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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 darbepeoin alfa (DA) were assessed in NDD CKD pts in a randomized, open-label, active-controlled phase 3 study.

Methods: Data from 3 completed randomized Phase 3 studies in NDD-CKD pts were analyzed individually and in the pooled population by iron status. Pts were randomized to roxadustat or placebo for up to 4 years. Baseline (BL) hemoglobin (Hb) and change from BL (CFB) were summarized overall and in pts with iron repletion or iron depletion. Iron repletion was defined as ferritin ≥100 μg/L and transferrin saturation (TSAT) ≥20%; the remainder were defined as iron depleted. Oral iron was allowed on study and IV iron was allowed as rescue.

Results: Across studies, 2391 and 1886 pts with NDD-CKD were treated with roxadustat and placebo, respectively. Mean (SD) BL Hb was 9.10 (0.74) g/dL (roxadustat) and 9.07 (0.73) g/dL (placebo). At BL, 1433 (60%) pts were iron replete for roxadustat and 1127 (60%) pts were iron replete for placebo. Mean CFB in Hb with roxadustat was summarized by study and iron status (Table 1). Hb CFB was similar in iron-replete and iron-depleted patients receiving roxadustat. Roxadustat dose and iron use in subgroups will be explored.

Conclusions: Roxadustat corrected and maintained Hb in patients with NDD-CKD and anemia regardless of iron status at baseline.

Funding: Commercial Support - Fibrogen, Inc.; AstA.Zene Inc; Astellas Pharma Inc.

Change from baseline in Hb overall and by iron status with roxadustat treatment across NDD studies over Weeks 28 to 52 regardless of rescue therapy.

TH-OR04
Roxadustat Is Not Associated with an Increased Risk of Neoplasm in Patients with CKD and Anemia
Daniel W. Coyne,1 Steven Fishbane,2 Pablo E. Pergola,3 Robert Leong,4 Ming Zhong,5 Dustin J. Little,3 Kin-Hung P. Yu,6 Washington University in Saint Louis School of Medicine, Saint Louis, MO; 2Northwell Health, Great Neck, NY; 3Renal Associates PA, San Antonio, TX; 4Fibrogen Inc, San Francisco, CA; 5AstraZeneca, Gaithersburg, MD.

Background: Roxadustat is a novel, orally bioavailable, small molecule that reversibly inhibits hypoxia-inducible factor (HIF) prolyl hydroxylase enzymes and activates HIF and transcription of HIF-responsive genes, including for erythropoietin. Preclinical studies of roxadustat in multiple animal species did not demonstrate a carcinogenic signal. We report neoplasm-related adverse events (AEs) and serious adverse events (SAEs) from the roxadustat global phase 3 program.

Methods: Data from six pivotal studies were pooled. 3 compared roxadustat to placebo in patients with non-dialysis-dependent (NDD) CKD, and 3 compared roxadustat to epoetin alfa in patients with dialysis-dependent (DD) CKD. Patients were excluded from the studies if they had a history of malignancy, except for those determined to be cured or in remission for ≥2 years, or for patients receiving chemotherapy for malignant disease.

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 BL 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%). Differentially, establishing roxadustat’s noninferiority to DA. Noninferiority of roxadustat to DA was demonstrated for MAP and time to first IV iron use, change in mean arterial pressure (MAP), and occurrence of hypertension. Treatment-emergent adverse events (TEAEs) were assessed.

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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. Neopterin-related AE rates were 2.5/100 PEY in both the roxadustat and placebo groups. Neopterin-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. Neopterin-related AE rates were 2.7/100 PEY and 2.3/100 PEY in the roxadustat and epoetin alfa groups. Neopterin-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 neopterin-related AE and SAE rates in the roxadustat phase 3 clinical trials.

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

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)

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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 ANDES (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 in those with low iron stores and poor treatment response. The primary endpoint was the mean change in Hb from baseline to the average over Weeks 28–52.

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).

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

Funding: Commercial Support - AstraZeneca

TH-OR06

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

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Background: Anemia in CKD is multifactorial, with contributions from reduced erythropoietin production and hepcidin-induced functional iron deficiency. Roxadustat, a hypoxia-inducible factor prolyl hydroxylase inhibitor, treats anemia by enhancing erythropoietin synthesis and increasing iron availability via reducing hepcidin and increasing iron transport. We assessed the effect of roxadustat on iron parameters in patients with DD-CKD.

Methods: Patients were randomized to open label roxadustat or epoetin alfa in 3 pivotal DD-CKD trials. Intravenous (IV) iron was administered per usual care with epoetin alfa and was limited to rescue therapy with roxadustat. Mean changes from baseline in Hb, hepcidin, and iron parameters were evaluated. Pooled results are reported.

Results: Overall, 3890 patients were evaluated (roxadustat N=1943; epoetin alfa N=1947; mean baseline Hb 9.7 g/dL for both groups), including 1515 incident dialysis patients and 1355 anemia patients (N=756 epoetin alfa N=799; overall mean baseline Hbvalues ~8.8 g/dL). Mean Hb increased more from baseline averaged over Weeks 28–52 with roxadustat vs epoetin alfa (1.21 vs 0.95 g/dL; P<0.0001). Roxadustat-treated patients used less IV iron, with mean monthly IV iron use over Weeks 28–52 of 80.3 mg for roxadustat and 108.2 mg for epoetin alfa (P<0.0001). Roxadustat reduced hepcidin and increased transferrin and serum iron; transferrin saturation did not change vs epoetin alfa (Figure). Reduction in ferritin occurred predominantly in patients with the highest baseline values when assessed by quartile (>800 μg/L).

Conclusions: Roxadustat facilitated iron transport and utilization by increasing both iron-carrying capacity (transferrin) and serum iron, in contrast to the effects on these parameters seen with epoetin alfa. Overall, these changes contributed to decreased need for IV iron use while achieving greater Hb increase from baseline with roxadustat vs epoetin alfa.

Funding: Commercial Support - AstraZeneca

TH-OR07

Renoprotective Effects of Ferric Citrate in a Mouse Model of CKD

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Background: Ferric citrate (FC) is an effective phosphate binder and iron replacement product. 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 Col4α2 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 intact 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 Dialysate Denusial 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 hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI), denusial, with conventional ESA treatment.

Methods: ASCEND-D (NCT02879305) recruited 2964 prevalent dialysis patients receiving ESA treatment (standardized to weekly intravenous [IV] epoetin) 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 ≥150 Units/kg/week. Predictors of ESA hyporesponsiveness were determined using a multivariable regression model. Alternate hyporesponder definitions were explored.

Results: Using the primary definition, 34% (122 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 (0.081).

Conclusions: This is the first global HIF-PHI study to report pre-defined predictors 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 inhibitory (HIF-PI) agent 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 chronic kidney disease (CKD)-dependent (DD) 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.; AstZeneca plc; Astellas Pharma Inc.
Results: Deletion of Hif1α delayed progression of CKD, as CDP mice showed reduced bone loss of BUN compared to age-matched Col4a3KO mice (−25%). CDP mice also showed lower FGF23 levels (−80%) vs. Col4a3KO and we obtained similar results in Col4a3KO mice administered with a HIF inhibitor (−80% FGF23, −30% BUN, vs. Ctr-Col4a3KO). CDP 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 Hif1α KO cultures compared to Ctr cells, and led to a 30% reduction in Fg23 expression. In contrast, Hif1α cells showed reduced osteogenic potential, with fewer ALP colonies and mineral deposits, and a blunted Fg23 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, resealing recycling and endosomal signaling. Mutations in the SLC9A6 gene encoding the NHE6 isoform cause severe X-linked mental retardation, epilepsy, autism and corticalbasal 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 knockout mice. In a next series of experiments, we used primary osteoblasts, extracted from calcified bone of newborn mice, to study NHE6 expression, proliferation, and cell-mediated mineralization in vitro. To determine the impact of the NHE6 isoforms on structural bone parameters, we performed high-resolution microcomputed tomography (mCT) studies on lumbar vertebral of wild-type and NHE6 knockout mice.

Results: NHE6 expression was observed in both primary osteoblasts and osteoclast precursors. In two studies with osteoclast precursors, derived from NHE6 knock-out mice demonstrated normal osteoclast differentiation and osteoblast proliferation. However, NHE6-deficient osteoblasts exhibited a resorptive 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.

Conclusions: 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 knockout 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, regulates its activity and its 24th 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 light phase at ZT2-ZT12 (ZT: zeitgeber time since lights on) for 4 weeks and blood and glands obtained again (N=39). CKD was induced by 5/6 nephrectomy and high phosphate (P) diet for 8 weeks and parathyroid glands were harvested every 4th-hour (N=44). Plasma PTH, P, total calcium, FGF23, and urea were measured. Parathyroid expression of core circadian clock genes was examined by qPCR.

Results: Circadian rhythm was found for PTH (p<0.0002), P (p<0.001), FGF23 (p<0.02), and urea (p<0.0001). Restricted feeding to the habitual inactive period inverted the acrophase timing of PTH (ZT9.6 → ZT23.6), P (ZT8.7 → ZT21), FGF23 (ZT7.4 → ZT22.9) and urea (ZT12.2 → ZT8.4). Restricted feeding did not significantly affect the period, acrophase timing, MESOR or amplitude of circadian clock genes. Bmal1, Per1, Per3, Cry1,2 and Rev-erba. The rhythmicity of parathyroid circadian clock genes was severely deregulated in CKD with significant upregulation of PER1 (p<0.0002), Per2 (p<0.03), and Rev-erba (p<0.004) and downregulation of Npas2 (p<0.05). The
significant rhythmicity 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-erbs increased.

**Conclusions:** Feeding restricted to the inactive period inverted the acrophase of plasma PTH, P and FGF23 and revealed 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 (gland cells missing homolog 2), PTH (parathyroid hormone), Cux1/c (calcium sensing 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 tsp1, paxk7, atp6v0b, rpl11, rps8 and etc (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 uricemic hyperparathyroidism glands.**

**TH-OR16**

Calcium Isotopes: A Novel Biomarker of Bone Mineralization in CKD

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**Background:** Calcium 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 44/42Ca in 128 children in CKD4-5 and on dialysis (CKD4-5D) and 117 healthy participants (age <30) underwent Ca isotope measurement, bone biomarkers, DXA and tibial peripheral quantitative CT (pQCT), an accurate measure of cortical BMD.

**Results:** In healthy children the 44/42Ca_int and 44/42Ca_pen were higher than in adults (p<0.001), reflecting avid Ca uptake during bone formation. Since urinary Ca excretion is impaired in CKD, 44/42Ca_int was higher and 44/42Ca_pen lower in CKD4-5D compared to controls (p<0.001 for both). In CKD2-5D 44/42Ca_int positively correlated with cholecalciferol (p=0.01) and alfacalcidol (p=0.002) doses, implying increased bone Ca uptake when cholecalciferol is increased. 44/42Ca_pen is positively correlated with biomarkers of bone formation (ALK, p=0.05) and inversely with resorption markers (PTH, p=0.01; TRAP5b, p=0.01 and CTX, p=0.006). 44/42Ca_int is positively correlated 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 44/42Ca_int (p=0.06, p=0.006) and PTH (p=0.39, 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.
SNF472 Consistently Slows Progression of Coronary Artery Calcification Across Subgroups of Patients on Hemodialysis

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Background: In the Cal.JP10 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 volume progression 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 formate 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 ≥40mg/dL, eGFR <45mL/min and POx>5μmol/L, n=10) and PH (UOx ≥40mg/dL, n=5) who received ≥7.500 of REL 5x/day with meals/snacks. Parameters assessed at baseline, and weeks 4, 8 and 12 included POx and UOx (only if eGFR >15mL/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 formate accumulation, as all samples were below or within normal range (1-9mg/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

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.v. 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 60-240pg/ml (recommended level of Japanese guideline) every 3 weeks between 25 and 300 mcg during 24 weeks of treatment. The primary endpoint was the percentage 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.
TH-OR21
Primary Cilia and the Glycocalyx Are Flow Sensors for Nitric Oxide Production by Thick Ascending Limbs
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Background: The primary cilium is an organelle found on essentially all epithelial cells. Similarly, the glycocalyx is a matrix-like layer of proteoglycans, glycosaminoglycans (GAGs) and proteins covering the surface of all cells. In vascular endothelial cells, primary cilium 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 cilium and the glycocalyx in NO production by thick ascending limbs is unknown. We hypothesized that primary cilium and the glycocalyx 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 glycocalyx 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 to 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 1.80±0.74 AU/min (p < 0.04); a higher concentration (0.4 U/ml) caused a greater decrease in basal NO from 1.86±0.41 AU/min (p < 0.006). Heat inactivation of heparinase (0.2 U/ml) abolished its effect (3.01±0.34 to 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 cilium and the glycocalyx 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 (Kir4.1/Kir5.1) multimers) potassium channels, a basolateral calcium sensing receptor (CaSR), and the claudin (Cla) family of proteins. Morphological heterogeneity of TAL cells has been reported, as well as mosaic expression of ROMK and Kir4.1. 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, Clδ-10 and Clδ-16 signals were analyzed by immunofluorescence, in situ hybridization (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 Kir4.1 protein expression showed conspicuous heterogeneity in a mutually exclusive pattern, with stronger pNKCC2 expression in the ROMK-negative, Kir4.1-positive cell type. CaSR and Clδ-16 signals were moderate to absent in ROMK-positive cells, but intensified in ROMK-negative cells, while Clδ-10 was strongly expressed only in ROMK-positive cells. ISH revealed no cell heterogeneity of ROMK mRNA. In Brattleboro rats, 72 h dDAVP increased the number of ROMK- and Kir4.1-positive cells and the overlap of both signals in mTAL, and stimulated NKCC2 phosphorylation. Clδ-10 expression was induced in the outer stripe of outer medulla. Morphological alterations in the TAL included proliferation of microvilli. WB showed 2.2-fold increase of ROMK and 1.3-fold increase of Kir4.1 abundance, but down-regulation of CaSR to 60%.

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

Conclusions: These results demonstrate mosaic expression of ROMK, Kir4.1, CaSR, Clδ-10, and Clδ-16 in TAL, which correlate with cell-heterogeneous levels of NKCC2 activation.

Funding: Government Support - Non-U.S.

TH-OR23
Optical Clearing and 3D Imaging Reveal a Sexual Dimorphism in the Structure and Remodeling Response of the Distal Convoluted Tubule
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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 high-resolution histological and ultrastructural analyses, we quantitatively assess DCT morphology in male and female mice and study remodeling response to furosemide.

Methods: Male and Female (3-month-old) 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 Clear, Unobstructed Brain/Body Imaging Cocktails and Computational Analysis (CUBIC) pipeline, co-stained with antibodies that label the early DCT (DCT1, parvalbumin) and the entire DCT (DCT1 & 2; 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 basel state. Surprisingly, the length of the DCT was longer in males (~620 μm) than female mice (~360 μm). Furosemide treatment significantly increased the abundance of NCC and pNCC in both sexes equally (~50%) and increased the 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 elongation effect 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 under conditions of high sodium delivery, yet have larger reserve and remodeling capacity to adapt to unique physiological stresses.

Funding: NIDDK Support, Private Foundation Support

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: NCC is activated via the CaSR-WNK4-KSP4-SPAK pathway. Glucose and other sugars act as positive allosteric modulators of the CaSR. This might be relevant in the distal convoluted tubule (DCT), since glucose is reabsorbed proximally and frankovose delivery to the DCT depends largely on dietary intake. Here we studied if positive allosteric modulation of the CaSR by glucose/fructose induces NCC activation via CaSR-WNK4-KSP4.

Methods: We used 1) HEK-293 cells cotransfected with SPAK, WNK4 and/or CaSR and exposed to 0.5 mM extracellular Ca 2+ with 0, 5.5 or 25mM of glucose/fructose. 2) Furosemide administered in the food (100 mg/kg per day) for seven days. Total NCC and pNCC protein abundance was analyzed by Western Blot. 3) Urinary exosomes from male healthy volunteers to assess NCC abundance and activity after exposure to placebo, cinacalcet 30mg at time 0 (n=4) or 5% fructose with +/- calcilytic NPS2143 (30 mg/kg oral gavage). Renal proteins for western blot were extracted 3 h latter. 3) Urinary exosomes from male healthy volunteers to assess NCC activity after exposure to placebo, cinacalcet 30mg at time 0 (n=4) or 5% fructose with water intake (n=3).

Results: Stimulation of HEK293 cells with glucose or fructose increased SPAK phosphorylation, but only if both WNK4 and CaSR were present (p<0.01). In mice, we observed increased pNCC in kidneys, together with increased activation of WNK4-SPAK (p<0.01), after exposure to 20% fructose. Dapagliflozin also induced activation of SPAK and NCC. These effects of fructose and dapagliflozin were abrogated by co-administration of NPS2143 (p<0.01). Preliminary data on human subjects show that when compared to baseline, urinary exosome pNCC/NCC ratio (~1.0), cinacalcet induced a 77% increase in pNCC/NCC ratio (1.77, p=0.018) and fructose induced a near two-fold increase in pNCC/NCC ratio (2.69, p=0.006).

Conclusions: In vitro glucose or fructose increase SPAK phosphorylation in a CaSR-WNK4-dependent manner. In vivo glucose (dapagliflozin) or fructose increases NCC abundance and activity, via increased CaSR and data suggest a calcimimetic-like behavior for glucose or fructose in the DCT. This effect appears to be reproduced in humans and represents the
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-WNK-SPAK pathway.

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

**TH-OR25**

**Cross-Talk Between Epithelial Sodium Channel and Basolateral K_4,1/-K_5,1 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 K_4,1 homomeric or K_4,1/K_5,1 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 K_4,1 inhibitor, VU0134992, on the activity of K_4,1, K_4,1/K_5,1, and ENaC. Channel activity was recorded in CHO cells transfected with respective channel subunits, cultured polarized epithelial mLCCD cells, and native freshly isolated rat and human CCD tubules. To test the effect of pharmacological K_4,1/ K_5,1 inhibition on electrolyte homeostasis in vivo, Dahl salt-sensitive rats were injected with amitriptyline (15 mg/kg/day).

**Results:** We found that inhibition of K_4,1/K_5,1, but not K_4,1 channel, substantially suppresses both amiloride-sensitive I_sc in mLCCD cells and single-channel ENaC activity in principal cells of rat and human CCD tubules. Furthermore, we demonstrate that the injection of K_4,1/K_5,1 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 K_4,1/K_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 Kir5.1 channels in the cortical collecting duct (CCD) are known to 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/K5.1 heteromeric K⁺ channels affects ENaC-mediated Na⁺ transport in the cortical collecting duct (CCD) principal cells.

**Methods:** Cross-talk between epithelial sodium channel and basolateral K_4,1/-K_5,1 channels in the cortical collecting duct was to determine how the inhibition of basolateral K_4,1 homomeric or K_4,1/K_5,1 heteromeric K⁺ channels affects ENaC-mediated Na⁺ transport in the cortical collecting duct (CCD) principal cells.

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

**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 ask if other proteins from this family, i.e. Tclc1d4, Tclc1d4 and Tclc1d2 interact with V-ATPase in kidney and if their TLDc domains mediate this interaction.

**Methods:** Interaction between endogenous , Tclc1d4, Tclc1d4 and Tclc1d2 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, Tclc1d4, Tclc1d4, and Tclc1d2, or mutant TLDc domains of Ncoa7 (G802A, G815A, R817A, G845A, G896A, L926A, E938A) followed by western blotting by B1.

**Results:** In Co-IP studies of mouse kidney lysates we found that endogenous Tclc1d4 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 Tclc1d4 or Tclc1d2 in Co-IPs, possibly due to low sensitivity of the anti-Tlclc1 and anti-Tlclc2 antibodies. Additionally, we found that the purified TLDc domains of Ncoa7, Oxr1 and Tclc1d4, but not Tclc1d4 or Tclc1d2, 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, Tclc1d4 and possibly Tclc1d2, 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 TLDc motif is a protein-protein interaction domain that defines a new class of V-ATPase interacting regulatory proteins. The evolutionarily 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 (AQ3P). The purpose of this study was to determine if lysine acetylated AQ3P (acAQ3P) affects water permeability.

**Methods:** We generated an antibody to detect acAQ3P and found acAQ3P 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, acAQ3P was also found in the IMCD. Next, we developed AQ3P K point mutation plasmids; an acetylated mimetic K282Q (AQ3P K282Q), and a deacetylated mimetic K282R (AQ3P K282R). 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 AQ3P K282Q, AQ3P K282R and littermate controls AQ3P WT/WT were placed on standard chow and: 1) ad lib water, 2) 5% sucrrose water for hydration, or 3) 24 h water deprivation and urine flow measured.

**Results:** Following osmotic stimulus, we found AQ3P WT/WT cells had the highest water permeability followed by the AQ3P K282Q cells and the AQ3P K282R cells. From our mutant mice, as adults, control and AQ3P WT mice had similar urinary flow on all protocols. However, the AQ3P K282R mice produced double the urine on protocols 1 and 2. Thus, maintenance of deacetylated AQ3P enhances fluid excretion under normal and hydrated conditions. To further determine whether the increased urinary flow was due to impaired water permeability, we immunolocalized AQ3P and AQ3P under ad lib conditions. AQ3P WT/WT mice had enhanced expression of AQ3P in the basolateral membrane, and reduced AQ3P expression in the apical membrane. In contrast, the AQ3P K282R mice had diffuse AQ3P localization in the CD, with no obvious change in AQ2P.

**Conclusions:** Together, these preliminary data suggest that acAQ3P promotes localization to the basolateral membrane of the CD and supports the hypothesis that acAQ3P 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. AVP facilitates aquaporin 2 (AQP2) translocation to the apical plasma membrane to augment water permeability of the collecting duct (CD). Inability of CD to respond to AVP signal causes NDI leading to polyuria, dehydration and thirst. Stimulation of CD water reabsorption by AVP can only occur in the presence of positive osmotic difference between the cytosol and luminal fluid. 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 urinary concentration remains unknown.

Methods: The employed techniques include 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 AVP-induced AQP2 trafficking to the apical membrane and metabolic cage balance studies.

Results: TRPC3 is a Ca2+-permeable mechanoo-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 urinary volume excretion after 24 h of water deprivation (WD) despite higher AVP 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. These results show 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 NDI-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 hypertonicity-driven transcription factor responsive to environmental osmotic changes. Sulfated glycosaminoglycans (GAGs) have been suggested to neutralize Na+-induced hypertonic effects by facilitating a dynamic non-osmotic Na+ storage compartment. Patients with diabetes mellitus type 1 (DM1) and hereditary multiple exostoses (HME) were separated by a 7-to-10-day washout period. After each diet, blood samples and skin biopsies were obtained. With immunohistochemistry, skin NFAT5 expression and GAG sulfation patterns were semi-quantitatively analyzed by researchers blinded for diet status. Disturbances in NFAT5 expression and GAG sulfation patterns were found, indicating 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 NDI-like phenotype.

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Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only. Underline represents presenting author.
and LV 1-47 (9.1% vs 4.3%, P=0.636) were high among patients with combined renal and cancer. In this specific compartment of kidney, patients with renal amyloidosis (LV 6-57 was more likely to have G-AL (42.9% vs 26.6%, P=0.399), and LV 1-51 was associated with V-AL (19.2% vs 3.3% vs 0, P=0.019). Patients with LV 2 family had a tendency at increased risk of developing into ESRD compared with other LV families (HR=0.27).

Conclusions: IGVL germline gene usage was associated with organ tropism, renal amyloid deposition patterns and renal survival in Chinese patients with AL amyloidosis. 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 (IgG1k) 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 with D monotherapy in a series of severe patients (pts) with AL amyloidosis and multiorgan 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-pro-BNP) 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 in proteinuria levels. These data were paralleled by the reduction of NT-proBNP values in the 3 pts with cardiac involvement.

Conclusions: Daratumumab monotherapy resulted in the disappearance of M-proteins in every pt, FLC ratio normalization 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 KTx recipients are lacking. ICIs are reported to be associated with higher acute rejection rate in KTx 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 KTx recipients treated with ICI. 66 KTx patients with a functioning allograft at the time of ICI initiation were collected from 18 institutions. In addition, historical control groups of KTx recipients with advanced stage melanoma (AICC stage III-IV, n=17) and cutaneous squamous cell carcinoma (cSCC; AJCC 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 immunosuppression drugs (P=0.009) 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 ICI 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 KTx recipients with ICI use compared to non-ICI control groups.

Funding: NIDDK Support, Private Foundation Support

TH-OR35
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±21) and 47 (43.5±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.

TH-OR36
Kidney and Cancer Outcomes with Standard vs. Kidney Protective Chemotherapy Regimens for First-Line Treatment of Metastatic Urothelial Carcinoma
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Background: Cisplatin-based combination chemotherapy regimen is the optimal initial treatment for metastatic urothelial carcinoma, but kidney function eligibility and nephrotoxicity are treatment-limiting for many patients. For patients unfit to receive cisplatin, other options include alternative administration schedules (e.g. split dose cisplatin), carboplatin-based regimens and non-platinum regimens. The aims of this study were to compare cancer outcomes and incidence of acute kidney injury (AKI) during treatment among 3 regimens of chemotherapy.

Methods: We conducted a single-center retrospective study of patients receiving first-line chemotherapy for metastatic urothelial carcinoma (2005-2019). We compared standard gemcitabine-cisplatin (gem-cis) to: 1) gemcitabine-cisplatin split dose regimen (split) with cisplatin divided over day 1 and 8, and 2) combination of gemcitabine-carboplatin or single-agent gemcitabine (gem-carbo). We used Fine and Gray hazard model. The cumulative incidence of AKI (considering the competing risk of death) 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 immunosuppression drugs (P=0.009) 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...
Results: We identified 183 patients (98 gem-cis, 32 split and 53 gem/gem-carbo). Median age was 67.4 years (range 27-89 yrs). Median number of cycles was 7 (IQR: 5-11). MDRD estimated GFR was 78 mL/min/1.73m² (IQR: 66-91) in gem-cis, 64 (48-77) in split, and 45 (33-57) in gem/gem-carbo. Patients receiving split and gem/gem-carbo were older, had worse performance status, and hypertension was more frequent. Split and gem/gem-carbo regimens were associated with higher mortality and progressive disease relative to gem-cis when adjusted for age, baseline eGFR, ECOG, hypertension and diabetes with hazard ratio (HR) of 1.56 (95%CI: 1.04-2.34; p = 0.03) and 2.02 (95%CI: 1.36-3.01; p = 0.01) respectively. Median time to progressive disease was 242 (IQR: 137-444), 182 (122-279) and 117 (72-207) days in gem-cis, split and gem/gem-carbo groups. There was no significant association between regimen type and AKI with HR of 1.32 (95%CI: 0.62-2.81; p = 0.47) and 0.98 (95%CI:0.46-2.09; p = 0.96) for split and gem/gem-carbo groups versus gem-cis.

Conclusions: Kidney protective chemotherapy regimens were associated with increased disease progression and mortality, without a significant difference in AKI. Alternative kidney protective strategies are needed for patients with CKD and urothelial cancer.

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TH-OR39

Risk Factors for Nephropathy with High-Dose Methotrexate (HDMTX) in Haematological Malignancies


Background: HDMTX is a key component for treatment of haematological malignancy. Nephrotoxicity remains a significant risk factor for HDMTX and therefore, hypotension, diuretics and urinary alkalisation are employed in its management but despite these measures, nephrotoxicity remains 2-12%. Determination of risk factors is key in order to further stratify 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 12/31/18. 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 nephropathy. 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), nephropathy 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 nephropathy.

Conclusions: Nephrotoxicity remains a significant complication with HDMTX despite current measures. The high 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.

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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 arteriolar glomerular pressure. The most accepted explanation is that Bevacizumab induces thrombomodulin GPIbαopathy. However, there is no current model or description of potential risk factors to identify at-risk patients who may need close monitoring. The aim of this study was to identify baseline and treatment dependent factors that impact proteinuria development.

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 1.68, 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, CI95%:3,204, p = 0.001) were not. ACE inhibitors had the following association: (Lisinopril; {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: A presence of a 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. Due to lack of randomization and incomplete data, further analysis is needed.

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TH-OR40

Assessment of Estimated Glomerular Filtration Rate in a Cohort of 1200 Cancer Patients Using Serum Creatinine and Cystatin C

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Background: eGFR using creatinine (eGFRcr) with the CKD-EPI equation is recommended as the first test for GFR evaluation in clinical practice, but CG equation is commonly used for the prescription of chemotherapy, despite increasing evidence of its inaccuracy compared to measured GFR (mGFR). eGFR using cystatin C (eGFRcys)
is less influenced by muscle mass or nutritional status, and eGFR using both markers (eGFRcys) is more accurate than either eGFRcr or eGFRcr-cys, but not 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 51Cr-EDTA indexed for body surface area. mGFR was the least accurate and was least accurate. eGFRcys underestimated mGFR and eGFRcr-cys had minimal bias and was the most accurate of all equations (Table).

**Conclusions:** All eGFR 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.

**TH-OR41**

**Hematopoietic-Specific Melanocortin 1 Receptor Signaling Protects Against Crescentic Glomerulonephritis and Mediates the Beneficial Effect of Melanocortin Therapy**

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**Background:** Emerging evidence suggests that melanocortin 1 receptor (MC1R) signaling may contribute to the beneficial action of melanocortins in glomerular diseases. However, whether hematopoietic MC1R signaling is implicated is unknown.

**Methods:** MC1R mutant (e/e) or wild-type (WT) mice were inoculated with rabbit nephrotoxic serum (NTS) and treated with melanocortins, including the Repository Corticotropic Inversion (RCI, Acthar® Gel, Mallinckrodt ARD, LLC), NDP-MSH, and the MC1R selective agonist MS05. Some mice received adoptive transfer of syngeneic bone marrow-derived cells (BMDC) beforehand. Kidney function and injuries were evaluated.

**Results:** Upon NTS injury, e/e mice developed more severe crescentic glomerulonephritis than WT mice, featured by heavier proteinuria, higher serum creatinine levels and exacerbated renal lesions, including crescent formation, renal inflammatory infiltration and fibrosis as well as podocyte damage, marked by loss of expression of podocyte homeostatic markers in glomeruli. Melanocortin therapy substantially improved renal injury in WT mice and this protective effect was blunted in e/e mice. In contrast, adoptive transfer of BMDC derived from WT mice to e/e mice markedly ameliorated NTS nephritis and reinstated the therapeutic efficacy of melanocortins in e/e mice. Mechanistically, the beneficial action of WT BMDC in e/e mice was associated with diminished glomerular deposition of autologous anti-rabbit IgG and reduced fixation of C5b-9 along glomerular capillary loops, entailing a regulatory effect of BMDC-specific MC1R signaling on humoral immune response to NTS antigens. In addition, melanocortin therapy prominently tilted macrophage polarization towards the anti-inflammatory M2 phenotype in NTS-injured kidneys in WT mice. MC1R signaling is likely involved in this modulation of macrophage behavior, because MC1R was evidently expressed in bone marrow-derived macrophage (BMM) prepared from WT mice but absent from e/e BMM. Furthermore, MS05 diminished M1 phenotypes and promoted M2 polarization in M1-primed WT BMM but not e/e BMM, thus denoting a pro-M2 skewing effect of MC1R signaling.

**Conclusions:** Hematopoietic MC1R signaling attenuates NTS nephritis via, at least in part, regulation of humoral immune response and a pro-M2 skewing effect on macrophage polarization.

**Funding:** Commercial Support - Mallinckrodt Pharmaceuticals

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

**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 (n=3) and female (n=3) mouse kidney and a healthy human cortical frozen kidney tissue sections. We utilized Space Ranger (10x Genomics), Scour 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-cell, nephron and tissue levels.

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

**St** provides transcriptome expression within intact kidney tissue sections. (A) H&E stained human cortical kidney tissue with scarred and non-scarred regions. (B) The same human cortical kidney tissue with the transcript capture spots coloured by clustering using t-SNE projection demonstrates distinct transcriptome expression in scarred and non-scarred regions.

**TH-OR43**

**Automated Atubular Glomeruli Detection Using 3D Glomerular Quantification Algorithms**

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**Background:** Atubular glomeruli are associated with decreased glomerular filtration rate and kidney disease progression. To identify atubular glomeruli requires serial sectioning with whole slide imaging (WSI). Atubular glomeruli have or does not have connection to the proximal tubule. This process is labor intensive and very time-consuming, limiting its use. We aimed to test feasibility of automatically detecting atubular glomeruli by using Multi-Object Association for Pathology in 3D (Map3D).

**Methods:** The Map3D was created including a glomerular detection algorithm, dual-path multi-object tracking algorithm, and pixel-wise large-scale glomerular association algorithm across routine serial sectioning with whole slide imaging (WSI). Atubular glomeruli counting was done in human mouse kidneys, and 3 mice with diphtheria toxin (DT)-mediated proximal tubule-specific injury in mice with tubular cell expression of the DT receptor, and 4 mice with patchy tubulo-interstitial fibrosis induced by folic acid (FA). Data from this automated approach was compared with standard manual assessment detailed above and correlated with functional and structural parameters.

**Results:** The Map3D substantially reduced the time needed for average atubular glomerular counting per sample (30 min Map3D vs. 30 hours human). Atubular glomerular size were smaller than normal glomeruli. The number of complete (i.e. from pole to pole) glomeruli assessed increased by 25.6% using GQuant-3D (68±8.8 per mouse) vs human counting (72±2.7 per mouse). GQuant-3D recognized 14.3±5.5 atubular glomeruli per mouse sample, slightly less (83%) than the 16.7±4.0 atubular glomeruli per mouse sample.

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**ST** provides transcriptome expression within intact kidney tissue sections. (A) H&E stained human cortical kidney tissue with scarred and non-scarred regions. (B) The same human cortical kidney tissue with the transcript capture spots coloured by clustering using t-SNE projection demonstrates distinct transcriptome expression in scarred and non-scarred regions.
recognised by manual human assessment. The percentage of atubular glomeruli by
±
with normal mice (6.0
±
2.15%) and FA mice (36.5
±
2.91%). The percentage of atubular glomeruli, counted by either
GQuant-3D was increased in DT mice (9.7
±
2.15%) and FA mice (36.5
±
2.91%) compared to normal mice (6.0
±
9.1%). The percentage of atubular glomeruli, counted by either
GQuant-3D or human, correlated with interstitial fibrosis (R=
0.49 or 0.61 respectively), but not with tubular injury marker, KIM-1 and N-GAL.

Conclusions: The Map-3D 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-OR44
A Deep-Learning Approach to Kidney Donor 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 tool to
pathologist. Non-sclerotic and sclerotic glomeruli were selected to test this approach.

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
AT). All WSI images were divided into two datasets for training and validation cohorts
(0.8:0.2) and non-Duke WSIs were used as testing dataset. QuPath was employed to
manually annotate non-sclerotic (22767) and sclerotic glomeruli (1366). A 9-layer
convolutional neural network (CNN), based on the common U-NET architecture, was
developed in Python, using randomly selected 256x256 patches from WSI and input
augmentation to boost generalization performance. CNN hyper-parameters were tuned
via cross-validation. The CNN’s performance was quantified based on the Dice Similarity
Coefficient (DSC) between the predicted and ground-truth annotations.

Results: For non-sclerotic glomeruli, the average DSC for train, validation and
testing was 0.93, 0.91, 0.90 respectively. The F1, Recall, and Precision for testing was
0.93, 0.96, 0.90 respectively. For sclerotic glomeruli, the average DSC for train,
validation and testing was 0.89, 0.87, 0.83 respectively. The F1, Recall, and Precision for
testing was 0.87, 0.93, 0.81 respectively. The CNN has higher performance in the regions
of high glomerular density and occasionally, outperformed the pathologists in glomerular
detection. Lower model performance was observed in the presence of image artifacts and
in regions of low glomerular density.

Conclusions: DL applied to image analysis may help standardize and improve
accuracy and reproducibility of quantification of histologic primitives in kidney frozen
sections, enabling the establishment of synergistic machine-human protocols that can
be deployed in clinical practice. The development of DL-segmentation of other relevant
histologic primitives is in process.

Funding: Private Foundation Support

TH-OR45
Evaluation of a Direct-to-Digital Histology Method for Rapid Evaluation of Kidney Biopsies
Sudhir Perinchery, Randy L. Luciano, Gilbert W. Moeckel, Richard Torres.
Yale University School of Medicine, New Haven, CT.

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 MultiPhoton 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 renal biopsy in routine use. We developed an objective scoring system based on
downstream 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
clinical workflow, using previously-described methods. Images were obtained from
entire core biopsies with a prototype fast, high resolution, multiphoton microscope
system (Applivate 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 detection analysis and quantitative
lesion comparison.

Results: Diagnostic quality remotely-reviewable renal images of 10-16 digital
slices were available within < 3 hours of receipt. H&E detected morphologic findings
were equally detectable in digital images compared to physical, paraffin-embedded
sections including cases showing tubular injury, proliferative glomerulonephritis,
glomerular degeneration 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 workflow 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

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. RNA was extracted and
hybridized with NanoString HOP 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
IFN-γ 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 Tgfβ1 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.
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

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**TH-OR48**

**Complement Activation Assay in an Ex Vivo Microfluidic Cell-Culture System**

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**Background:** Discrimination between different diseases in patients suffering from thrombotic microangiopathies is often challenging. Measuring C5b9 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 C5b9-ELISA to measure C5b9-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 C5b9-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 C5b9-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 Tukeys-multiple comparisons test.

**Conclusions:** We described a novel, fast and reproducible ELISA to identify aHUS-patients by measuring C5b9-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.

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**TH-OR49**

**Barriers and Opportunities to Improve Variability in CKD Laboratory Methodology and Reporting: Results from the College of American Pathologists (CAP) 2019 Survey**

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**Background:** Variability in laboratory practices for estimated GFR (eGFR) and urine albumin-creatinine ratio (uACR) is a barrier to optimal CKD testing and interpretation by clinicians. The CAP serial surveys assess CKD laboratory methodology and reporting.

**Methods:** The CAP 2019 General Chemistry Survey conducted in December, included 9 questions regarding CKD tests.

**Results:** Respondents included 7,105 laboratories (83.8% U.S. and 16.2% international) with a response rate of 87.5%. Laboratory reporting of eGFR based on serum creatinine has increased overall from 3% to 92% in CAP surveys between 2003 and 2019. The Figure shows 76% of laboratories were using an isotope dilution mass spectrometry (IDMS) traceable version of the MDRD 4-variable equation (45%) or the CKD-EPI equation (31%), but an incorrect equation was used for IDMS creatinine by 23% of the respondents, resulting in systematic over estimation of kidney function. Barriers for the pediatric population less than 18 years include only 10% of laboratories report the correct bedside Schwartz equation and 20% of laboratories applied an incorrect adult eGFR equation for children. The microalbumin term that KDIGO and KDOQI recommend be included 9 questions regarding CKD tests.

**Conclusions:** Laboratory variability is a call to action for nephrologists to collaborate with clinical laboratories to improve appropriate CKD testing.
Polyclonal Variants Immunotactoid Glomerulopathy: A Rare Entity with Monoclonal and Pathology of Kidney Diseases: Novel Mechanisms and Clinical Correlations

monoclonal ITG and polyclonal ITG. Prognosis is good if the underlying hematologic patients who received kidney transplants.

As compared to polyclonal ITG, monoclonal ITG had a higher incidence of lymphoma composition. This finding was used to distinguish monoclonal ITG from polyclonal ITG.

Immunofluorescence revealed IgG-dominant staining which was light chain restricted and microtubular deposits with diameter of 14-60 nm, hollow cores, frequent parallel staining for DNAJB9 was negative on all cases tested. Electron microscopy showed membranoproliferative (29%) and membranous (29%) patterns. Immunohistochemical had hypocomplementemia. Light microscopy revealed endocapillary proliferative (35%), in 26% (most commonly MGRS). 14% had underlying autoimmune disease and 33%

proteinuria (median 6.6 g/day, 58% with full nephrotic syndrome), hematuria (86%), and renal dysfunction, and 24% progressed to ESRD. The median survival (not reaching (53% vs. 11%), multiple myeloma (8% vs. 0), and MGRS (22% vs. 0). On follow up 0.03, 1.47 [1.04, 2.07].

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 (RCT) 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%, 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.

FR-OR02

A Parsimonious Model for Diagnosis of Biopsy-Proven Acute Interstitial 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 interstitial 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), serum bicarbonate (0.70), albumin protein (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
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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.

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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 CRRT 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 CRRT 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 75% 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 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+ 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
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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, 71.9) 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.

Funding: Private Foundation Support

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/SCD remains limited. We aimed to describe the relative risk for AKI in SCT/SCD and the effect of AKI on eGFR decline in AA.

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/SCD (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 ≥72 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.

Funding: Private Foundation Support

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Conclusions: The risk for AKI is increased in both SCT (Sustained) and SCD (all forms) and may contribute to faster eGFR decline in SCT/D. 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

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 secretory clearance is not currently measured in the ICU. To estimate the kidney clearance of secretory solutes 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 secretory solutes using liquid chromatography-tandem mass spectrometry. We computed a composite secretion score incorporating all seven solutes, and evaluated its associations with 28-day major adverse kidney events (MAKE28), defined as doubling of SCr, dialysis dependence, or death.

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 urine/plasma ratio of six of seven secretory solutes was associated with a 52% lower risk of MAKE28 and did not die in the non-AKI group (m: 9.97 vs 9.21 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 = 0.23). In a multivariate 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 = 0.0089).

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

FR-OR10
Endotrophin, Released During Collagen Type VI Formation, Predicts Long-Term Mortality After AKI
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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 (ARD) 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 = 0.23). In a multivariate 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 = 0.0089).

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

FR-OR11
Association of Use of Kidney Disease Education Benefit with ESKD-Related Outcomes
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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 receipt of KDE and ESKD outcomes in this matched cohort using logistic regression. We examined patient characteristics associated with receipt of KDE. We matched each KDE recipient with 4 controls using propensity scores and estimated the association between receipt of KDE and ESKD outcomes in this matched cohort using logistic regression.

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. We examined patient characteristics associated with receipt of KDE. We matched each KDE recipient with 4 controls using propensity scores and estimated the association between receipt of KDE and ESKD outcomes in this matched cohort using logistic regression.

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

FR-OR12
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Oral Abstract/Friday
Conclusions: Make future studies more feasible. Prevent relapse. Treatment of AKI is important. AKI is associated with a 52% lower risk of MAKE28 and did not die in the non-AKI group (m: 9.97 vs 9.21 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 = 0.23). In a multivariate 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 = 0.0089).

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

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

18
FR-OR12
Correlation Between Patient Activation and Quality of Life Among Patients with CKD
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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: 6.87; 7.4; P= 0.01); Burden of Kidney Disease (BKD) (SE: 5.44; CI: 1.24; 9.64; 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= 0.001); 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-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?
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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 1Cr-ethylendiaminetetraacetic acid (1Cr-EDTA) clearance assays. Patients with albumin <30g/dl, ethnicity referrals, <18 years old, non-white or black, mixed ethnicities were excluded. Accuracy of CKD-EPI and MDRD eGFR equations compared to 1Cr-EDTA GFR were assessed with and without correction factor.

Results: 2,776 1Cr-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 GFR>60ml/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 1Cr-EDTA clearance for people of Black and White ethnicities according to 1Cr-EDTA GFR categories

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 1/2/3/4/5: 636 ± 98; 1020 ± 120; 1943 ± 326; 4421 ± 1042; 12781 ± 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] 0.89; 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, 87%; PPV, 98%; NPV, 61%). At 886 ppb, the sensitivity increased to 80% but the specificity decreased to 69%. For a non-liveness or non-serious CKD, breath ammonia at a cut-off concentration of 886 ppb 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-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 at eGFR assessment. 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.
**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

**FR-OR16**

**Incidence of CKD and Environmental Inequities: An Integration of Ecological and Spatial Approaches in US Veterans**

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**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 identified for individuals with eGFR < 60 mL/min/1.73m² and without prior indication of CKD for at least 3 years. The county-level incidence rate of CKD was number of cases/1000 person-years during 2016-18. County-level environmental factors included Townsend deprivation index; neighborhood indices; number of recreational facilities and fast-food restaurants. A geographically-weighted regression model (GWR) was 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.c). Townsend deprivation index associated with higher incident rate in the Midwest, Northern California and Texas (Fig 1.a). PM2.5 was associated with higher incident rate in the East North Central and East West Central regions (Fig 1.c). Townsend deprivation index associated with higher incident rate in the Midwest, Northern California and Texas (Fig 1.b). PM2.5 was associated with higher incident rate in the East North Central and East West Central regions (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**

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**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 bumetanide (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. -10.2±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. -0.75±1.78 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±4.76 vs. -0.24±1.42 (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
FR-OR18

Benefits of Icosepat Ethyl Across a Range of Baseline Renal Function in Patients with Established Cardiovascular Disease or Diabetes: Results of REDUCE-IT RENAL

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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 Icosepat Ethyl-Intervention Trial (REDUCE-IT) randomized patients with CVD or diabetes and one additional risk factor to treatment with icosepat ethyl or placebo. Patients from REDUCE-IT were categorized by prespecified eGFR categories for analysis of the effect of icosepat 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 0.3%, p=0.01).

Conclusions: In REDUCE-IT, icosepat 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 (HFHFrE), denying these patients a life-saving therapy.

Methods: The risk of developing mild hyperkalaemia (potassium ≥5.5 mmol/L) and moderate/severe hyperkalaemia (>6.0 mmol/L) was examined in the Dapagliflozin And Prevention of Adverse-outcomes in Heart Failure trial (DAPA-HF) according to background MRA use, and randomized treatment assignment, by use of Cox regression analyses.

Results: Overall, 3370 (70.1%) patients in DAPA-HF were treated with an MRA. Mild hyperkalaemia occurred in 182 (11.1%) and 213 (14.1%) patients treated with dapagliflozin as compared to 204 (12.6%) and 40 (2.4%) of patients given placebo (Table and Figure). This yielded a hazard ratio (HR) of 0.86 (0.70-1.05) for mild hyperkalaemia and 0.50 (0.29, 0.85) for moderate/severe hyperkalaemia, compared to placebo.

Conclusions: Patients with HFHFrE and taking an MRA who were randomized to dapagliflozin had half the incidence of moderate/severe hyperkalaemia, compared to those randomized to placebo.

Funding: Commercial Support - AstraZeneca

Cumulative incidence of hyperkalaemia in patients taking MRA at baseline

FR-OR20

Metformin Improves Vascular Function in CKD Patients with Metabolic Syndrome

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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 CKD3a and 1000 mg/day in CKD 3b. Co-therapies for optimal CV risk reduction were continued. The co-primary outcomes included change in noninvasive carotid intima-media thickness (CIMT) in common (CCA) and internal (ICA) carotid arteries at 16 weeks. Last-observed value 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; HLD 46.4 ± 15 mg/dl; fasting glucose (FG) 92.3 ± 10.3 mg/dl; HbA1C 5.7 ± 0.24%; HOHA-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 FMDmax (baseline: 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. F CAA (P=0.10) L CCA (P=0.96) R ICA (P=0.74) L ICA(P=0.44).

Conclusions: Treatment with metformin improved FMDmax, 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 ESCR Special Needs Plans and Outcomes
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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 (separately) 1) dialedyzed in the same facility as the C-SPN patient but had not enrolled in the C-SPN, 2) dialedyzed 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 ESCR Seamless Care Organizations
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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, 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=0.06), fewer dialysis facilities (8.7 vs 17, p=0.07), a smaller non-Hispanic Black population (14% vs 22%, p=0.06), and higher median household income ($59k vs $49k, p=0.01). 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 higher median household income ($58k vs $48k, p<0.01). 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 disparity in ESCO composition and savings 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 Ravindhran, Erikka J. Woolfolk, Lauren Moccia, Due 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 implement new strategies for prevention 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)
Thomas D. Wooldridge,1 Kieran Mccafferty,2 Michael Schoemig,3 Botond Szaboles Csky,2 Rafal Zwiech,1 Warren Wen,2 Catherine Munera,1 Frederique Menezghi,3 Nephrology and Hypertension Associates, Ltd., Tupelo, MS;3 The Royal London Hospital - Barts Health NHS Trust, London, United Kingdom;1 Dialysezentrum Heilbronn, Heilbronn, Germany;3 Norbert Barlitzki Memorial Teaching Hospital No. 1 of the Medical University of Lodz, Lodz, Poland;3 Cara Therapeutics, Stamford, CT;3 FMC Satellitza Dialysis Center Pecs, Pecs, Hungary.

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 (DFFK), 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 DFFK in HD pts with CKD-aP (KALM-2).2 NCT03636269.

Methods: HD pts with CKD-aP were randomized to receive intravenous DFFK 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 Numerical Rating Scale (WI-NRS) score at wk 12. Secondary endpoints were the proportion of pts who achieved a≥4-point improvement in WI-NRS score and mean change in itch-related QoL scores (5-10 itch and SkinEx10) from BL to wk 12.

Results: BL mean weekly WI-NRS scores were 7.3 and 7.1 in the DFF and PBO groups. The primary endpoint was met, with 54% of pts who received DFF achieving Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
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). ICH reduction was evident at wk 1 and was sustained through wk 12. Improvement in itch-related QoL assessed by 5-D Itch and Skindex-10 was observed. Treatment-emergent AEs ≥5% with DFK vs PBO were: diarrhea (8.1% vs 5.5%), fall (6.8% 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 second phase 3 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. Endpoints evaluated were: mean change from baseline (CFB) in hemoglobin (Hb) averaged over Weeks 28-52 regardless of rescue therapy and Hb CFB averaged over Weeks 28-36 censored for rescue therapy. Safety and tolerability were assessed by reported treatment-emergent adverse events (TEAEs).

Results: In the DD-CKD study population, 90% (515/587) 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 (RD) CKD group and 9.61 (1.31) in the epoetin alfa (EA) group. Patients achieved a larger mean (SD) CFB to Weeks 28–52 in Hb with roxadustat vs. epoetin alfa (1.49 [0.98] vs. 0.89 [1.51]), corresponding to a least-squares mean (LSM) difference of 0.25 (95% CI: 0.19, 0.31) (p=0.0001). Patients achieved a larger mean (SD) CFB to Weeks 28-36 in Hb with roxadustat vs. epoetin alfa (1.27 [1.63] vs. 1.02 [1.60]), corresponding to a 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 DD-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
Cachet Wenzinger,1 John Sy,1 Maria V. Marroquin,2 Kamary Kalantar-Zadeh,3 Csaba P. Kovousy,4 Elleni Straja.1 1Harold Simmons Center for Kidney Disease Research and Epidemiology, Orange, CA; 2The University of Tennessee Health Science Center, Memphis, TN; 3VA Long Beach Healthcare System, Long Beach, CA; 4Memphis VA Medical Center, Memphis, TN

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 patients with atrial fibrillation (AF) who then initiated dialysis. Patients 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 ESRD patients from rates of 0.3% to 7.5% and from 11.5% to 37.5%, respectively, by 2025 will improve 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

FR-OR27
Forecasting the Distribution of Dialytic Modalities in the Era of Advancing American Kidney Health
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Background: The Executive Order on Advancing American Kidney Health aims to increase home dialysis utilization in patients with end stage kidney disease (ESKD).

Methods: We constructed a simulation projecting dialytic modality distributions between 2019 and 2030 as a function of changing modality transition rates.

Results: 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.

Conclusions: 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 will improve 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.

Funding: Commercial Support - Fresenius Medical Care

FR-OR28
Hospitalization and Day of the Week: Comparing Peritoneal Dialysis, Home Hemodialysis, and In-Center Hemodialysis
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Background: Studies have shown that there are daily variations in mortality for patients receiving in-center hemodialysis (HD) but not home HD, peritoneal dialysis or more frequent in-center HD. Less is known about daily variations in hospitalization according to dialysis modality.

Methods: We analyzed all chronic dialysis patients in Canada (excluding Manitoba and Quebec) from 1 Jan 2005 to 31 Dec 2014 using the Canadian Organ Replacement Register (CORR). Dialysis modalities were defined (using CORR) as peritoneal dialysis, conventional HD or frequent HD (nightly or short daily) and HD modalities were further categorized as home versus in-center. All switches between modalities after dialysis initiation were included provided the duration of the switch was >30 days.

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

<table>
<thead>
<tr>
<th>Treatment Group</th>
<th>Total</th>
<th>Monday</th>
<th>Tuesday</th>
<th>Wednesday</th>
<th>Thursday</th>
<th>Friday</th>
<th>Saturday</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional In-Center HD</td>
<td>16,177</td>
<td>2,867 (17.8%)</td>
<td>2,574 (16.0%)</td>
<td>2,289 (14.2%)</td>
<td>2,150 (13.5%)</td>
<td>2,150 (13.5%)</td>
<td>2,000 (12.4%)</td>
</tr>
<tr>
<td>Frequent In-Center HD</td>
<td>1,476</td>
<td>237 (16.1%)</td>
<td>237 (16.1%)</td>
<td>229 (15.6%)</td>
<td>229 (15.6%)</td>
<td>229 (15.6%)</td>
<td>237 (16.1%)</td>
</tr>
<tr>
<td>Conventional Home HD</td>
<td>1,401</td>
<td>232 (16.5%)</td>
<td>229 (16.5%)</td>
<td>232 (16.5%)</td>
<td>232 (16.5%)</td>
<td>232 (16.5%)</td>
<td>229 (16.5%)</td>
</tr>
<tr>
<td>Frequent Home HD</td>
<td>1,459</td>
<td>232 (15.9%)</td>
<td>232 (15.9%)</td>
<td>232 (15.9%)</td>
<td>232 (15.9%)</td>
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<td>232 (15.9%)</td>
</tr>
<tr>
<td>Peritoneal Dialysis</td>
<td>2413</td>
<td>452 (18.7%)</td>
<td>464 (19.2%)</td>
<td>464 (19.2%)</td>
<td>464 (19.2%)</td>
<td>464 (19.2%)</td>
<td>464 (19.2%)</td>
</tr>
</tbody>
</table>

Day of the week hospitalization for each dialysis treatment type (%)

FR-OR29

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

*Alvin H. Moss,1 Annette Aldous,2 Glenda Harbert,1 Amanda C. Nicklas,3 Louis Diamond,3 Nancy Armistead,3 Dale Lupu,1 2West Virginia University Health Sciences Center, Morgantown, WV; 2George Washington University School of Public Health and Health Services, The George Washington University Milken Institute of Public Health, Washington, DC; 3The George Washington University School of Nursing, Ashburn, VA.*

**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 I 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-OR31

**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.
present impaired permeability to albumin, due to a dysfunctional assembly of the GBM, typically localized to the GBM and binds to COL4A3/laminin to inhibit podocyte adhesion. Mice lacking ROBO2/SLIT2 signaling negatively regulates nephrin-induced actin polymerization and destabilizes podocyte focal adhesions and attachment 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 injuries. Here we provide evidence to support the 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 vesicoureteral 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 and 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 terminal half-life of about 6 hours in rat and 8 days in monkey. Treatment with ROBO2-Fc reduced proteinuria, shortened podocyte foot process width, and increased slit-diameter density in the rat PHN model. Mechanistically, we found that SLIT2 is localized to the GBM and binds to COL4A3/laminin to inhibit podocyte adhesion.

**Conclusions:** We have generated a novel therapeutic ROBO2 fusion protein that functionally inhibits SLIT ligand-podocyte injury pathway in clinical demand. 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**

**Sanjeev Sethi,**1 Hanna Debiec,2 Benjamin J. Madden,1 Marina Vivarelli,2 Cristine Charlesworth,1 Ashiwayra Ravindran,1 Louann Gross,2 David Buob,2 Cheryl L. Tran,1 Francesco Emma,4 Francesca Diomed-Camassaci,4 Fernando C. Fervenza,1 Pierre M. Ronco,2,21 Mayo Clinic, Rochester, MN; 2Sorbonne Universite, Paris, France; 3Tenon Hospital, Paris, France; 4Ospedale Pediatrico Bambino Gesu, Roma, Italy.

**Background:** Membranous nephropathy (MN) results from subepithelial antigen-antibody 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 3 validation cohorts (2 French and 1 Italian) of 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 hereditary forms of MN. Sema3B was expressed in tubular basement membrane (TBM) IgG deposits, the TBM deposits were negative for Sema3B. WB analysis in 5 available sera showed reactivity to reduced Sema3B in 4 of 4 patients with active disease and no reactivity in 1 patient in clinical remission; there was also no reactivity in control sera. Eight (73%) of the 11 cases of Sema3B-associated MN were pediatric cases. In 5 of the 8 children, the disease started below the age of 2 years.

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

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**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**

**Laith Al-Rabadi,**1 Tiffany Caza,2 Claire Avillard,3 Aylin R. Rodan,4 B. Williams,1 Josephine Abraham,1 Monica P. Revelo Penafiel,1 Nicole K. Andeen,1 I. Kawai,1 Frederic Clayton,1 Timothy Cummins,1 Michael Merchant,2 Jon B. Klein,1 Christopher P. Larsen,3 Laurence H. Beck.2 (HTRA) for Sema3B-associated MN was performed to confirm MS results. Next, we analyzed 3 validation cohorts (2 French and 1 Italian) of 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).

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

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**Figure 1** shows bright granular capillary wall staining for Sema3B in 3 cases of Sema3B-associated 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 hHTRA1, 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 colocalized 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
Sanjeev FR-OR36
Charlesworth,1 Hanna Madden,1 Charles Debiec,2
1Mayo Clinic, Rochester, MN; 2Sorbonne Universite, Paris, France, Tenon Hospital, Paris, France.

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 DNAJB9 (4 cases of fibillary 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 subclassing 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 g/mL (+/- 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.

Funding: Commercial Support - Calliditas

FR-OR37
Nefcon® (Budesonide) Selectively Reduces Circulating Levels of BAFF (BLYS) and Soluble BCMA and TACI in IgA Nephropathy
Karen Molyneux, Jonathan Barratt, David H. Wimbury. Mayer IgA Nephropathy Laboratory, University of Leicester, UK, Leicester, United Kingdom.

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 gut memory B cells 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 interactor (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-release formulation of budesonide (Nefcon®), 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 Nefcon® 16 mg/day, 51 patients received Nefcon® 8 mg/day, and 50 patients received placebo. As a result, Nefcon® 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 Nefcon® 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 at p<0.05.

Results: A significant, dose-dependent reduction in serum BAFF levels was seen with Nefcon®, which reversed on cessation of Nefcon®. 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 levels with Nefcon®.

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

Funding: Commercial Support - Kezar Life Sciences

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 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 immune effector cell 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 PLAR2-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 reacting 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 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 antibodies.
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 vivo could allow for non-invasive monitoring.
Funding: Other NIH Support - SIRI funding from the National Institute on Minority Health and Health Disparities, awarded to Dr. Christopher Larsen

FR-OR40
Alpha-1-Antitrypsin Diminishes Neutrophil Activation by PR3-ANCA and Endothelial Injury by Neutrophil Serine Proteases
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Background: Neutrophil serine proteases (NSPs) contribute to ANCA-associated vasculitis (AAV). PR3 is a unique NSP family member because it is both a proteolytic enzyme and an ANCA antigen. Alpha-1-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 recombinant wild-type (wt) AAT and a mutant (mu) form that does not inhibit proteolytic NSP activity. We used flow cytometry to study membrane PR3 (mPR3) and MPO (mMPO), ferricytochrome C assay for superoxide release, FRET assays for proteolytic NSP activity, human neutrophils and glomerular microvascular endothelial cells (gMVEC) for confocal and electron microscopy, and assessed ECs by phalloidin staining and gene expression.
Results: Wt-AAT reduced mPR3 on TNF-primed neutrophils dose-dependently from 0.1 to 10 μM (n=5). Five μM wt-AAT, but not mu-AAT, reduced neutrophil mMPO 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 wt-AAT, but not mu-AAT, reduced neutrophil mPR3 in TNF-primed neutrophils dose-dependently.
Conclusions: AAT has protective effects by reducing neutrophil activation in response to PR3-ANCA, and NSP-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.
Funding: Government Support - Non-U.S.

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 5 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

FR-OR42
Proteomics Reveals Extracellular Matrix Injury in the Glomeruli and Tubulointerstitium of Kidney Allografts with Early Antibody-Mediated Rejection
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Background: As donor leukocytes persist within the allograft and can play any role in rejection as of yet unknown, in part because of limited techniques for distinguishing recipient and donor cells. We studied 30 kidney transplant recipients with early AMR, acute cellular rejection (ACR) or acute tubular necrosis (ATN). We targeted microdissected glomeruli and tubulointerstitium and subjected them to unbiased proteomic analysis.
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 122 tubulointerstitial proteins significantly differentially expressed in AMR vs ACR (p<0.05). Similarly, 112 (glomeruli) and 124 (tubulointerstitium) 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 LAMC1 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 (GSE36059) also demonstrated increased galectin-1 expression and linked 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 TNFα-treated proximal tubular epithelial cells.

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

FR-OR43
Interim Update of the MDR-101-MLK Phase 3 Trial: MERCURY Study
Dixon Kaufman,1 Mark D. Stegall,2 Ethan P. Marin,3 Ahmed O. Gaber,4 Titte Srinivas,5 Erik Stites,6 Stephan Busque,7 Martin L. Mai,8 Matthew Cooper,9 Suzanne Crowley,1 James B. Piper,10 Asher P. Shah,1 Sanjeev Akkina,1 Kenneth Chavin,4 Mercury Study Group1 University of Wisconsin System, Madison, WI; Mayo Clinic Minnesota, Rochester, MN; Yale University Department of Internal Medicine, New Haven, CT; Houston Methodist, Houston, TX; University of Colorado, Denver, CO; Stanford University School of Medicine, Stanford, CA; Mayo Clinic’s Campus in Florida, Jacksonville, FL; MedStar Georgetown University Hospital, Washington, DC; University Hospitals, Cleveland, OH; Medeor Therapeutic, South San Francisco, CA; Inova Health Systems, Falls Church, VA; Jefferson Health, Wayne, PA; Loyola University Health System, Maywood, IL.

Background: The goals of tolerance in patients with kidney transplants (Ktxp) are to eliminate 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).

Methods: Eligible adult pairs (donor/receiver) of a first kidney allograft from an HLA-identical LD were enrolled and randomized 2:1 to either the Investigational Arm (IA; n=20) or Control Arm (CA; n=10). Donors in the IA received G-CSF mobilization for 5 days before undergoing apheresis (1 or 2 cycles). IA recipients receive ATG conditioning, low-dose total lymphoid irradiation (TLI) over 10 days and IS followed by an infusion of MDR-101 on d11. After 180 days of persistent mixed chimerism, IA subjects initiated a 6-month taper of CNIs and could withdraw all IS on D365. CA subjects initiated a 6-month taper of CNIs and could withdraw all IS on D365. CA subjects were treated as institutional SOC.

Results: As of June 1 2020, 26 subject pairs (donor/receiver) have been enrolled, comprising 18 pairs randomized to the IA and 8 pairs randomized to the CA. MDR-101 infusion was completed in 12 subjects in the IA, and 9 subjects in the IA have reached Day 180 with 6 months of positive mixed chimerism. Five subjects have reached D365 and were able to withdraw all IS. Two subjects lost chimerism – 1 at D545 (off IS) and 1 at D245 continue to wear IS. There have been no events of GvHD, biopsy proven acute rejection, dnDSA. There have been no graft losses or deaths in either group.

Conclusions: Administration of MDR-101 in HLA-identical LD Ktxp recipients conditioned with ATG and TLI have produced promising results to date. These results show that MDR-101 induces mixed chimerism without GvHD and permits withdrawal of IS without rejection or dnDSA. Further analysis continues.

Funding: Veterans Affairs Support, Commercial Support - Medeor Therapeutics

FR-OR44
Single-Cell Profiling of Peripheral Blood Mononuclear Cell Identifies Immune Populations Associated with High Risk of Early Acute Rejection
Weijia Zhang, Samina S. Farouk, Zeguo Sun, Zhengzi Yi, Jia Fu, Chengguo Wei, Miguel Fribourg, John C. He, Paolo Cravedi, Barbara T. Murphy. Icahn School of Medicine at Mount Sinai, New York, NY.

Background: Our previous transcriptomic analysis of pre-peritransplant peripheral blood of 235 kidney transplant recipients in a multi-center GoCAR cohort revealed a 23-gene set predictive of early acute rejection (EAR) post kidney transplant, but the associated immune profile is unknown.

Methods: We first developed a reliable targeted RNA expression (TREX) sequencing assay based on the EAR prediction gene set and applied the assay to assess the EAR risk of 21 dialysis patients who were recruited at Mount Sinai Hospital. We next performed extensive single-cell immune profiling of PBMCs of these patients using 33 surface markers with CyTOF technology. Lastly, using 10X genomics technology, we performed single cell RNA sequencing (scRNAseq) of the PBMCs to identify immune cell (sub) populations and their transcriptomic signatures from two patients with high and low risk of EAR, respectively.

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

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**FR-OR46**

**Modified Immune Cell Infusion in Kidney Transplantation**

Christian Morath, 1 Matthias Schauer, 1 Eman H. Ibrahim, 1 Wei Li, 1 Christian Kleist, 1 Gerhard Opelz, 1 Caner Süssel, 1 Mostafa G. Aly, 1 Claudius Speer, 1 Florian Käßle, 1 Christian Nussbag, 2 Luiza Pego Silva, 3 Claudia Sommerer, 1 Angela Hückelhoven-Krauss, 3 Arianeh Mehrabi, 3 Carsten Mueller-Tidow, 3 Jochen Reiser, 2 Martin G. Zeier, 1 Michael Schmitt, 1 Peter Ternes, 1 Anita Schmitt, 1 Volker Daniel, 1 *Ruprecht Karls Universität Heidelberg, Heidelberg, Germany; 2Rush University Medical Center, Chicago, IL.*

**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 68-fold increase in the frequency of immunosuppressive CD19+CD24hiCD38hi transitional B lymphocytes 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 1.5x10^9/MIC per kg b.w. on day -7 before living donor kidney transplantation and who were on low 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. CD19/CD24/CD38+ and CD19+CD24+CD38+ Breg were with 2.2x and 1.0x, respectively strikingly higher than the 0.0x (P=0.001) and 0.0x (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+ (P=0.0071), CD19+CD24+CD38+ (P=0.0077), CD19+CD25+CD73-CD71+ (P=0.013), CD19+CD25+CD73+CD71 (P=0.0011), CD19+CD24+CD27+ memory (P=0.029), and IL10+CD19+CD24+CD27+ memory Breg (P=0.042). No such differences were observed for CD4+CD25+CD73+Fox3+ Treg (P=0.60) 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.

**Funding:** Commercial Support - Tolerogenix GmbH, Government Support - Non-U.S. Commercial Support - Tolerogenix GmbH, Government Support - Non-U.S.

**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 DCDF injury compared to cold storage (SCS); 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 8 hours of NEVKP or SCS, and auto-transplantation.

**Results:** Of 6593 proteins quantified, 70 were differentially expressed between NEVKP and SCS groups (2-way ANOVA, q<0.05). Proteins increased in NEVKP mediated key metabolic processes including fatty acid ß-oxidation; the TCA cycle and oxidative phosphorylation. 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 PPARG1A, PPARA/G/D and RXRA/B as the upstream regulators of our dataset, and we confirmed our 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 SCS. 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 Glycopalx**

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**Background:** Calcineurin inhibitors are associated with nephrotoxicity, 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-inhibited 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 (CyaA) on EC injury, complement activation (C3a, C9) and regulation (CD46, CD55 and complement factor H [CFH]) on EC surfaces, and on the EC glycopalx, utilising flow cytometry, Western blot, and immunofluorescence imaging. Functional activity of CFH was assessed via CFH co-factor assay. Co-immunoprecipitation of Angiopoietin-2 (Angpt-2), Angiopoietin-1 (Angpt-1) and Tie2 was assessed by Western blot.

**Results:** CyaA resulted in a dose and time dependent enhancement of EC complement damage. The ELISA for C3a, C9, CD46, CD55 and CD59 and complement factor H [CFH] on EC surfaces, and on the EC glycopalx, utilising flow cytometry, Western blot, and immunofluorescence imaging. Functional activity of CFH was assessed via CFH co-factor assay. Co-immunoprecipitation of Angiopoietin-2 (Angpt-2), Angiopoietin-1 (Angpt-1) and Tie2 was assessed by Western blot.

**Conclusions:** Our findings confirm a role for complement in CyaA-induced EC injury, and suggest Angpt-2 mediated glycopalx abolishment, induced by CyaA, as a mechanism leading to complement alternative pathway dysregulation via decreased CFH surface binding and surface co-factor activity.

**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.

**Methods:** We performed an unbiased methylation analysis of 28 kidney biopsies obtained at 3 timepoints from pig kidneys subjected to 30-minutes of warm ischemia, followed by 8 hours of NEVKP or SCS, and auto-transplantation.

**Results:** Of 6593 proteins quantified, 70 were differentially expressed between NEVKP and SCS groups (2-way ANOVA, q<0.05). Proteins increased in NEVKP mediated key metabolic processes including fatty acid ß-oxidation; the TCA cycle and oxidative phosphorylation. 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 PPARG1A, PPARA/G/D and RXRA/B as the upstream regulators of our dataset, and we confirmed our 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 SCS. These effects may be coordinated by PPAR-family transcription factors, and may represent novel therapeutic targets in ischemia-reperfusion injury.
Methods: Epigene-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 pval<0.01 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. SPAN1) and genes with prior chronic kidney disease associations (e.g. FNTA). A DMR was also identified within the long intergenic non-protein coding RNA LINC01344, suggesting a possible regulatory function. Additionally, Partek® Pathway® identified enrichment of DMR in the mitogen-activated protein kinase (MAPK) signalling 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 transplantation.

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.

Results: In vitro: We observed significantly increased expression of NLRP1 inflammasome protein and Caspase-1 in cells subjected to CS/REW. Using Imagestream flow cytometry we observed spatial overlap between two different fluorescent labels of Caspase-1 and NLRP1 in RTECs exposed to CS/REW compared to control cells. In vivo studies: Wild-type kidneys subjected to CI+Txp demonstrated significantly increased Caspase-1 and NLRP1 protein expression. Caspase-1 deletion results in significantly decreased RTEC apoptosis in transplanted Casp1KO vs WT kidneys. Renal function, brush border injury, cast formation, tubular simplification were similar in both groups and not significantly different [Table 1].

Conclusions: CS/REW and CI+Txp increase NLRP1 and Caspase-1 expression and co-localization. Deletion of Caspase-1 improves tubular cell apoptosis following CI+Txp. However, Caspase-1 deletion did not prevent AKI and necrosis in kidneys subjected to CI+Txp, suggesting that other triggers of inflammation and programmed necrosis may need to be included in addition to deletion of Caspase-1 to fully prevent AKI after kidney transplantation.

Funding: Veterans Affairs Support

Histological assessment of transplanted kidneys

**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 transplantation.

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.

Results: In vitro: We observed significantly increased expression of NLRP1 inflammasome protein and Caspase-1 in cells subjected to CS/REW. Using Imagestream flow cytometry we observed spatial overlap between two different fluorescent labels of Caspase-1 and NLRP1 in RTECs exposed to CS/REW compared to control cells. In vivo studies: Wild-type kidneys subjected to CI+Txp demonstrated significantly increased Caspase-1 and NLRP1 protein expression. Caspase-1 deletion results in significantly decreased RTEC apoptosis in transplanted Casp1KO vs WT kidneys. Renal function, brush border injury, cast formation, tubular simplification were similar in both groups and not significantly different [Table 1].

Conclusions: CS/REW and CI+Txp increase NLRP1 and Caspase-1 expression and co-localization. Deletion of Caspase-1 improves tubular cell apoptosis following CI+Txp. However, Caspase-1 deletion did not prevent AKI and necrosis in kidneys subjected to CI+Txp, suggesting that other triggers of inflammation and programmed necrosis may need to be included in addition to deletion of Caspase-1 to fully prevent AKI after kidney transplantation.

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 transcriptional 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 (Nephrotic syndrome and SARS-CO2-2) using R. Pathway analysis was performed using WebGestalt. Possible drugs correcting the skewed gene expression in FSGS and SARS-CO2-2 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 upregulated and upregulated in COVID-19 and FSGS/MCD (B2M, EIF2AK2, IFIT1, IFIT2, TC7M and UBE2L6). Strikingly, IFIT2 has been recently reported as a maker 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 eMAP data and identified 59 drugs significantly inversely associated with SARS-CO2-2 and 72 for FSGS. Out of these, 7 drugs were in common, representing novel potential drugs for COVID-19 and podocytopathies.

Conclusion: Overall, our results suggest transcriptional congruency between NS and SARS-CO2-2 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 (MSH) 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 (MSHS). 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.

Conclusion: A machine-learned model using admission features had good performance for dialysis prediction and could be used for resource allocation.
SA-OR03
SARS-CoV-2 Detection in Urine Sediment 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 hypothesized 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 sediments 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 tubulitis of COVID-19 patients. In some tubules, positive SARS-CoV-2 overlapped with ACE2, the receptor for viral entry. Virus was detected in 61% of urine sediments, with 6-fold greater viral load in AKI- versus non-AKI patients (copies/ng RNA: AKI, 7432±1338 vs No-AKI: 1523±404; p<0.05, n=52). The highest viral loads were detected three weeks post-AKI at 11,374±2248 copies/ng RNA (p<0.01). Among COVID-19 AKI-patients who died, the urine viral load exceeded 8800 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 serve as an early warning signal. This 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 hypothesized that 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.

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 (COVID-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 LDL, 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 (bb.flatironinstitute.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-CoV2 infected cells.

Conclusions: A consistent ACE2-coregulated 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

SA-OR05
Genomic Datasets from Traditional Murine Models of AKI and AKI-Lung Cross-Talk Reveal Molecular Pathways Relevant to COVID-19 Infection
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Background: COVID-19 infection leads to ARDS and AKI, and there are established mechanistic links between acute kidney injury (AKI) and lung injury. SARS-CoV-2 uses cell entry angiotensin-converting enzyme 2 (ACE2) and transmembrane protease, serine 2 (TMPRSS2), which are expressed in kidney and lung. Using publicly available genomic datasets of ischemia and sepsis induced AKI in mice, we searched for established and novel molecular players of AKI and AKI-lung cross-talk relevant to COVID-19.

Methods: The microarray datasets GSE6730 (AP17 Renal 2007, JASN 2008) and GSE60088 (Shock 2016) were downloaded from Gene Expression Omnibus (GEO). GSE6730: lungs from mice with moderate and severe ischemic AKI were studied at 6h and 36h. GSE60088: kidneys were studied from mice after 6h of pneumonia+mechanical ventilation (PMV). Isolated RNA was hybridized to MG_430 microarray. To identify differentially expressed genes, GEO-built in GEO2R tool was used.

Results: AKI led to downregulated kidney ACE2 gene at both 6h (fold change (FC)=−2.41) and 36h (FC=−3.23) after severe (60min clamp) but not moderate ischemia (30 min clamp; 6 h: FC=+1.3, 36h: FC=+1.16). In lung from AKI mice, ACE2 was significantly downregulated (FC=−2.89, P=5.56e10). Ischemic AKI and PMV led to a decrease in lung TPRSS2 FC=−1.83, P=1.19e10 and FC=−1.68, P=6.58e10, respectively. The filtering for known genes with P-value<0.01 and FC>4 identified 53 kidney genes upregulated by PMV; and 254 lung genes upregulated by AKI, of which 9 genes were common to both organs. 3 of 9 genes were previously linked to kidney-lung crosstalk: Len2 (FC=+8.6, FC=+6.32), Socs3 (FC=+10.5, FC=+10.4), Inhib (FC=+12.0, FC=+6.17). This finding validates our approach and makes other 6 genes appealing candidates, especially Maff (FC=+7.21, FC=+5.98). This gene participates in the cellular stress response and also binds the oxytocin receptor promoter, which may be involved in gender differences in disease severity.

Conclusions: We identified changes in COVID-19 related genes ACE2 and TPRSS2 in traditional mouse models of AKI and lung cross talk. We also found new candidate genes activated in kidney during pneumonia+mechanical ventilation and in lung during AKI, which warrants further investigation of their involvement in the combined kidney-lung injury during COVID-19.

Funding: NIDDK 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 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). Patients requiring 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: 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 results 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.
SA-OR09
Urgent Peritoneal Dialysis Catheter Placement at a New York City Hospital During the COVID-19 Pandemic

**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 (CKRT) 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 CKRT 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 time 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 antiocoagulants. 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 exudation.

**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<0.0006). Use of anticoagulants (16% vs 51%, p=0.0001) 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.
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. Podocyte-derived extracellular vesicles (EVs) was isolated and identified by specific morphology and surface markers. Immunofluorescence, PCR, western blot, electron microscope, and tranwell were conducted to assess the de-differentiation of PTECs. The expression level of miRNA in EVs was detected and Cy3-labeled mimics was used to demonstrate its direct transfer into target cells. A dual-luciferase reporting 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 siRNA. In addition, Streptozotocin-induced diabetic mice and a models were constructed, and miRNA antagonem were used to explore its role in proximal tubule injury.

Results: Podocytes induced de-differentiation of PTECs in high-glucose conditions and induced cell-cell interaction. The podocyte-derived EVs was extracted and identified as exosome, 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 DDK2, 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 determinants 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 with structural parameters.

Results: Using WGS to evaluate this family, we identified a rare loss-of-function mutation in adiponectin (ADIPOQ) (p.R662C), 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 ADIPOQ wildtype diabetic patients). In cell culture, we observed that ADIPOQ (p.R662C) is degraded by the proteosome. Likely due to its incorporation to trimeric adiponectin, over-expression of the mutant protein decreases stability of wildtype adiponectin and exerts a dominant-negative effect that results in reduced adiponectin levels.

Conclusions: This is the first human family with a dominant-negative mutation in adiponectin. Importantly, while adiponectin is known to play important roles in insulin sensitivity, it also has a protective role in mitigating renal injury in patients with diabetes. Moreover, adiponectin knockout mice are prone to DN and podocyte apoptosis. Together these data provide evidence supporting the role of adiponectin in kidney disease in patients with diabetes.

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 intrareally with adeno virus 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 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 macropage recruitment (p<0.001), inflammatory cytokine (p<0.01) and fibrotic markers (p<0.01), kidney ADMA levels (p<0.05), and urinary thiobarbituric acid reactive substances excretion (p<0.01), along with a significant reduction in kidney DDAH activity (p<0.05) and kidney NOS3 mRNA (p<0.05) compared to normal mice. In contrast, Ad-h-DDAH-1 treatment of diabetic mice reversed these effects.

Conclusions: 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 217 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 (sPEC) unique to T2D, was dominated by apoptosis and glycolysis 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 mouse survival in a murine model of DKD.
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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 an important role in DN progression. DN reversal following 10 years (10Y) of euglycemia after pancreas transplantation (PTx) is documented (N Engl J Med 2016;375:69-75). We hypothesized that if PC loss has occurred, 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/gluomerulus [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=0.0008) or 10Y (p=0.002) was greater than C with no significant change found 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 mesangial extracellular dynamics in DN in T1D. Moreover, despite long-term nornormoglycemia, 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, FinnDiane) to identify urinary proteins associated with rapid eGFR loss. Cases and controls were defined by annual eGFR decline ≥3 ml/min/1.73 m2 and <1 ml/min/1.73 m2, respectively. We developed a targeted liquid chromatography-tandem mass spectrometry assay to measure 38 peptides of 20 proteins implicated in diabetic kidney disease (DKD), the mechanism mediating this process remains to be explored.
Results: Out of 38 urine peptides, 2 cathepsin D (CatD) peptides were associated with rapid eGFR loss adjusting for demographic but not clinical variables (1.26, 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 loss among those with UACR ≥30 mg/gCr in 36% were included. Over 8 years median follow-up, mean eGFR slope was -5.65 and 0.57 ml/min/1.73 m2 per year for cases and controls, respectively. Out of 38 urine peptides, 2 cathepsin 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 mg/gCr 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 1.10-3.19; 1.84, 95% CI 1.08-3.13) sets. Across several Nephroseq cohorts, CatD transcription was increased in tubulointerstitial and not glomerular specimens in diabetic kidney disease compared to healthy living donors.
Funding: Private Foundation Support

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

Figure 1: Heatmap of HRG in T2D

SA-OR16
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/SCO2:db/db and Sco2/SCO2:db/db mice. Sco2/SCO2, 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 compared to healthy donors. 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+/+ and SCO2+/- mice had a significant reduction in albuminuria, serum creatinine, glomerular hypertrophy, glomerular oxidative stress (8-oxoG staining) with an increase in podocyte number (WT vs cells per glomerular cross-sectional area), synaptopodin expression, and overall survival. SCO2+/+ and SCO2+/- mice also exhibited less glomerular endothelial injury with a decrease in glomerular capillary loop dilatation and a trend towards decrease in Vv(Mes/glom) and Vv(Cam1) and an increase in Angpt1, Vegfa, Kdr and Klf2 expression as compared to db/db mice.
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.

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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 (≥60 mL/min/1.73 m² and <60 mL/min/1.73 m²) and by eGFR slope from BL was calculated; an interaction p-value <0.05 indicated difference between slope. The estimated treatment difference (ETD) at 1 year between annual rates of decline in eGFR were analyzed using a linear random regression model with individual intercept and baseline eGFR slope from BL.

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 ≥60 mL/min/1.73 m² subgroups and eGFR slope, 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 function categories; the data suggest the main benefit might be observed in those with kidney disease.

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SA-OR20
Patience 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, patience (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 ≤45 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 % of pts on SPIRO, was 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. Four 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.

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SA-OR21
Single-Cell Transcriptomic Analysis to Define Cellular Heterogeneity in Human ADPKD
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Background: Deciphering the molecular pathogenesis of human autosomal dominant polycystic kidney disease (ADPKD) requires a detailed understanding of the distinct cell types and cell states driving cyst growth. Unlike single cell RNA-seq, single nucleus RNA-seq can be performed on cryopreserved samples, and we hypothesized that it might reveal unique cell states from biobanked human ADPKD samples.

Methods: We performed snRNA-seq on 8 ADPKD kidney samples (4 males and 4 females, mean = 50 +/- 8.5 years old, all had ESRD). Cystic kidneys weighed 1631 +/- 728 g. Nuclear preparations were processed using 10x Genomics Chromium 3’ kit and sequenced by NovaSeq. Reads were counted with CellRanger 3.1.0 and analyzed with Scanpy v1.7.0. Gene expression was validated by fluorescence in situ hybridization (FISH).

Results: Samples were stored at -80°C prior to processing (median, 20 mo; range 7-40 mo). All samples yielded good libraries (Avg. genes/nucleus = 1560 +/- 526). 63,289 nuclei originating from all 8 ADPKD kidneys passed quality control filters. Large clusters of cystic epithelial cells could be distinctly identified as originating from PT, TAL and CD. Compared to non-cystic epithelia, TAL-derived cystic epithelia showed strong induction of ERBB4 and gene ontology terms including fibroblasts/ECM and secretion of TGFβ. CDH6 high cystic epithelia expressed the PT injury markers CDH6 and LRPs2 and cystic epithelia expressed the PT injury markers CDH6 and LRPs2 and cystic epithelia expressed the PT injury markers CDH6 and LRPs2.

Conclusions: To our knowledge this is the first single cell transcriptomic atlas of human ADPKD. We demonstrate the utility of this approach by revealing (1) excellent gene expression from all samples including those stored > 3 yrs, (2) segment specific cystic epithelial expression profiles, (3) activated interstitial fibroblast subsets and (4) pro-inflammatory macrophage cell types and states.

Funding: NIDDK Support, Commercial Support - Chinook Therapeutics
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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Background: 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 mice (n=4) and cilia mutant mice after renal injury, such as cyclosporin A (CsA) or meropenem (a primary cilium inhibitor). We then performed cell-cell interaction analysis using NicheNet.

Results: Single cell RNA sequencing data from sham- and injured-cilia mutant mice indicate that renal injury results 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 NicheNet 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 altered cystic phenotype as assessed by kidney weight/body weight ratio, ANOVA interaction p=0.0017. In vitro binding studies indicated that CUD062 interacts with PKD domains 2-17 and most tightly with domains 15-17 in an SDS stable manner. We further showed that extracellular application of pure CUD062 activated cystin-1 (PC1) current (p<0.05). On a cellular level, the receptor for CUD062 is not known. In vivo, CUD062 was shown to be expressed most prominently in the vasa recta (VR) and the endothelium of large blood vessels but not in kidney tubules.

Conclusions: These data suggest that CUD062 might be a circulating ligand for PC1 and carbonic anhydrase 2 (CAII) and Tsc1 (TSC1/2) KO mice as its genetic deletion leads to a milder phenotype than that observed in Pkd1 homozygous null mice.

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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 gene responsible for the disease, we are still far from understanding 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 investigated the effects on PKD.

Methods: AMPK activation mouse models were generated by expressing the AMPKα1 isoform 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 cages, serum and urine samples were collected for analysis. Kidneys were collected and snap-frozen for biochemical studies or wax-embedded for histological studies. 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 mice (n=4) and cilia mutant mice after renal injury, such as cyclosporin A (CsA) or meropenem (a primary cilium inhibitor).

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 decreased urine osmolality and polydipsia, kidney damage and compromised renal function. Cysts were observed in the collecting ducts of these mice, consistent with the distal nephron being most heavily affected in PKD. Mechanistically, the cystic kidneys had increased AMPK 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, thus 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-OR25

Intercellular Transmitted and the Cell Signaling Factor FOXI1 Drive the Kidney Cystogenesis in Tuberous Sclerosis Complex

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Background: The 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 (angiomylipomatomata) 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 Foxi1 and Tsc1 (Foxi1/Tsc1 double KO) or carbonic anhydrase 2 (CAII) and Tsc1 (CAII/Tsc1 double KO) were generated based on RNA-seq and expression studies.

Results: Foxi1 KO mice showed numerous kidney cortical cysts, which were overexpressed in A-intercalated (A-IC) cells that express Foxi1. In Foxi1/Tsc1 dKO mice (Kidney MRI in image 1) 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.

Conclusions: We propose that A-IC cells, V H -ATPase and CAII are critical to cystogenesis and their inhibition may be associated with the significant protection against cyst generation and/or enlargement in TSC. Carbonic anhydrase inhibitors may be viable treatments for the prevention of kidney cyst expansion in TSC. Supplementation of carbonic anhydrase inhibitors with HCO3- (to minimize the untoward side effects of metabolic acidosis) may be the way forward.

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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 outcomes 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 SPATA8L1/GATM (rs24846722, p = 1.7 x 10^-10). Of these, 19 represented previously reported loci from GWAS of kidney function or CKD. Known CKD genes from case-control studies such as APAOL1 (rs73885319 p=9.09x10-28) 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 (rs10991574 p = 2.97x10^-10) associated with accelerated atherosclerosis and lipid metabolism through PPAR alpha, PIK3AP1 (rs5647676 p = 3.1 x 10^-10) associated with lescolocyte count and BCL-xL (rs9646829 p=2.49 10^-8) associated with colorectal adenoma. Some of the strongest signals previously reported for kidney phenotypes included: DAB2 (rs2542713 p=1.5 x 10^-8), OCT2 (rs2279463, p=1.98 10^-10), UNCX (rs62435145 p=1.97 10^-10) and PRKAG2 (rs10253736 p=3.0 x 10^-10). 70 SNPs were exonic variants overall. SNPs within UMOD/PDLP3, the top hits for kidney function GWAS and CKD progression among European-Americans, did not reach genome-wide (p=9.19x10^-8) significance.

Conclusions: In this large GWAS of eGFR among African Americans to date, we replicate over 19 previously identified loci, identify 3 novel loci associated 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 can systematically map out 3D genome architecture. However until now, technical and cost limitations have prevented these powerful approaches from being applied to intact human kidney tissues.

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 deeply sequenced to >400 million mapped reads 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 will provide an 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.

SA-OR28

Clonal Hematopoiesis of Indeterminate Potential and Somatic Mutation Role in CKD: The First Study

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Background: Clonal hematopoiesis of indeterminate potential (CHIP) is an age-related somatic mutagenesis associated with inflammation and increased risk of death due to cardiovascular disease. Chronic kidney disease (CKD) is strongly associated with cardiovascular disease, suggesting shared pathophysiologic mechanisms. Inflammation is a well-established component of CKD but CHIP has never been investigated in CKD.

Methods: We analyzed whole-exome sequencing data to determine CHIP prevalence and variant allele frequency (VAF) in a cohort of 2,187 CKD patients and 1,686 age-matched controls. Somatic variants were called using MuTect2 and filtered using strict standard criteria. The presence of CHIP mutations was evaluated for associations with demographic and clinical variables, including age, sex, CKD etiology, treatment with immunosuppressive therapies, end-stage renal disease (ESRD), and history of renal transplant.

Results: In a multivariate logistic regression model focused on the most frequently mutated CHIP genes (DNMT3A, TET2, ASXL1, JAK2), we observed an age-independent association between CHIP and CKD, where both prevalence (p=0.04, OR: 1.62) and VAF (3.48% vs. 1.89%, p=0.004) were higher in CKD cases than in controls. Among CKD cases, CHIP was independently associated with history of renal transplant >10 years (p=0.01, OR: 5.8) and treatment with immunosuppressive therapies (p<0.01, OR: 2.6).

Conclusions: Our analysis of a large case-control cohort suggests an independent association between CHIP and CKD. This association was most evident in patients with ongoing inflammation due to renal transplantation or immune-mediated conditions. These data will require replication in larger human cohorts and validation in animal models.

SA-OR29

Loss of Diacylglycerol Kinase α Causes Thrombotic Microangiopathy by Impairing Endothelial Vascular Endothelial Growth Factor A Signaling

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Background: Atypical hemolytic uremic syndrome (aHUS) is a thrombotic microangiopathy (TMA) accompanied by hemolytic anemia, thrombocytopenia, and acute renal failure due to glomerular damage. Mutations in complement genes have been identified in about 50% of aHUS cases. We reported that mutations in the gene DGKK, encoding the lipid kinase diacylglycerol kinase epsilon (DGKK) that is unrelated to the

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

Underline represents presenting author.
complement system, also cause aHUS. In the glomeruli, DGKE is expressed in endothelial cells and podocytes. The molecular mechanisms by which DGKeB causes TMA are not known. Phosphatidylinositol phosphate [PtdIns(4,5)P_2] 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 VEGF signaling in endothelial cells due to shortage of PtdIns(4,5)P_2.

**Methods:** To test this hypothesis, we performed in vitro studies on DGKE knockdown human umbilical vein endothelial cells (HUVECs) and generated endothelial-specific Tie2Cre;DGKE 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)P_2. Endothelial-specific Tie2Cre;DGKE conditional knockout mice spontaneously developed thrombocytopenia, schistocytosis, 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 signaling downstream of VEGFR2 in endothelial cells by decreasing cellular levels of PtdIns(4,5)P_2, 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.

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**SA-OR30**

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

Rusell P. Thompson, Colles M. Asp-348, Glu-355, Yanny Lee, Nadia Terra, Jayne Raper

**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 unrelated channel forming proteins. Here we introduce a new model of APOL1 channel structure and topology based on functional characterization of divergent APOL1 orthologs and interspecies chimeras in a planar lipid bilayer system.

**Methods:** We tested interspecies APOL1 chimeras and point mutations in planar lipid bilayers to identify molecular determinants of pH dependence and ion selectivity. **Results:** Strikingly, we demonstrate that cation conductance depends on the C-terminus domain, rather than the N-terminal region as previously suggested, with both pH gating and selectivity functions largely governed by a single residue - aspartate-348. Dual substitution of Asp-348 and nearby glutamate-355 eliminated pH gating, with tyrosine-351 having a steric influence. Acidic residues within a putative hairpin region (residues 177-228) affected the pH-dependence of channel formation.

**Conclusions:** Based on these data we present a radically updated domain structure of APOL1, including a putative 4-pass transmembrane topology and a pore-lining helix near the C-terminus (see Image abstract). We propose a mechanism of channel gating based on dual proton-sensing residues (Asp-348 and Glu-355) within the pore-lining helix, with Asp-348 also determining selectivity for cations over anions.

**Funding:** Other U.S. Government Support

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**SA-OR31**

**Small Molecule Inhibitor of TMEM16A Chloride Channel Blocks Vascular Smooth Muscle Contraction and Lowers Blood Pressure in Spontaneously Hypertensive Rats**

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**Background:** Hypertension is a major cause of cardiovascular morbidity and mortality, despite the availability of antihypertensive drugs with different targets and mechanisms of action. There is an unmet need for antihypertensive drugs with novel mechanisms of action for better BP control. TMEM16A (transmembrane member 16A or anoctamin-1) is a Ca<sup>2+</sup>-activated Cl<sup>-</sup> channel expressed in vascular smooth muscle. TMEM16A activation produces membrane depolarization that results in secondary activation of voltage-dependent ion channels that modulate vasoconstriction. TMEM16A is a potential target for hypertension treatment.

**Methods:** We recently identified by high-throughput screening and subsequent medicinal chemistry, small molecule TMEM16A inhibitor TM<sub>23</sub>-23 that inhibits TMEM16A current fully, with IC<sub>50</sub> = 30 nM. Here we tested TM<sub>23</sub>-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:** TM<sub>23</sub>-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 TM<sub>23</sub>-23 to rodents at 10 mg/kg produced sustained systolic blood pressure (SBP) reductions of ~90 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 TM<sub>23</sub>-23 (10 mg/kg, ip) compared to vehicle administration, with BP gradually returning to baseline values within 6-8 hours after TM<sub>23</sub>-23 pretreatment. Minimal effect on BP (less than 10 mmHg decrease in SBP) was seen in wild-type rats and mice with TM<sub>23</sub>-23 treatment (10 mg/kg, ip). Chronic 5-day treatment of SHR with TM<sub>23</sub>-23 (10 mg/kg, ip, twice daily) caused sustained decreases (~25 mmHg) in daily average SBP, DBP and MAP during the treatment period. TM<sub>23</sub>-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 TM<sub>23</sub>-23 as an antihypertensive with a novel mechanism of action.

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

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**SA-OR32**

**Intravitreal Imaging of Afferent 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 renal 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( Ca<sup>2+</sup>)<sub>max</sub> were observed in a few AA VSMCs at the glomerular entrance, which appeared to function as an afferent cell. The diameter of the AA (9.2±3.7 μm WT, vs. 11.3±3.7 μm KO) and EA (7.18±0.36 μm WT, vs. 8.59±0.30 μm 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±0.15 μm/s WT, vs. 2.0±0.12 μm/s 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( Ca<sup>2+</sup>)<sub>max</sub> in VSMCs during every contraction (A( Ca<sup>2+</sup>)<sub>max</sub> ~ 556±855 AU). In contrast, KO animals showed highly heterogeneous and irregular AA vascular activity. In those AAs that did exhibit some myogenic tone or contractile contractions, a higher frequency was observed (0.28±0.02 Hz), however the magnitude of A( Ca<sup>2+</sup>)<sub>max</sub> in AA VSMCs was much lower than in the WT (A( Ca<sup>2+</sup>)<sub>max</sub> ~ 395±249 AU). In both WT and KO animals, treatment with suramin rapidly blocked AA VSMC calcium increases and the myogenic contractions, and the AA became dilated.

**Conclusions:** AA sphincter cells have robust effects on AA (Ca<sup>2+</sup>)<sub>max</sub> 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 Nitrite Supplementation Improves Endothelial Function with Aging: Translational Evidence for Suppression of Mitochondria-Derived Oxidative Stress
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Background: We previously observed improvements in vascular endothelial function with inorganic nitrite 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 nitrite (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 C57BL6 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 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 was increased by 28% vs. baseline after nitrite supplementation (p<0.05), but unchanged with placebo.

Conclusions: Nitrite supplementation improves age-related endothelial dysfunction and is associated with increased NO, reduced mito ROS and improved mitochondrial stress resistance.

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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 myocardic 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 is unknown if FGF23 does not affect cardiac fibroblasts by regulating paracrine signal mediators in myocytes.

Methods: We treated cultured cardiac myocytes with FGF23 and determined expression levels of established paracrine signal mediators (IL6, LIF, TGFβ) or with high phosphate and analyzed FGF23 expression, all by qPCR. We isolated cardiac fibroblasts from wildtype mice on a high phosphate diet or control chow (0.7%) for 4 days to titrate P[K] over a narrow range (3.7mM (LK), 4.4mM (MK), 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 of [K] to BP.

Results: BP decreased by ~10 mmHg when [K] increased from 3.7 to 5.1 mM in control mice, coincident with the inactivation of [K]. When the switch was on (LK and MK groups), HNa significantly elevated BP and had no effect when the switch was inactivated by HCTZ. 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 hypothesis that low K dietary 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.’

Conclusions: Kinase-activating mutations were introduced in SPPAK. Expression of the constitutively active (CA) SPPAK mutant was limited to the early DCT and resulted in NCC hyperactivation. BP responses to small changes in plasma [K] in CA-SPPAK were compared to control mice. Dietary K content was varied over 4 days to titrate [K] over a narrow range (3.7mM (LK), 4.4mM (MK), 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 of [K] to BP.

Funding: NIDDK Support, Other NIH Support - NIH RO1 AG13038, NIH/NCATS

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 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 SPPAK. Expression of the constitutively active (CA) SPPAK mutant was limited to the early DCT and resulted in NCC hyperactivation. BP responses to small changes in plasma [K] in CA-SPPAK were compared to control mice. Dietary K content was varied over 4 days to titrate [K] over a narrow range (3.7mM (LK), 4.4mM (MK), 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 of [K] to BP.

Results: BP decreased by ~10 mmHg when [K] increased from 3.7 to 5.1 mM in control mice, coincident with the inactivation of [K]. When the switch was on (LK and MK groups), HNa significantly elevated BP and had no effect when the switch was inactivated by HCTZ. 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 hypothesis that low K dietary 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.’

Conclusions: Kinase-activating mutations were introduced in SPPAK. Expression of the constitutively active (CA) SPPAK mutant was limited to the early DCT and resulted in NCC hyperactivation. BP responses to small changes in plasma [K] in CA-SPPAK were compared to control mice. Dietary K content was varied over 4 days to titrate [K] over a narrow range (3.7mM (LK), 4.4mM (MK), 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 of [K] to BP.

Funding: NIDDK Support, Other NIH Support - NIH RO1 AG13038, NIH/NCATS

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, ascertainment 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 before versus 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
Leila R. Zelnick,1 Michael Shlipak,2 Elsayed Z. Soliman,3 Amanda H. Anderson,4 Robert Christenson,7 James P. Lash,8 Rajat Deo,6 Panduranga S. Rao,4 Farsad Afshininia,5 Jing Chen,4 Jiang He,4 Stephen L. Seliger,7 Raymond R. Townsend,1 Debbie L. Cohen,6 Alan S. Go,9 Nisha Bansal.1 1University of Washington Department of Medicine, Seattle, WA; 2University of California San Francisco, San Francisco, CA; 3Wake Forest University, Winston-Salem, NC; 4Tulane University, New Orleans, LA; 5University of Maryland School of Medicine, Baltimore, MD; 6University of Illinois at Chicago, Chicago, IL; 7University of Pennsylvania, Philadelphia, PA; 8University of Michigan, Ann Arbor, MI; 9Kaiser Permanente Northern California, Oakland, CA.

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, we developed a clinically informed clinical only model (CHARGE-AF) using machine learning methods, as well as a previously validated clinical prediction model (CHARGE-AF, using both original and re-estimated coefficients) to predict incident AF. Discriminatory ability of each 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 25% with CKD stage 4-5. The median follow-up (years) was 2.8; 251 incident AF events occurred during 7.3 (SD 2.8) years of follow-up. The AUC of the CHARGE-AF model was 0.75 (0.73, 0.76); the AUC of the clinical only model was 0.69 (0.67, 0.71). The difference was statistically significant (p < 0.002).

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

Funding: NIDDK Support

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
Robert Provenzano,1 Lynda Szeczech,2 Ming Zhong,2 Bryant Lai,2 Robert Leong,2 Dustin J. Little,2 Kin-Hung P. Yu,2 Wayne State University, Detroit, MI; 2FibroGen Inc, San Francisco, CA; 1AstraZeneca, Gaithersburg, MD.

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, 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 (>65 years) to 40% in patients on dialysis.

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 subgroup of incident-dialysis (ID-DD) patients. Patients with baseline (BL) moderate to severe CHF were not enrolled. CHF hospitalization events were a component of the MAE-plus endpoints that were adjudicated by a blinded independent committee, and analyzed by a Cox proportional hazards regression model; these analyses were not powered for individual endpoint outcomes.

Results: In the pooled NDD studies, 4270 patients were analyzed (2386 roxadustat; 1884 placebo). BL CHF history was comparable between roxadustat (25.7%) 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, 1.12) for roxadustat vs placebo.

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

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

Underline represents presenting author.
Effect of Apabetalone on Major Adverse Cardiovascular Events 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 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 infarction 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 [1.66, 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: CKD is a major risk factor for major adverse cardiovascular events in patients with recent acute coronary syndrome. Hence, the efficacy of BET inhibition (BETi) treatment with apabetalone (APB) was substantially reduced in patients with CKD.

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

Kyle Merrill,1 Shirley Galbiati,2 Mark Mitsnefes,3,4 on behalf of NAPRTCS Investigators 1Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; 2EMMES, Rockville, MD; 3University of Cincinnati, Cincinnati, OH.

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, and LVMi values based on outlying 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, hyperension (OR 2.9, 95% CI 1.4-6.3), anemia

SA-OR40

SA-OR41

SA-OR42

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
SA-OR43

Biomarker Panels for Discriminating Risk of CKD Progression in Children

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Background: We used multivariate survival trees 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 plasma and 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 8.8-15), 405(62%) were male, 195(30%) had a glomerular cause of CKD, and baseline eGFR was assessed annually using the bedside and complete CKiD 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. 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 CKiD 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

SA-OR44

Puberty Is Associated with Decline in Estimated Glomerular Filtration Rate in Children with CKD

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Background: Puberty is a high-risk period for decline in kidney function among children with CKD. We aimed to describe changes in eGFR before and after pubertal onset using different objective markers of puberty among children with CKD.

Methods: We conducted a prospective cohort study using data from the Chronic Kidney Disease in Children (CKiD) study. Children who had onset of CKD after pubertal onset were excluded. GFR was estimated annually using the bedside and complete CKiD 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. 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 CKiD 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

Figure: The best-sized multivariate survival tree and corresponding survival curves to predict CKD progression in children.

SA-OR45

CLYS1 H310Y Is a Novel Cause of Familial Childhood Steroid-Sensitive Nephrotic Syndrome

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Background: Nephrotic syndrome (NS) is the most common glomerular disease seen in children. It is estimated that up to 30% of steroid resistant NS (SRNS) may be due to mutations in one of sixty genes reported in cohort of patients with familial or idiopathic SRNS. However, the genetic causes of the more common steroid sensitive NS (SSNS) and the molecular basis for variability in glucocorticoid response have remained elusive. Our overarching hypothesis is that single gene causes of SSNS can be identified in cohorts of children with SRNS. We then hypothesized that mutations in the NS3 complex may contribute to the variability in glucocorticoid response.

Methods: To identify single gene causes of SSNS in a cohort of patients with familial SSNS and examine the molecular basis of glucocorticoid response, we carried out whole genome sequencing in forty families with hereditary SSNS. After identifying a potential disease-causing variant, we examined the effects of loss of gene function in cultured human podocytes through the creation of lentiviral shRNA knockdown and CRISPR-Cas9 knockout cell lines as well as morpholino-based gene knockdown in zebrafish.
Results: We identified a rare homozygous variant, CLVS1 H310Y, that segregates with disease in a consanguineous family with two affected siblings and a cousin. CLVS1 encodes clavinulin, a component of clathrin mediated endocytosis. This variant was not present in a homozygous state in >200,000 chromosomes and is predicted to be pathogenic by in silico analyses. Morpholino knockdown of the orthologous CLVS1 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 CLVS1 mRNA but not the H310Y variant. Knockdown of CLVS1 in cultured human podocytes as well as overexpression of the H310Y variant in HEK 293 cells decreased endocytosis of the fluorescently labeled dextrans and increased susceptibility to apoptosis. The rare variants podocyte phenotypes could be rescued in the presence of glucocorticoid, mimicking the steroid responsive phenotype in patients bearing the CLVS1 H310Y variant.

Conclusions: We identified a mutation in CLVS1 as a new cause of hereditary SSNS. Our data demonstrates the requirement of functional mRNA but not the gene in silico

CLVS1 with disease in a consanguineous family with two affected siblings and a cousin.

SA-OR46
Cross-Talk Between Neutrophils and Macrophages Dictates the Outcome of Acute Pyelonephritis
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Background: Pediatric urinary tract infections (UTI) 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 Tgfb2 is coupled to the distal tubule differentiation. After cell specification, terminal differentiation was strongly linked to metabolic nuclear receptors such as Estra and Ppara for proximal tubules and Estb and Pparg1a in loop of Henle. We also implemented snATAC-seq data to leverage our understanding of human kidney disease development. By overlapping the chromatin landscape with kidney disease GWAS signals, we inferred key cell types for GWAS loci in the proximity of Shroom3 and Dab2 genes. Interestingly, we observed that some kidney disease-associated loci, such as those in the vicinity of Uncx, are only accessible in the developing kidney cells, indicating a developmental stage regulatory role of genetic variants.

Conclusions: Here we present a comprehensive open chromatin and gene expression landscape for developing mouse kidney and illustrate the use of single-cell multi-omics data to study gene regulatory dynamics and its relationship to complex human disease genetics.

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. We implemented in vitro monitoring and expansion methods to study gene regulatory dynamics and its relationship to complex human disease genetics.

Methods: 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. 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 Tgfb2 is coupled to the distal tubule differentiation. After cell specification, terminal differentiation was strongly linked to metabolic nuclear receptors such as Estra and Ppara for proximal tubules and Estb and Pparg1a in loop of Henle. We also implemented in vitro monitoring and expansion methods to leverage our understanding of human kidney disease development. By overlapping the chromatin landscape with kidney disease GWAS signals, we inferred key cell types for GWAS loci in the proximity of Shroom3 and Dab2 genes. Interestingly, we observed that some kidney disease-associated loci, such as those in the vicinity of Uncx, are only accessible in the developing kidney cells, indicating a developmental stage regulatory role of genetic variants.

Conclusions: Here we present a comprehensive open chromatin and gene expression landscape for developing mouse kidney and illustrate the use of single-cell multi-omics data to study gene regulatory dynamics and its relationship to complex human disease genetics.

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

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
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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. 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 Tgfb2 is coupled to the distal tubule differentiation. After cell specification, terminal differentiation was strongly linked to metabolic nuclear receptors such as Estra and Ppara for proximal tubules and Estb and Pparg1a in loop of Henle. We also implemented snATAC-seq data to leverage our understanding of human kidney disease development. By overlapping the chromatin landscape with kidney disease GWAS signals, we inferred key cell types for GWAS loci in the proximity of Shroom3 and Dab2 genes. Interestingly, we observed that some kidney disease-associated loci, such as those in the vicinity of Uncx, are only accessible in the developing kidney cells, indicating a developmental stage regulatory role of genetic variants.

Conclusions: Here we present a comprehensive open chromatin and gene expression landscape for developing mouse kidney and illustrate the use of single-cell multi-omics data to study gene regulatory dynamics and its relationship to complex human disease genetics.

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

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SA-OR05

Rhesus Macaque Serves as a Model for Human Lateral Branching Nephrogenesis
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Background: Premature infants are at risk for chronic kidney disease later in life due to low nephron endowment. Lateral branching nephrogenesis (LBN), not occurring in the mouse, is a poorly understood but critical form of human nephrogenesis. Here, we analyze third trimester LBN in the rhesus macaque at the molecular and morphological level.

Methods: The morphology of third trimester rhesus kidneys was assessed by immunostaining after tissue clearing. 3D renderings were created using Bitplane Imaris. Single-cell RNA sequencing (scRNA-seq) and single-nucleus RNA sequencing (snRNA-seq) were performed on 4 kidneys from 4 rhesus using cold protease digestion and 10xGenomics platform. Unsupervised analyses using ICG2 were used to identify distinct cell populations and GO-Elite was used to compare rhesus with human and mouse datasets.

Results: The gestational period of the rhesus lasts 165 days. We determined that cessation of rhesus nephrogenesis occurs between 136- and 138-days gestational age (GA). LBN was observed along the ureteric stalks at 126-138 days GA. We noted rosette-like patterns of ureteric tips and nephron progenitor cells (NPC) in both rhesus and human third trimester archival samples. scRNA-seq was performed on 4 cortical enriched rhesus samples 129-131 days GA revealing 3 transcriptionally distinct cell clusters. C25 was predicted to contain the naïve NPC and included CITED1, MEOX1, and EYA1. snRNA-seq yielded 5,972 nuclei, corresponding to 29 ICGS2 clusters. We found a single cluster (c26), with a near identical GO-Elite enrichment profile to that of the naïve NPC scRNA-seq cluster (c25). snRNA-seq c26 contained many unique markers not found in the naïve NPC markers, BMPR, BFGF, BMPR1A, BMP7, BMPR2, IGF1, PDGFR, and SMAD5. The late-gestation rhesus NPC markers more closely aligned to late-gestation murine NPCs, whereas the 2nd trimester human NPCs more closely aligned to mid-gestation murine NPCs. Novel surface markers predicted in the rhesus include CACNA1E, KIRREL3, and KIRREL2.

Conclusions: The rhesus is the first animal model to demonstrate LBN, suggesting that LBN is conserved in old world primates. We identified novel genes upregulated during LBN and surface markers that could be used for cell-sorting.

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SU-OR02

Cyclin G1/CDK5-Mediated Dedifferentiation of Proximal Tubular Cells Drives AKI-to-CKD Transition
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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 redifferentiation 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 if CG1 regulates dedifferentiation of PTCs through interaction with kinase CDK5.

Methods: 1) Ablation of experimental AKI 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 (UO) was performed and kidneys were harvested on day 9. 3) To determine the interaction of CG1, immunoprecipitation (IP) was performed in CG1-overexpressing LLC-PK1 cells treated with AA. 4) To examine the pathological role of CDK5, 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 CDK5 with SOX9 was confirmed by the observation that CG1 binds to SOX9 knockout mice (CG1KO). Genetic or pharmacological inhibition of CDK5 preserved E-cadherin in AA-induced cellular injury with reduction of profibrotic markers; however, it provided no additive 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 diseases 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 with a membrane dye and Day 25 kidney organoids revealed that USCs were 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 formed iPSCs expressed the kidney cell type markers Ecad (dual tubule), GATA3 (collecting duct), LTL (proximal tubule) and NEPHRIN (Glomeruli) at Day 21. The organoids were then treated with 5 x 10^5 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
Chunyu Zhang, Jie Wu, Lingling Wu, Xiangmei Chen, Chinese PLA General Hospital, Beijing, China; Nanjian 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 vivo 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. This study developed an RGD-scaffold to increase the 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 providing a new feasible treatment for potentiated AKI.

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**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 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 biartigenic doxycycline-inducible system (VeptRNAiR, RosA26RiTAiR, tetO-Cre)1 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 KO mice (p<0.0055). Global gene expression analysis indicated minimal kidney transcriptome change at base line whereas in the setting of IRI, VEPTP KO mice showed a less activated renal endothelium and downregulation of acute stress response genes signature. A corresponding decrease in pro-fibrotic genes was observed in VE-PTP KO mice on day 7. In the pharmacological study, systemic administration of C4BP-ANG1 activated Tie2 and its downstream AKT/eNOS/NO pathways in mouse kidneys 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**

**Pannexin 1 Channel Regulates Mitochondrial Function and Cell Survival During AKI**

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**Background:** Pannexin 1 (Pannx1) 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 Panx1 in mice prior to injury is protective against renal ischemia-reperfusion injury (IRI). How Panx1 contributes to acute kidney injury (AKI) pathology is unknown. We hypothesized that Panx1 induces cell death by mediating both intracellular and extracellular events.

**Methods:** We subjected a novel human Panx1 overexpressing mouse (hPanx1-Tg) to IRI or cisplatin-mediated AKI and assessed plasma creatinine and renal expression of neutrophil gelatin associated lipocalin (Ngal). For in vitro studies, Panx1 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 oxygen consumption rate, mitochondrial membrane potential and ROS production. mRNA expression was assessed using real-time PCR.

**Results:** hPanx1-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 Hif-1 after cisplatin exposure. Assessment of mitochondria showed that OX cells had reduced mitochondrial DNA, Ppargc 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.

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Underline represents presenting author.
SU-OR08
Enhancer and Super-Enhancer Dynamics in Repair After Ischemic AKI
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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: Using RNA-seq and ChIP-seq (H3K2ac, H3K4m3, BRD4, BRD2, BRD3, Pol II, HNF4A, GR, STAT3 and STAT5) were performed on samples from repairing kidney cortex 2 days after ischemia/reperfusion injury (IRI) to identify activated genes, transcription factor binding, enhancer and super-enhancers associated with kidney repair. Further, we investigated the role of enhancers in kidney repair through pharmacological BET inhibition using the small molecule JQ1 in AKI models in vivo.

Results: Response to injury leads to genome-wide alteration in enhancer repertoire in vivo. We identified 16,781 enhancer and 380 super-enhancer sites (H3K2ac and BRD4 positive) with a high density of binding in SHAM and IRI samples; 6,516 enhancer, 164 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 factor-binding sites show specific binding at corresponding enhancer sites with high 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 attention to potential caveats for use of BET inhibitors that are currently being tested in clinical trials. Understanding of enhancer dynamics after acute kidney injury in vivo has the potential to lead to indentation of new targets for therapeutic intervention.

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

SU-OR09
Developmental Reprogramming of Kidney Resident Macrophages During Human AKI and Its Implications to CKD
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Background: Kidney tissue-resident macrophages (KRM) promote naturally occurring or AKI-induced cystic renal disease in mice. AKI also reprograms KRM into a disease state that promotes fibrosis. Understanding of enhancer dynamics after kidney injury in vivo has the potential to lead to identification of new targets for therapeutic intervention.

Methods: We performed RNA-seq and ChIP-seq (H3K2ac and H3K4m3) data from the Mouse Cell Atlas. We identified 16,781 enhancer and 380 super-enhancer sites (H3K2ac and BRD4 positive) with a high density of binding in SHAM and IRI samples; 6,516 enhancer, 164 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 factor-binding sites show specific binding at corresponding enhancer sites with high 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 attention to potential caveats for use of BET inhibitors that are currently being tested in clinical trials. Understanding of enhancer dynamics after acute kidney injury in vivo has the potential to lead to identification of new targets for therapeutic intervention.

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

SU-OR10
Endothelial-Derived mir-17–92 Promotes Angiogenesis to Protect Against Renal Ischemia-Reperfusion Injury
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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-17–92deo-/-) 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 mirRNA mimics during renal IRI to test its therapeutic efficacies.

Results: We demonstrate that mir-17–92, -18a, -20a, and -19b are up-regulated in renal endothelial cells after renal IRI in mice. mir-17–92deo-/- exacerbates ischemic AKI in male and female mice. Specifically, mir-17–92deo-/- promotes renal tubular injury, increases renal blood flow, promotes microvascular rarefaction, increases renal oxidative stress and promotes macrophage infiltration to injured kidneys. The potent anti-angiogenic factor, thrombospondin 1 (TSP1), is highly expressed in renal endothelium in mir-17–92deo-/- after renal IRI and is a target of mir-18a and mir-19b. Beyond defining a critical role for mir-17–92 in the angiogenic response after ischemic AKI, we show that co-treatment with a combination of mir-18a and mir-19b mimics is sufficient to mitigate ischemic AKI.

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
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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 present in various kidney biopsies and in 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. The first model, a CKD-like injury induced by uninephrectomy/angiotensin II administration. In each of these models, we inhibited CDH11 genetically using transgenic mice and pharmacologically with the administration of a functional blocking antibody to CDH11.

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 cytotoxic production (TGF-β 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 signaling pathway by which CDH11 mitigates PT injury is still under investigation, preliminary data shows that inhibition of CDH11 increases Wnt/β-catenin activity in the kidneys of injured mice. Wnt/β-catenin signaling promotes cell survival, which in this context could result in reduced tubular atrophy, cytotoxic 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 reduces 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)

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
SU-OR12
METTL10: A Kidney Disease Risk Gene by Altering Protein Methylation
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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 cell 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 mice of Mettl10 KO mice. The reduction in eEF1A activity lead to lower protein translation and tubule cell proliferation. Mettl10 KO mice were more susceptible to kidney disease, it showed higher 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
Poonam Dhillon,1 Jhwan Park,1 Carmen Hurtado del Pozo,2 Lingzhi Li,2 Shizheng Li,1 Royesh Shrestha,1 Nuria Montserrat,1 Katalin Susztak,1 Susztak Lab 1University of Pennsylvania, Philadelphia, PA; 2Barcelona Institute of Science and Technology, Barcelona, Spain.

Background: Kidney proximal tubule (PT) cells have high mitochondrial density to perform their highly energizing demand 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 ESRR.

Results: Single cell metabolomic 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 adult, and developing mouse PT cells and organoids. Single cell epigenetics data identified the critical role of nuclear receptors; HNF4A, HNF1B, PPARa, and ESRR 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. Genetic and pharmacological deletion of these transcription factors lead to marked changes in differentiation state of cultured PT cells. Analysis of healthy and disease human kidney samples and mice with ESRR deletion showed a defect in FAO, OXPHOS and PT differentiation and was more susceptible for injury, defining a novel role for ESRR in PT cells and CKD.

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

Funding: NIDDK Support

SU-OR14
COX17-Mediated Abnormal Mitochondrial Copper Metabolism Promotes Renal Fibrosis
Saiya Zhu, Chen Yu. Department of Nephrology, Tongji Hospital, Tongji University, Shanghai, China.

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 mechanism of the accumulation of copper in mitochondria 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) AKI and diabetic nephropathy (DN) kidneys. The regulation role of COX17 was investigated in renal tubule epithelium cell line (NRK-52E) and rat fibroblasts(NRK-49F) by treating with copper or copper chelator tetrathiomolybdate (copper-chelating agent). ICP-MS, mitoXO, electron microscopy, realtime-PCR 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 dysfunction of mitochondrial species analysis were significantly upregulated. More importantly, mitochondrial copper content and coll, fibronectin expression were reduced and mitochondrial function was improved after transfecting with COX17 shRNA. Meanwhile, treatment with copper chelator tetrathiomolybdate 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
Jing Li, Chuan-Ming Hao. Division of Nephrology, Huashan Hospital Fudan University, Shanghai, China.

Background: Inadequate repairing process to injury has been reported to play a critical role in renal fibrosis. Mounting evidence suggests that prostaglandins are important in serving as a “buffer” in response to physiological or pathophysiologic insults to tissues including the kidney. Importantly, under certain conditions such as aging and hypertension, prostacyclin (PGI1), an active production of COX/PGI2, 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 30 minutes on D0. After 4 weeks, the right kidneys were removed. The mice were treated with beraprost sodium (300 μg/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. Losing one allele of PGIS significantly attenuated the increase of PGIS expression after UUO and aggravated UUO-induced renal fibrosis. IR model was performed on wild-type mice. Treatment with beraprost sodium (BPS), a analog of PGI2, inhibited the expression of fibronectin, collagen I and α-SMA in the kidney and ameliorated extracellular matrix deposition in the kidney tissue study. Furthermore, the level of phosphorylated FAK 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 fibroconnectin, collagen I and α-SMA in rat renal fibroblasts (NRK-49F), which were induced by TGF-β.

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

SU-OR16
Proteomic Risk Assessment of CKD Progression in the Chronic Renal Insufficiency Cohort
Ruth F. Dubin,1 Rajat Deo,2 Zihe Zheng,2 Haochang Shou,2 Yue Ren,2 Hongzhe Li,3 Mark Segal,1 Harold I. Feldman,2 Peter Ganz,2 1University of California San Francisco, San Francisco, CA; 2University of Pennsylvania, Philadelphia, PA.

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 patient sera from the regular 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, estimated glomerular filtration rate (eGFR) 42 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 Eq.
Biomarkers that predict the risk of CKD progression. The proteomic risk model has a c-statistic of 0.860 (95% CI: 0.834, 0.885) in the validation set, indicating a strong predictive value. Additionally, we identified 58 protein biomarkers that are unique to progression of diabetic vs. non-diabetic CKD.

Conclusions: Through large-scale proteomics, we discovered numerous novel biomarkers that predict the risk of CKD progression. The proteomic risk model has excellent discrimination, equal to the refit clinical model. Ongoing analyses of the biological functions of the newly discovered biomarkers may identify new therapeutic targets to slow CKD progression.

Funding: NIDDK Support

SU-OR17

Molecular Mechanisms Underlying Sex-Specific Association of Circulating Transforming Growth Factor β1 with the Risk of Accelerated Kidney Function Decline

Jon V. Norvik,1,2 Inger Therese T. Enoksen,2 Christopher L. O’Connor,2 Marit D. Solbu,1 Vivi Nørby,1 Matthias Kretzler,2 Wenjun Ju,1 Bjorn O. Eriksen,1 Marit D. Mølën,1,2,3 Universitetstryketskuelen Nord-Norge, Tromsø, Norway; 2UiT Norges arktiske universitet Det helsevitenskapelige fakultet, Tromsø, Norway; 3Universitetet i Bergen, Bergen, Norway.

Background: Study of sex differences in kidney function decline and risk of chronic kidney disease (CKD) is a stated research goal. We recently found serum transforming growth factor β1 (TGF-β1), a key mediator in kidney fibrosis development, to be associated with risk of accelerated age-related loss of glomerular filtration rate (GFR) in women, but not men, in the general population. We therefore investigated the effect of sex on intrarenal TGF-β1 pathway and structural damage in kidney biopsies from a cohort of patients with early kidney impairment.

Methods: Kidney tissue samples from 22 female and 33 male patients undergoing nephrectomy included in the PRECISE study (age 31 to 83 years) were used for transcriptomic analysis of micro-dissected glomeruli (Affymetrix Human Gene 2.1 ST Array). Interaction of the expression of genes in the TGF-β1 signaling pathway with sex was evaluated between expression level and global glomerulosclerosis (GGS), a structural parameter of kidney disease. Genes exhibiting significant interaction with sex were used to generate a sex-dependent TGF-β1 pathway activity score.

Results: Out of the 136 genes downstream of TGF-β1, expression of 20 genes exhibited significant interaction with sex for GGS. BMP6, ID1, MYC, and TNF were among the genes that showed the most significant interaction. An increased activity score for sex-specific TGF-β1 downstream effectors was associated with higher degree of GGS in women (p < 0.001), but with less GGS in men (p = 0.01, p for interaction sex < 0.001, Figure 1).

Conclusions: Higher levels of the sex-specific TGF-β1 pathway activity was associated with higher GGS in women, but with less GGS in men. These results, along with our findings of an association between higher serum TGF-β1 and accelerated GFR decline in women only, point to a sex-specific TGF-β1 driven mechanism of kidney fibrosis that may shed light on sex differences in age-related GFR loss and CKD.

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

SU-OR18

Defining the Correlation Between Kidney Function and Histopathological Changes

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Background: Estimated glomerular filtration rate (eGFR) is an imperfect measure of kidney function and does not correlate well with prognosis. Histopathologic analysis of renal biopsy is considered the gold standard to establish disease etiology and prognosis. Kidney biopsy, however, is rarely performed in patients with diabetes due to its associated risks. Here we examined whether we could predict the degree of histological damage and kidney function decline based on clinical and demographic information.

Methods: Descriptive based histopathological analysis was performed in 759 human kidney tissue samples obtained from unaffected portion of tumor nephrectomies. Samples were limited to healthy, hypertensive and diabetic kidney disease. Changes in the glomeruli, arteriolar intima, and the vasculature were scored in an unbiased manner. Regression analyses were performed to assess the association between histopathology based on eGFR quantiles. Decline in renal function over time (eGFR slope in ml/min/1.73m2 per year) was assessed in subjects with at least 3 months of follow up. Validation analysis was performed on 467 clinically indicated kidney biopsies.

Results: Mean subject age was 61, eGFR was 66 ml/min/1.73m2, 70% had hypertension and 37% had diabetes. The association between eGFR and interstitial fibrosis was relatively weak (r2 = 0.3, p < 0.001). There was no association between fibrosis and GFR greater than 45 ml/min/1.73m2. Samples with eGFR below 45 ml/min/1.73m2 showed a reasonably strong association between eGFR and fibrosis (r2 = 0.51, p < 0.001) indicating a non-linear relationship. Hypertension and black race were independently associated with more severe histopathologic changes (p < 0.05). Similar non-linear trends and significant associations were observed in our validation cohort. There was an association between sex and structural histopathologic findings in kidney biopsies with which did not reach significance in the primary cohort but was significant in the validation cohort.

Conclusions: The eGFR is a poor predictor of fibrosis at values > 45 ml/min/1.73m2 but predicts renal structural changes well at lower eGFR. Hypertension and black race were independently associated with renal fibrosis, which may warrant more aggressive therapy in these cohorts. Predictions of kidney function decline are enhanced when eGFR and histopathology are used in combination.

Funding: NIDDK Support, Other NIH Support - ST32DK007006-45

SU-OR19

Low Birth Weight for Gestational Age and Risk of Different Groups of Kidney Disease 50 Years During the First 50 Years of Life

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Background: Previous studies have shown that Low Birth Weight (LBW) is associated with increased risk of end-stage renal disease. Few population based studies have investigated risk of Small for Gestational Age (SGA) on kidney disease. Our study investigates SGA and risk of chronic kidney disease (CKD), other kidney diagnoses as well as different stages of kidney failure.

Methods: The Norwegian Patient Registry (NPR) has registered ICD diagnostic codes for all admissions and outpatient visits to Norwegian hospitals since 2008. The Norwegian Medical Birth Registry (MBR) has registered birth weight, gestational age, and several other data on maternal and offspring health for all birth in Norway since 1967. Data from these registries were linked and risk of CKD and other groups of kidney disease were analyzed with logistic regression statistics. Based on birth weight, gestational age and gender, a z-score of birth weight for gestational age has been calculated. SGA defined as birth weight less than the 10th percentile for gestational age and gender with cut-off -1.30 for male and -1.28 for female. LBW (less than the 10th percentile) and preterm birth were independently associated with renal fibrosis, which may warrant more aggressive therapy in these cohorts. Analyses of kidney function decline are enhanced when eGFR and histopathology are used in combination.

Results: Of the 2,663,100 included subjects, 4495 had been diagnosed with CKD and 12,818 with acute kidney disease, glomerulonephritis, hereditary kidney disease or kidney disease due to kidney or urinary tract malformations. SGA was associated with odds ratio (OR) 1.14 (95% CI 1.03-1.23) for acute kidney disease, 1.18 (1.070-1.30) for glomerulonephritis, 1.31 (1.12-1.52) for hereditary kidney disease and 1.13 (1.03-1.23) for kidney disease due to kidney or urinary tract malformations.

Conclusions: SGA is a strong risk maker for diagnosis of all stages of CKD during the first 50 years. The risks seem to increase also for other groups of kidney disease.

SU-OR20

Large-Scale Kidney Volumetry from MRI: Initial Results and Relations to Sex, Age, and Body Size in UK Biobank

Joel Kullberg,1 Taro Langner,1 Salvador Daniel Rivas-Carrillo,2 Iris Friedli,2 Tove Hall,1 Robin Strand,1 Håkan Ahlström,1 Lars Johansson,2 Uppsala University, Department of Medical Biochemistry and Microbiology, Uppsala, Sweden; 1Uppsala University, Department of Medical Sciences, Molecular Epidemiology, Uppsala, Sweden; 2Uppsala University, Department of Information Technology, Uppsala, Sweden.

Background: Kidney volume has been associated with age, kidney function, diabetes, and other cardiovascular risk factors. Body size, body surface area (BSA) and lean body mass are important parameters in UK Biobank (UKB) is a large-scale study aiming to examine 100,000 subjects aged 44 to 82 years using MRI. Resulting images allow measurements of kidney volume. Currently 40,264 scans have been released.
Methods: A deep learning-based method for direct kidney parenchymal volume (KPV) segmentations 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 biomechanical analysis (BIA-FBM) and lean tissue volume from MRI (MRI-LT) were studied using linear regression. Rate changes were compared between and above group means 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: Resulting KPVs from 37,468 subjects (47.6% males) and age changes are shown in Fig. A and Table I. Correlations between total KPV and BSA and MRI-LT over age are shown in Fig. B. The associated overall correlations were (males / females): Body weight: 0.568/0.460, BSA: 0.574/0.496, BIA-FBM: 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 I

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Total KPV</th>
<th>BIA-FBM</th>
<th>MRI-LT</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-20 yrs</td>
<td>20.7</td>
<td>20.5</td>
<td>20.1</td>
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<td>21-30 yrs</td>
<td>18.9</td>
<td>18.5</td>
<td>18.2</td>
</tr>
<tr>
<td>31-40 yrs</td>
<td>17.0</td>
<td>16.5</td>
<td>16.2</td>
</tr>
<tr>
<td>41-50 yrs</td>
<td>15.2</td>
<td>14.8</td>
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</tr>
<tr>
<td>51-60 yrs</td>
<td>13.4</td>
<td>13.1</td>
<td>12.8</td>
</tr>
</tbody>
</table>

A) Scatter plot of total KPV and age for males and females including regression lines for mean age.

Age changes are given as two regression slopes, from below and above the specific mean 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, the cure was defined as the absence of a peritonitis relapse or recurrence, PD catheter removal, transition to hemodialysis or death during the 50 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. cefazidime=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 (AHRQ)

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 Young Jee Cho,1,2 Carmel Hawley,1,2 Elaine Pascoe,3 Andrea K. Vicielli,1,2 Scott B. Campbell,1,2 Carolyn L. Van Eps,1,2 Nicole Isbel,1,2 Bruce A. Cooper,4 David Harris,4,5 Carol A. Pollock,4,6 Muh Geot Wong,6,7 David W. Johnson.1,2 Centre Hospitalier de L’Universite de Montreal, Montreal, QC, Canada; 3Princess Alexandra Hospital, Woolloongabba, QLD, Australia; 4The University of Queensland Faculty of Medicine, Herston, QLD, Australia; 5Westmead Institute for Medical Research, Westmead, NSW, Australia; 6The University of Sydney School of Medicine, Sydney, NSW, Australia; 7Royal North Shore Hospital, St Leonards, NSW, Australia; 8George Institute for Global Health, Camperdown, NSW, Australia.

Background: Residual kidney function (RKF) is associated with improved survival and quality of life in dialysis patients. Previous studies have suggested that commencement of peritoneal dialysis (PD) may slow RKF decline compared to the pre-dialysis period. We sought to evaluate the association between PD initiation and RKF 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 RKF 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 RKF decline was slower after PD commencement (-2.69±1.8 L/min/1.73m²/yr) compared to before PD commencement (-4.09±0.33 L/min/1.73m²/yr); change in slope = -1.19 L/min/1.73m²/yr, 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=-1.34—0.01, p=0.04).

No differences were observed between the early- and late-start groups with respect to RKF decline, urine volume decline or time to anuria.

Conclusions: Commencement of PD was associated with a slower decline of RKF 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 vs. 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 solutions (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 (646±256, 739±312, 863±380 ml for 11, 14, 20 g/h) vs. PET (162±242 ml, p<0.001). 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 usage was made 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

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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 is associated with different incidence rates of anemia and clinical outcomes. Therefore, evaluating the safety and efficacy of roxadustat in patients with dialysis-dependent (DD) CKD on peritoneal dialysis (PD) is of clinical importance.

Methods: Pooled data from three pivotal, phase 3, randomized, open-label, epoetin alfalpha-controlled studies of roxadustat for the treatment of anemia in patients with DD-CKD were assessed in the subgroup of patients on PD. Endpoints evaluated were: mean change from baseline (CFB) in hemoglobin (Hb) averaged over Weeks 28–52 regardless of rescue therapy, Hb CFB averaged over Weeks 28–36 censored for rescue therapy, and risk for blood/RBC transfusion during the treatment period. Safety and tolerability were assessed by reported treatment-emergent adverse events (TEAEs).

Results: In the DD-CKD study population, 10% (372/3887) of patients were on PD (roxadustat 1800, epoetin alfa–122). Baseline characteristics were generally similar between treatment groups. Mean (SD) Hb levels (g/dL) at baseline were 9.5±1.2 (223) in the roxadustat alfa group. Patients achieved a larger mean (SD) CFB to Weeks 28–52 in Hb (g/dL) with roxadustat vs. epoetin alfa (1.41 ± 1.45 vs. 1.08 ± 1.53), corresponding to a least-squares mean (LSM) treatment difference of 0.37 (95% CI: 0.11, 0.63) (p=0.0048). Patients achieved a larger mean (SD) CFB to Weeks 28–52 in Hb (g/dL) with roxadustat vs. epoetin alfa (1.53 ± 1.54 vs. 1.01 ± 1.63), corresponding to a LSM treatment difference of 0.46 (95% CI: 0.17, 0.74) (p=0.0018). Risk for blood/RBC transfusion was significantly reduced with roxadustat vs. epoetin alfa (HR, 0.50 [95% CI: 0.26, 0.98]; p=0.0422). TEAE rates were comparable between treatment groups.

Conclusions: Roxadustat was efficacious vs. epoetin alfa for increasing/maintaining Hb levels and reducing the risk for blood/RBC transfusion in patients with DD-CKD on PD. 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.
SU-OR26
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: OR = 0.13 vs. 0.10%, OR: 1.44, 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 ($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.

Table 1

<table>
<thead>
<tr>
<th>Cardiovascular Thromboembolic Outcomes</th>
<th>Incidence (%)</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical Complications</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Cerebrovascular accident</td>
<td>0.13</td>
<td>1.44</td>
<td>(1.31-1.57)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Deep Vein Thromboses</td>
<td>0.10</td>
<td>1.75</td>
<td>(1.62-1.88)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Medical Complications + 90-Day Readmissions Rate</td>
<td>0.10</td>
<td>1.44</td>
<td>(1.31-1.57)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Outcome comparisons by dialysis modality following TKA.

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±13.9 years; 99 (58.9%) were men. Median PD effluent (PDE) sediment mtDNA was 255.4 ng/ml (IQR: 157.5-451.3); median PDE sediment mtDNA was 206.16 ng/ml (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 episodes (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) (Fig. 1). AA, tortuosity, and NA were not significantly different between the two groups. AA was approximately 40° in both groups.

Conclusions: The AA of our AVF rat model is similar to the AA in human radiopaque AVFs in the literature. Sildenafil leads to significantly higher flow rate and larger lumen in both vein and artery than controls. Vorticity, WSS, and OSI are 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 (Wavelinq). 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. Experience 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**

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**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-period to 0.36/100 CVC days after AmBC implementation. Hospitalization rates were lower during the post-period versus the pre-period overall and within each calendar month; 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) could not be quantified.

**SU-OR32**

**Complement C5a Receptor Inhibitor Avacopan Improves Renal Function in ANCA Vasculitis**

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**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 function 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 arms. 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, 57.7%, 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 (week 4=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 compared to week 52: avacopan eGFR +13.7 vs. prednisone +8.2 (P=0.01).

**Conclusions:** Treatment with avacopan for ANCA vasculitis compared with standard glucocorticoid therapy (both combined with either CYP or RTX) is as 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**

Nicolas Induction Therapy in ANCA Vasculitides

Richard Karras.1,2 Thomas A. Kelleher,2 Pierre A. Merkel.3 1Division of Rheumatology, University of Washington, Seattle, WA; 2Addenbrooke’s Hospital, Cambridge, United Kingdom; 3University of Cambridge, Cambridge, United Kingdom.

**Background:** Persistent proteinuria and hematuria (P&P) can occur in ANCA vasculitis patients treated with induction therapy. The long-term significance of P&P is uncertain.

**Methods:** This multicenter, retrospective observational study included 97 patients with ANCA vasculitis who achieved remission induction at 26 weeks, and were followed up to week 104. Patients were followed if they had proteinuria at week 26 (P+26) or week 52 (P+52). Proteinuria and hematuria were recorded at each follow-up visit.

**Results:** At week 26, 34 patients showed P+26, of whom 15 had P+26 and 19 had P+26 + hematuria. At week 52, 53 patients showed P+52, of whom 21 had P+52 and 32 had P+52 + hematuria. At week 104, 13 patients showed P+104, of whom 6 had P+104 and 7 had P+104 + hematuria.

**Conclusions:** P&P at week 26, 52, and 104 were associated with worse renal outcomes, including doubling of serum creatinine, decrease of eGFR, and death. In addition, patients with P&P at week 26 were less likely to achieve sustained remission.

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

Underline represents presenting author.
Methods: This is a post hoc study including participants of 5 European randomized clinical trials: AAV (MAINRITSAN, MAINRITSAN2, RUTUXAS, MYCCY-IMPROVE). We examined the association of PCR (urine protein-creatinine ratio) and hematuria on spot urine samples collected at the end of induction therapy with the occurrence of (i) a combined endpoint of death and/or end stage renal disease (ESRD), and (ii) renal relapse during follow-up.

Results: Among 571 patients (59% men, median age 60 years), 60% had PRR-ANCA, 35% had MPO-ANCA, 77% had renal involvement. After induction therapy, 157/526 (29.8%) had persistent hematuria, 165/481 (34.3%) had PCR ≥ 0.5 g/mmol, 136/444 (30.6%) relapsed, and at median follow-up of 12 months (IQR: 18-42), an adjustment for age, gender, antigenic serotype, initial eGFR, persistent hematuria, a PCR ≥ 0.5 g/mmol after induction was associated with risk of death and/or ESRD (adjusted Hazard Ratio (HR) = 4.08, 95% confidence interval (CI) 1.48-11.25, p = 0.006). Persistent hematuria was associated with risk of renal relapse (adjusted subdistribution HR = 2.18, CI 95% 1.14-4.18, p = 0.019) but not with any relapse (adjusted aHR = 1.10, CI 0.78-1.56, p = 0.59) nor with death and/or ESRD (adjusted HR = 1.88, CI 95% 0.83-4.29, p = 0.132).

Conclusions: In this large cohort of AAV patients, persistent proteinuria after induction therapy was an independent predictor of death and/or ESRD, whereas persistent hematuria after induction therapy was an independent predictor of renal relapse. These parameters must be taken into account to assess long-term renal prognosis of AAV patients.

SU-OR34

Belimumab (BEL) Improves Renal Outcomes in Active Lupus Nephritis (LN): A Phase 3 Randomized, Placebo (PBO)-Controlled Trial

Brad H. Rovin,1 Frederic Houssiau,2 Richard Furie,3 Ana Malvar,6 Yoe Kie Onno Teng,7 Chi chiu Mok,9 Gabriel Contreras,4 Xueqing Yu,9 Sebastian Dolff,1 Beulah Ji,3 David A. Roth,3 Christi Kleoudis,10 Susan Makowik,9 Anuradha Madan,6 Jennifer Gilbride,9 Yulia Green,9 Division of Nephrology, The Ohio State University, Columbus, OH, 1Pôle de Pathologies Rhumatismales Inflammatoires et Systémiques, Institut de Recherche Expérimentale et Clinique, Université Catholique de Louvain and Service de Rhumatologie, Cliniques Universitaires Saint-Luc, Brussels, Belgium; 2Division of Nephrology, Northwell Health, Great Neck, NY, 3Organización Medica de Investigacion, Buenos Aires, Argentina; 4Expert Center for Lupus-, Vasculitis- and Complement-mediated Systemic Diseases, Department of Internal Medicine – section Nephrology, Leiden University Medical Center, Leiden, Netherlands; 5Division of Nephrology, Division of Hypertension, Department of Medicine, University of Miami Miller School of Medicine, Miami, FL; 6Department of Nephrology, Guangdong Provincial People’s Hospital, Guangzhou, China; 7GlaxoSmithKline, Uxbridge, United Kingdom; 8GlaxoSmithKline, Collegeville, PA; 9Parexel, Durham, NC; 10GlaxoSmithKline, Stevenage, United Kingdom; 11Tuen Mun Hospital Department of Medicine and Geriatrics, Hong Kong, Hong Kong; 12Department of Infectious Diseases, University Hospital Essen, University of Duisburg-Essen, Essen, Germany.

Background: BEL is approved for patients (pts) with systemic lupus erythematosus (SLE) in Europe and the United States (US) for active LN. However, data on its efficacy in active LN are limited.

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 Efficacy Renal Response (PERR = urine protein/creatinine ratio ≤0.5; eGFR no more than 10% below pre-flare value ≤0.5 g/mmol/1.73m²; 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 during follow-up.

Results: 224 pts were randomized to each arm. At Week 104, there were significantly more PERR and CRR responders on BEL vs PBO: (45.0% vs 32.3%, OR [95% CI] 1.6 [1.1-2.3], p = 0.012; 30.6% vs 19.7%, OR [95% CI] 1.7 [1.1-2.7], p = 0.012), respectively. Risk of renal relapse or renal death was lower in BEL pts relative to PBO (HR [95% CI] 0.5 [0.3, 0.8]; p = 0.01). Week 104 PERR response rates in pts on CyC/AZA were significantly higher (27.1% vs 16.3%, OR [95% CI] 1.9 [1.3-2.9], p = 0.002) than for pts on MMF (16.7% vs 10.5%, OR [95% CI] 1.6 [1.1-2.3], p = 0.003). Significant improvements in renal endpoints were also observed with BEL compared with PBO (eGFR ≥0.05 g/mmol after induction was significantly improved in patients treated with BEL (p < 0.001). These results suggest that BEL may improve renal outcomes in patients with active LN.

Conclusions: BEL significantly improved renal responses with no unexpected safety signals. Funding: Commercial Support - EMD Serono Research & Development Institute, Inc. (a business of Merck KGaA, Darmstadt, Germany), Billerica, MA; 6Center University Medical Center, New York, NY.

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 polymeric IgA1 (Gd-IgA1) that often deposit in the kidneys (causing inflammation and scarring) and trigger formation of IgA/G autoantibodies. Atacicept, a human TACI-Ig fusion protein, inhibits B cell-stimulating factors BLyS and APRIL and is associated with reduced serum IgA/G, mature B cells and plasma cells. This Phase II study (NCT02808429) examines atacicept safety and efficacy in reducing Gd-IgA1 and renal activity in IgAN.

Methods: Patients with active IgAN (eGFR ≥ 30 ml/min/1.73m²) and ≥ 0.75 mg/mg on 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; and Gd-IgA1.

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 (placebo vs with placebo (Fig 1B); eGFR remained stable. TEAEs were reported by 81% of patients (mild/moderate, none severe), with no serious related events, severe hypogammaglobulinemia, or fatal outcomes.

Conclusions: These results provide proof of concept for the potential treatment of patients with IgAN and persistent proteinuria with atacicept. Funding: Commercial Support - GSK.

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 individually. However, no research has evaluated the prognosis of IgAN patients using the 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 new grading classification system (O-grade) that utilized the total score of each MEST-C score (O-grade I = 0-1, II = 2-4, and III = 5-7 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 vs. O-grade I were 1.7 (1.2-2.4) and 2.5 (1.9-3.4), respectively. The 20-year renal prognosis was analyzed, and the O-grade combined with the Japanese clinical classification (C-grade) was also evaluated.

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.
mean blood pressure and renal function, proteinuria, and O-grade (HR, 1.39; 95% CI, 1.05-1.83) were independent factors predicting the renal prognosis. The O-grade in the nine groups classified by the O-grade combined with the C-grade showed HR of 33.7 (P<0.001) in the severest group with reference to the mildest group.

Conclusions: The O-grade classified by the total score of the Oxford classification was associated with renal CR, and renal prognosis could be accurate in predicting the total activity and chronicity of IgAN and prediction of the renal prognosis of this disease.

SU-OR37
Development of a Deep Learning Model to Predict ESKD in Patients with Immunoglobulin A Nephropathy (IgAN) at Kidney Biopsy Time

Background: Many prediction models to support clinical decision making have been developed for decades but they are based on traditional statistic 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 progression in IgAN 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 IgAN patients of the VALIGA and Greek cohort. Then, the tool was validated in an independent cohort of 167 IgAN patients from 6 nephrology units. After Cox’s regression analysis 7 variables (age, sex, blood pressure values, serum creatinine, daily proteinuria, MESTC 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 IgAN 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 IgAN patients at high risk of ESKD (iii) This tool may stratify patients in the context of a personalized therapy.

Funding: Government Support - Non-U.S.

SU-OR38
Complete Remission of Proteinuria in Patients with Focal Segmental Glomerulosclerosis Treated with Sparsradan, a Dual Endothelin and Angiotensin Receptor Antagonist, in the DUET Trial

Background: In FSGS, partial remission (FSGS partial remission endpoint [FPRE]: 40% reduction of the proteinuria/creatinine ratio at 12w [PC1] <1.5 g/m²) and complete remission (CR) of proteinuria are strong predictors of kidney survival. In the DUET trial, sparsradan (SPAR) resulted in greater reductions in proteinuria and higher rate of FPRE vs irbesartan (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/l) of proteinuria in DUET. Here we analyze patients who achieved CR (UP/C <0.3 g/l) of proteinuria in DUET.

Methods: DUET randomized patients age 8-75 years with biopsy-proven FSGS, UP/C <1 g/l, and eGFR>30 mL/min to SPAR or IRB for 8 weeks, followed by OLE with all patients receiving SPAR; the UP/C and other proteinuria measures were 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, 86 (79.6%) reached CR and other patients reached partial 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/l vs 2.65 g/l), and higher proportion of baseline immunosuppression (45% vs 35%), in particular with mycophenolate mofetil (18% vs 12%). AChromatic cohort 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 observations support the long-term nephroprotective potential of SPAR.

Funding: Commercial Support - Retrophin, 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 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. 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-OR42

Exploration of Racial Disparities in the Kidney Transplant Process Among Dialysis Patients

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Background: Kidney transplant is generally considered the best long-term treatment for dialysis patients. Before receiving a transplant, a patient must be referred to a transplant center, undergo extensive clinical evaluation, and then be placed on a wait list. Previous studies have observed that black patients are less likely to receive kidney transplants than white patients. However, it is unclear at which points in the transplant process inequity is imparted. In this analysis, we used a single source of data to compare the entire transplant process among black and white patients at a large dialysis organization.

Methods: Eligible patients were those who, between Jul 2015-Jun 2018, were 18-80 years old; were incident to dialysis and began care at the LDO within 30 days of first ever dialysis; and had not undergone a transplant evaluation or listing prior to dialysis start. Exposure was measured based on race as documented in LDO medical records (black or white). Patients were followed forward in time from study entry until 31 Mar 2019 or censoring or loss to follow-up. Transplant referrals, listings, and receipts were compared across exposure categories using time-to-event models adjusted for demographics, comorbidities, biochemistries, and socioeconomic factors.

Results: We identified 60,229 eligible incident patients (23,499 black; 36,730 white). Compared to whites, black patients were 23% more likely to be referred for transplant (hazard ratio [HR] and 95% confidence interval [CI] = 1.23 [1.20, 1.27]). Among referred patients, black patients were 19% less likely to be placed on a wait list than whites (HR [95% CI] = 0.81 [0.77, 0.86]). Among wait-listed patients, black patients were 52% less likely to receive a transplant than whites (HR [95% CI] = 0.48 [0.41, 0.56]). Overall, black patients were only 46% as likely to receive transplants as white patients (HR [95% CI] = 0.46 [0.39, 0.53]).

Conclusions: These results support prior findings that racial disparities exist within the kidney transplant process and indicate that these disparities occur downstream of the referral.

Funding: NIDDK Support, Private Foundation Support
SU-OR45

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

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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 transplantations 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 imported from 46 different OPOs and 29% from our local OPO. Mean donor age (±SE) was 45.7±6.9. Donor ethnicity distribution was W 180 (60.6%); AA 66 (22.2%) and H 50 (16.8%). Overall 226 (76.1%) donors’ NOK authorized for research and 71 (23.9%) declined research. Donor age <35yr had a lower rate of authorization 62.9% vs 81.3% and 80.6% for 35-49yr and ≥50yr respectively p=0.006. Table 1 shows ethnic distribution on rate of NOK authorization for research, which was significantly lower in multiethnic and genetically diverse cohorts.

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 multiethnic and genetically diverse cohorts.

Funding: NIDDK Support

SU-OR46

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

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Background: Thrombotic Microangiopathy (TMA) 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 accurate diagnosis integrating morphological, clinical, laboratory and molecular findings, where available. 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 82,677 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, nephrologists 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

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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 two years following MIA detection (HR 1.83, 95% CI 1.07-2.96).

Conclusions: Two years after documenting MIA in kidney transplanted patients, their CVD risk was increased, most likely, as a result of endothelial dysfunction. This should prompt the caregiver for strict primary prevention and risk factors modification.

Kaplan-Meier analysis showing rate of CV outcome or death in relation to MIA. X axis shows days since urine collection, Y axis shows cumulative survival. Blue curve – patients without MIA, red curve – patients with MIA.

SU-OR49

Renal Graft Outcomes in Simultaneous Kidney-Heart Transplant Recipients: Analysis of the UNOS Database from 1987-2018

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Background: Simultaneous kidney and heart transplants (SKHT) are employed for patients with both end-stage heart failure and severely impaired kidney function. Renal outcomes in such recipients have been described, albeit in single-center cohorts. We analyzed the United Network for Organ Sharing (UNOS) dataset comprising of 1702 simultaneous kidney-heart transplant recipients since 1987.

Methods: This is a retrospective analysis of SKHT recipients in the UNOS dataset who received transplants between October 1987 and December 2018. We compared the incidence and risk factors of renal allograft loss in SKHT recipients versus deceased donor kidney (DDKT) alone recipients. The Student t-test or Kruskal Wallis tests were used to compare continuous variables, and the Chi2 test for categorical variables between groups. Cox regression hazard model was used to study the factors associated with graft failure.

Results: SKHT recipients were mostly white, males, 5-years older than DDKT recipients. The SKHT donors were younger than DDKT donors, predominantly white males who died from a CVA. Five year patient survival was similar in both the groups (80%) but 1-year mortality was 3 times higher in the SKHT group (12.5%) than DDKT (4.6%). Nearly 20% recipients in both groups died with a functioning graft. Renal graft survival in SKHT group was lower in the first year but equalized with DDKT group 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 (30%) 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 graft 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

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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 medium 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 occurred 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.

Methods: Renal ischemic reperfusion injury (IRI) rat model was established and RDN was performed. Animals were randomized to IRI with or without RDN. Tyrosine hydroxylase (TH), renal functions, tubular cell apoptosis and histology staining were examined at 24 hours, and renal fibrosis and capillary vessels were measured at 2 weeks. What is more, the expression of miRNAs in injured kidney was determined by micro-array and the target genes were analyzed. Lastly, human renal biopsy samples with chronic kidney disease were picked for the TH and fibrosis analysis.

Results: TH was eliminated and renal functions were improved in the denervation group at 24 hours. RDN reduce tubular cell apoptosis and mitigate the histological lesion. Meanwhile, the increase of capillary vessel density was determined at 24 hours and 2 weeks, and the miRNA targeted pro-angiogenesis, anti-fibrosis and inflammatory pathways were modulated. Lastly, less fibrosis regions were found in TH high expression regions of human renal biopsy samples.

Conclusions: RDN was a reliable method in alleviating IRI induced acute and chronic kidney injury, and the modulation of miRNA related pro-angiogenesis, anti-fibrosis or inflammatory pathways involved in this process.

PO2616

Obesity Has Opposing Effects on Acute vs. Chronic Kidney Disease
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Background: With an accumulation of lipid droplets, mitochondria become incapable of upregulating the glucose-dependent response to ischemia and the cell becomes dependent upon glycolysis to satisfy metabolic need. This dysregulation has contributed to the exacerbation of ischemic injury in various tissues in diet-induced obese (DIO) mice. However, very little is known in how DIO can contribute to ischemic kidney disease. We hypothesized that obesity may dampen the response to acute kidney injury (AKI) and further exacerbate the development of dysfunction in chronic kidney disease. In this study, the increase of capillary vessel density was determined at 24 hours and 2 weeks, and the miRNA targeted pro-angiogenesis, anti-fibrosis and inflammatory pathways were modulated. Lastly, less fibrosis regions were found in TH high expression regions of human renal biopsy samples.

Conclusions: RDN was a reliable method in alleviating IRI induced acute and chronic kidney injury, and the modulation of miRNA related pro-angiogenesis, anti-fibrosis or inflammatory pathways involved in this process.

PO2617

Protective Effects of Apelin on Contrast-Induced Nephropathy
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Background: Contrast induced nephropathy (CIN) has no proven preventive measures yet except for saline administration. Apelin is a endogenous ligand to apelin receptor in body, which has physiologic roles such as increasing cardiac output and peripheral vasodilatation. This study aims to examine the protective effect of apelin on CIN.

Methods: A total of 22 rats were divided into 4 groups: Control, Apelin, Contrast and Apelin+Contrast. In order to effectively induce CIN, 50 mg/kg of gentamycin IV was injected daily to all rats from Day-1 to Day-6. On Day-7, the rats were pre-treated as follows; Control and Contrast groups: Saline SQ, Apelin and Apelin/Contrast groups: apelin (500 ng/kg) IV. Apelin/Contrast groups were associated with no treatment, main treatments were followed; Control and Apelin groups: Saline IV. Contrast and Apelin/Contrast groups: Ioxagol-350 mg id/mL, 1.8 g id/kg IV. We performed serum and 24-hour urine tests on Day-0 and Day-9 which was 48 hours after contrast administration. We collected the kidney with sacrifice on Day-9.

Results: The significant increase in serum creatinine (Cr) in only Contrast group (p=0.039). In Contrast (p=0.015) and Apelin/Contrast (p=0.007) groups, urinary Cr excretion significantly increased indicating renal tubular injury. The immunohistochemistry for caspase-3 indicated that Contrast group had significant increase in number of positive cells compared to Control group at 24 hours. The immunohistochemistry for TH, renal functions, tubular cell apoptosis and histology staining were examined at 24 hours, and renal fibrosis and capillary vessels were measured at 2 weeks. What is more, the expression of miRNAs in injured kidney was determined by micro-array and the target genes were analyzed. Lastly, human renal biopsy samples with chronic kidney disease were picked for the TH and fibrosis analysis.

Conclusions: We could identify the protective effects of apelin against CIN in the study.

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) 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 (P<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=0.005) 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; P<0.05). Male SHR also exhibited greater decreases in glomerular filtration rate (GFR; P=0.025; P=0.12) and increases in systolic BP (P=0.0001; P=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

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 mROS and released mtDNA from PT cells. BAM15 attenuated generation of mROS 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

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:

\[
\text{mRAI} = \frac{1}{X} \times \left[ \frac{1}{X} \times \left( \frac{SCr_1 - SCr_2}{SCr_2 - SCr_3} \right) \right]
\]

where X is the number of days between SCr measurements.

Results: Younger adults (age < 65) were less at risk of AKI as compared to older adults (age ≥ 65). The incidence of AKI at 3-7 days of hospital or ICU stay was 52.7%. Most patients fulfilled the AKI sCr criteria. Our results showed that mRAI had robust predictive capacity to identify hospitalized 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

Table: Performance of the mRAI for the prediction of AKI in hospitalized patients

<table>
<thead>
<tr>
<th>Statistic</th>
<th>Value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>89.6%</td>
<td>72.6%–97.8%</td>
</tr>
<tr>
<td>Specificity</td>
<td>76.9%</td>
<td>56.3%–91.0%</td>
</tr>
<tr>
<td>Positive Likelihood Ratio</td>
<td>3.89</td>
<td>1.91–7.92</td>
</tr>
<tr>
<td>Negative Likelihood Ratio</td>
<td>0.13</td>
<td>0.05–0.40</td>
</tr>
<tr>
<td>PPV</td>
<td>81.2%</td>
<td>68.0%–98.9%</td>
</tr>
<tr>
<td>NPV</td>
<td>86.9%</td>
<td>69.1%–95.2%</td>
</tr>
</tbody>
</table>

*Table: Performance of the mRAI for the prediction of AKI in hospitalized patients.*

PO2621
Grb2 Promotes Cardiorenal Syndrome Type 3: Roles of Cardiomyocyte Contractile Cytoskeleton, Mitochondria Damage, and Inflammation
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Background: Cardiorenal syndrome type-3 (CRS-3) is a damage to heart following acute kidney injury. Although many experiments have found that inflammation, oxidative stress, and cardiomyocyte death are involved in cardiomyocyte pathophysiological alterations during CRS-3, it lacks a non-bias analysis to figure out the primary mediator of cardiac dysfunction. Herein, the aim of our study is to figure out the primary upstream regulator of these intracellular molecular biological events.

Methods: In this study, proteomic analysis was performed in CRS-3 and growth factor receptor-bound protein 2 (Grb2) was identified as a regulator involving AKI-related myocardial damage.

Results: Increased Grb2 was associated with cardiac diastolic dysfunction, mild cardiomyocyte death and prominent myocardial inflammation; these pathological changes could be reversed through administration of Grb2-blocking peptide after AKI. Molecular investigation illustrated that augmented Grb2 promoted cardiomyocytes contractile cytoskeleton degradation through inhibiting the expression of Myosin. In addition, increased Grb2 triggered mitochondrial fission, inactivated mitochondrial autophagy, induced mitochondrial potential reduction, and triggered caspase-9/3 activation. Pro-inflammatory signaling pathways, including NF-κB, MAPK/ Erk, and MAPK/P38, were activated by Grb2 in cardiomyocytes following AKI.

Conclusions: Our results identify CRS-3 is caused by Grb2 upregulation which contributes to cardiac dysfunction, cardiomyocyte apoptosis and myocardial inflammation. This finding provides a potential target for the clinical treatment of patients with CRS-3.

PO0001
AKI Identification: Use of Electronic AKI Alerts vs. Electronic Health Records in Hospital Episode Statistics
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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). Herein, we aimed to evaluate the performance of the e-alert system in hospitalised patients. The performance of the e-alert system in hospitalised patients is measured in 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) in patients aged ≥ 18 years, between 01/01/2017 and 31/12/2017 were linked to HES data to identify a hospitalised AKI population. Descriptive analyses were conducted to describe the demographics and to investigate whether those with an AKI e-alert also had an International Classification of Diseases (ICD)-10 code for AKI (N17) in HES.

Results: From 01/01/2017 to 31/12/2017, 301,504 hospitalised adults received an AKI e-alert. AKI severity was positively associated with the percentage of AKI alerts coded in HES. There was a significant variation in HES coding between hospitals, most pronounced for AKI stage 1 (mean 48.2% SD 14) versus AKI 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 at 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.

Early Prediction of Hospital-Acquired AKI from Electronic Health Records Using Machine Learning

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Background: Hospital-acquired acute kidney injury (HA-AKI) leads to increased mortality and morbidity. Early prediction of HA-AKI using Electronic Health Records may enable clinicians to modify treatment to minimize risk and AKI severity.

Methods: Inpatient admissions from 7/13/2012 – 7/11/2018 who had 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, logistic 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 based on the balance between model simplicity and performance. Variables included in the 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 requiring CRRT for AKI. Renal recovery was defined by CRRT discontinuation. Intermittent hemodialysis was excluded. Only articles utilizing multivariate analysis were included. We divided our analyses into two cohorts based on the primary outcomes: renal recovery cohort and overall mortality cohort.

Results: For renal recovery cohort (n = 4,497 from 14 studies), the mean effluent dose of CRRT was 24.93 ± 5.87 ml/kg/h with a median duration of CRRT of 3.75 days (IQR 2.45). Increasing urine output at time of CRRT discontinuation (per 100 ml/day), elevated initial SOFA score (per 1 score) and serum creatinine level at CRRT initiation (per 10 mg/dl) were predictive of renal recovery with odds ratio of 1.021 (95% CI, 1.012-1.031), 0.890 (95% CI, 0.805-0.984) and 0.995 (95% CI, 0.991-0.999), respectively. For overall mortality cohort (n = 16,948 from 11 studies), the mean effluent dose of CRRT was 26.22 ± 4.67 ml/kg/h with a median CRRT duration of 4.5 days (IQR 3.40). Age (per 1 year) and presence of sepsis were significantly associated with overall mortality with odds ratio of 1.023 (95% CI, 1.006-1.040) and 2.031 (95% CI, 1.267-3.257), respectively. All analyses remained significant through sensitivity analyses. No potential publication bias was identified.

Conclusions: Urine output at CRRT discontinuation, initial SOFA score, and serum creatinine level are predictive of renal recovery and successful CRRT discontinuation. Increasing age and the presence of sepsis are independent risk factors for elevated overall mortality.

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 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.

Funding: NIDDK Support

AKI Epidemiology, Risk Factors, and Prevention: Clinical Research

Poster

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 also predicted 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.

Funding: Other NIH Support - National Institute of Allergy and Infectious Diseases of the National Institutes of Health under Award Number K23AI43882; National Center for Advancing Translational Sciences Grant Number UL1 TR002377; National Institute on Aging of the National Institutes of Health Award Number R01AG036476.

Risk Factors for Mortality and Hospital Readmission Following AKI

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Background: Acute kidney injury (AKI) occurs in over 20% of hospitalized patients and is associated with increased short-term and 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 admission or discharge to a 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 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), prior cardiovascular disease (HR=1.15, CI 1.13-1.17, p<0.001), short-term inpatient mortality (HR=1.12, CI 1.30-1.33, p<0.001), chronic kidney disease (HR=1.15, CI 1.13-1.17, p<0.001), creatinine at time of admission (HR=1.012, CI 1.009-1.015, p<0.001) and increase from pre-admission values (HR=1.045, CI 1.041-1.048, p<0.001). The same patient characteristics were significant predictors of readmission for a renal indication. The odds ratios for death and readmission were 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, 0.858 (95% CI:0.850-0.867), 0.858 (95% CI:0.850-0.866), 0.859 (95% CI:0.840-0.870), 0.864 (95% CI:0.851-0.876) and validated in MIMIC were 0.799 (95% CI:0.710-0.824), 0.809 (95% CI:0.730-0.833), 0.814 (95% CI:0.791-0.837), 0.800 (95% CI:0.776-0.825), respectively. When training the model using MIMIC dataset, the intra-ICU mortality AUC of LR, XGBoost, RF and MLE 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 MLE were 0.864 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 than the usual practice in predicting mortality of patients requiring RRT in ICU. All of the models almost had excellent performance in both databases.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
**PO0011**
Region-wide Implementation of Best Practice in AKI
Anirudh Rao, Kottatharil 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 guideline implementation period. Five hospitals were excluded due to guideline implementation pre-roll out (2), implementation dates not provided (2) & no pre-post guideline implementation period. Five hospitals were excluded due to guideline implementation pre-roll out (2), implementation dates not provided (2) & no pre-post guideline implementation period. Five hospitals were excluded due to guideline implementation pre-roll out (2), implementation dates not provided (2) & no pre-post guideline implementation period. Five hospitals were excluded due to guideline implementation pre-roll out (2), implementation dates not provided (2) & no pre-post guideline implementation period. Five hospitals were excluded due to guideline implementation pre-roll out (2), implementation dates not provided (2) & no pre-post guideline implementation period. Five hospitals were excluded due to guideline implementation pre-roll out (2), implementation dates not provided (2) & no pre-post guideline implementation period. Five hospitals were excluded due to guideline implementation pre-roll out (2), implementation dates not provided (2) & no pre-post guideline implementation period. Five hospitals were excluded due to guideline implementation pre-roll out (2), implementation dates not provided (2) & no pre-post guideline implementation period. Five hospitals were excluded due to guideline implementation pre-roll out (2), implementation dates not provided (2) & no pre-post guideline implementation period. Five hospitals were excluded due to guideline implementation pre-roll out (2), implementation dates not provided (2) & no pre-post guideline implementation period. Five hospitals were excluded due to guideline implementation pre-roll out (2), implementation dates not provided (2) & no pre-post guideline implementation period.

**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 year and overall AKI incidence (P=0.53), the study year was negatively correlated with incidence of severe AKI requiring replacement therapy (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 36% developed severe AKI requiring RRT. There was 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.
Results: From January 1 to March 3, 124 cases of AKI were identified among patients presenting to the ED, 114 (92%) of whom participated in the study. The mean (SD) age of the 114 AKI cases and the 228 controls was 68.7±15.2 years and 68.8±15.0 years, respectively. 43% of cases and controls were female. AKI cases were significantly more likely than controls to have been taking non-steroidal anti-inflammatory drugs (NSAIDs) (36.0% vs 20.6%, p=0.01) in the week preceding the ED visit. In both cases and controls, the usage of OTC NSAIDs was more common than prescription NSAIDs (72.2% and 66.0%). No significant difference was observed between AKI cases and controls in the use of ACE-inhibitors/angiotensin receptor blockers (45.6% vs 39.9%, p=0.314). The use of proton pump inhibitors was less common among AKI cases than controls (27.2% vs 41.7%, p=0.01) and same was true for statins (22.8% vs 33.3%, p=0.045).

Conclusions: These preliminary results suggest a significant contribution of OTC NSAID use to AKI among patients presenting to the ED. A detailed information on adverse events should be provided when these medications are sold over the counter.

Funding: Government Support - Non-U.S.

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 <16 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.

Methods: We examined the association of race and future development of SRC in an SSc cohort.

Results: From January 1 to March 3, 2013 to December 2018. We classified included patients into pure AKI and ACKD two etiology, and renal recovery of biopsy-proven AKI patients.

Background: We retrospectively analyzed the clinical and pathological data of AKI patients who underwent PCI at Duke University Medical Center, Durham, NC.

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 Cardiac Database 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, predisposing 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 63.6 years [IQR 54 to 72]); 33% female; 75% white, 22% 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: p 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.
Results: The study included 207 AKI patients who had undertaken renal biopsy, while 553 patients were excluded for the total biopsy cases and 31.7% of the total hospitalized AKI cases during the same period. The majority of AKI patients were male (65.1%), with an average age of 42±16.5 years, pure AKI and ACKD account for 21.6% and 78.4%, respectively. Pure AKI mainly presented as AKI-3 (74.8%), while ACKD mostly presented as AKI-1 (53%). The proportion of patients undergoing renal replacement therapy in pure ACKD group was significantly higher than ACKD group (29.3% vs. 11.9%, P < 0.001). In pure ACKD group, acute interstitial nephritis (AIN) was most common (56.1%), followed by acute tubular necrosis (ATN) (34.6%). The main cause of AIN was due to drugs (84.9%) and infections (14%) and more patients required dialysis. AKI patients had a wide spectrum of pathological diseases, and the prognosis of renal recovery was worse than pure AKI.

Funding: Private Foundation Support

PO0019
Higher Ambient Level of Nitrogen Dioxide Is Associated with an Increased Risk of AKI
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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, PM10, 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 11,293 AKI cases that met the inclusion and exclusion criteria were selected, of which, 3175 (28.1%) were severe AKI (stage 2 or 3). In univariable analysis, the ambient levels of NO2 and SO2 were significantly associated with the risk of AKI in the group. 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.

Conclusions: Among biopsy-proven AKI patients, pure AKI was relatively rare while ACKD accounts for the majority. Pure AKI tends to be more severe than ACKD and more patients required dialysis. ACKD patients had a wide spectrum of pathological diseases, and the prognosis of renal recovery was worse than pure AKI.

Funding: Private Foundation Support

PO0020
AKI After Procedures of Orthoptic Liver Transplant: Risk Factors, Renal Outcomes and Survival

Background: The incidence of acute renal injury (AKI) after orthotopic liver transplantation (OLT) ranges between 40 and 70%. The etiology of this syndrome is multifactorial.

Methods: Medical records of patients undergoing OLT in the period from January 2012 to August 2019 were reviewed. A total of 355 patients were included. 171 patients presented AKI. Baseline characteristics, variables during surgery and variables during their stay in intensive were analyzed. Renal outcomes and survival were also analyzed.

Results: In the group without AKI age mean was 45.8 years and 37% were men, in the group with AKI the age mean was 51.2 years and 54% were men (P < 0.001). Mean baseline creatinine was 0.77 vs while 0.88 mg/dl (P < 0.001). Fuorescure prior to transplantation was found; 51.6% vs 71.9%, P < 0.001. A difference was also found between the incidence of AKI in the group that underwent transplants in the 3 months prior to transplantation (50%), the 3–6 months prior to transplantation (43.7% vs. P < 0.001) and (0.21 vs. 0.53) During surgery. Difference was found in maximum lactate, maximum dose of norepinephrine and vasopressin use during surgery: (5.1 vs. 5.8 P < 0.014), (0.59 vs. 0.34 P < 0.001), (36% vs. 51% P < 0.003). Differences were also found in drained anesles and anehepatic period: (1508 vs 973 SD vs 1871 P < 0.021) and (52.9 vs 57.4 P = 0.014). In the stay in the ICU, there was a difference in the income of liquidst first and second 8 hours after transplant (1319 vs 1984 P = 0.001) and (1208 vs 1606 P = 0.009), norepinephrine dose in the first 24 hours (0.14 vs 0.27 P < 0.001), use of vasopressin and strakladalin (27.1% vs 42.1% P = 0.02) and (3.8% vs. 13.9 P = 0.001), transfusion of blodd derivatives 33.1% vs 59% (P < 0.001). There was difference in creatinine and GFR at the end of hospitalization (0.67 vs 0.97 P < 0.001) and (104 vs 82.6 P = 0.001). Survival at 7 days after the transplant 100% vs 96.5% P = 0.01. Survival at 1 year: 99.5% vs 93.6% P = 0.002.

Conclusions: The incidence of AKI in the first 7 days was 48%, which is consistent with that reported in the world literature. The development of AKI seems to be multifactorial influencing baseline characteristics of patients before transplantation and renal function during surgery and intensive care stay. AKI was associated with higher mortality at 7 and 30 days, in addition to lower GFR at patient discharge and higher risk of CKD.

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PO0021
Anemia Following AKI After Non-Carcinoid Surgery and Long-Term Outcomes: The NARA-AKI Cohort Study
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Background: The aim of this study was to investigate whether acute kidney injury (AKI) is an independent predictor of anemia and whether anemia following AKI is a mediator of mortality after AKI.

Methods: This is a retrospective cohort study. Adults who underwent non-cardiac surgery from 2007 to 2011 were included. Those with obstetric or urological surgery, missing data for analyses, or preoperative dialysis were excluded. Subjects were followed until the end of 2015 or loss to follow-up. The exposure of interest was postoperative AKI defined by KDIGO criteria. The outcome variables were hematocrit values measured at 3, 6, and 12 months postoperatively and mortality. Associations between AKI and hematocrit or association between AKI and mortality were examined by multivariable linear regression or cox regression analyses, respectively. Data were adjusted for potential confounders.

Results: Among 6692 subjects, 445 (6.6%) developed AKI. Among those with postoperative data, AKI was independently associated with lower hematocrit values at 3, 6, and 12 months postoperatively, with coefficients [95% confidence interval] of [−0.79 to −1.47] to [−0.11], n=1750, −1.35 [−2.11 to −0.60], n=1558, and −0.91 [−1.59 to −0.22], n=2463, respectively. Higher stages of AKI and longer duration of AKI were associated with more severe anemia. AKI was associated with higher mortality after 3 months postoperatively with hazard ratio [95% confidence interval] of 1.54 [1.12 to 2.12]. Further adjustment with hematocrit values at 3 months attenuated the association (1.45 [1.05 to 2.00]). Median effect was significant (p=0.02) by mediation analysis.

Conclusions: AKI was an independent predictor of anemia following AKI. This might be due to permanent interval damage and impaired erythropoietin production. Higher mortality associated with AKI was at least partially mediated by anemia following AKI. Whether correction of anemia following AKI improves outcome of AKI requires further research.

Funding: Private Foundation Support

Poster
PO0023
Decreased Urinary Uromodulin Is Potentially Associated with AKI: A Systemic Review and Meta-Analysis
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**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 Databases (up to 2020). 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 promising diagnostic values and mechanisms in protecting AKI.

**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.

PO0024
Independent Predictors of Checkpoint Inhibitor-Associated AKI

**Background:** Checkpoint inhibitors (CPI)-associated acute renal injury (AKI) is an adverse effect of these therapies and its incidence is 13-29%. Clinical characteristics and risk factors of CPI-associated AKI were investigated.

**Methods:** Clinical and demographic data of patients receiving CPI March 2018-May 2019 were evaluated. Patients were divided into two groups depending on the development of AKI.

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Underline represents presenting author.

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 between 2013-2015. Patient data were obtained from the electronic hospitalization information system. We selected 57589 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 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 57589 adult analysed, 20599 (35.8%) used diuretics, 17077 (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.

**Funding:** Government Support - Non-U.S.
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 30,222 nephrology outpatients with CKD stages 2-5 in 2016 and their prescriptions. Drug prescriptions and their duration were collected prospectively. We used cause-specific Cox proportional hazard models to estimate hazard ratios (HRs) 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, 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): 1.1% per-person years (IQR, 6.2-2.2)) and 414 patients had at least one interval between two continuous SCr testing <14 days during the first 30 days of hospitalization and medication data from 6 months before until 30 days after first prescription. The greater nephrotoxicity of ibuprofen use was associated with significantly increased risk of HA-AKI (hazard ratios, HR 2.29; 95% CI, 1.41-3.73) compared to the other two groups (82.8% vs. 60.0% vs. 36.1%, P < 0.001).

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

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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 2013 to 2015 at 25 academic medical centers in China. Patient-level data were obtained from the electronic hospitalization information system. We included 50,420 hospitalized children aged between 1 month to 18 years who had at least one SCr test during the first 3 days of hospitalization and at least one interval between two continuous SCr testing <14 days during the first 30 days of hospitalization, excluding those with end-stage renal disease, community-acquired AKI, insufficient SCr testing and without prescription. AKI was defined as an increase of at least 0.3 mg/dL in serum creatinine (SCr) and/or any interval between two continuous SCr testing <14 days during the first 30 days after prescription.

Results: We studied 3896 individuals (mean age 64.5 ± 13.3 years) with incident prescriptions: 138 in the NSAID group and 3738 in the non-NSAID group. 30-day AKI and/or hyperkalemia occurred in 525 individuals (13.5%). After adjusting for age, gender, plasma baseline SCr, eGFR, serum potassium, NSAID, RAAS blocker and diuretic, baseline SCr (adjusted OR 1.41, 95% CI 1.03-1.91, p=0.01), RAAS blocker (adjusted OR 1.42, 95% CI 1.15-1.75, p<0.001), diuretic (adjusted OR 1.91, 95% CI 1.53-2.38, p<0.001) and higher baseline serum potassium (adjusted OR 1.36, 95% CI 1.19-1.57, p<0.001) were independent predictors for the outcome. NSAID prescription for patients with a history of AKI was associated with a higher risk of AKI (adjusted OR 1.62, 95% CI 1.09-2.65, p=0.05). 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 1.99-10.08, p=0.04).

Conclusions: NSAID prescription in individuals with DM may be associated with AKI and/or hyperkalemia, especially with concurrent RAAS blocker or diuretic.

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PO0029

A Retrospective Cohort Study of Chemotherapy-Related AKI

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Background: Chemotherapy-related acute kidney injury (CR-AKI) is increasing worldwide. However, there is limited information available about CR-AKI in China.

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).

Conclusions: Of 258 CR-AKI patients, 61 (23.0%) reached AKI stage 3, and 37 (14.3%) received RRT in the hospital mortality. 14.9% (38/258) of the 207 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 gender, age, 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 (37.1% 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.
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 therapy 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 determined 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 reported 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.

Baseline Urinary Protein Biomarkers as Predictors of eGFR Decline in Cancer Patients Receiving Cisplatin

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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 3-7 days of stay. Exclusion criteria consisted of age ≥ 75 years, baseline eGFR <60 ml/min/1.73m², ESKD, or CKD stage 5. AKI was defined as a change of serum creatinine level ≥ 0.3 mg/dL or ≥ 1.5 times in contrast to normal baseline value within 48 hours. We evaluated if the microscopic examination of the urine sediment (score ≥ 2) could be used 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 stage 3 (6.6%). Performance metrics of the urinary score used are reported in Table. A urinary 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: 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

Table: Performance of the urinary sediment score for the prediction of AKI in hospitalized patients
Methods: 107 patients (23-77 years, 53 females) when they were first prescribed RASb for primary hypertension (PHT) (n=25), diabetic nephropathy (DN) (n=12), PHT+DN (n=8), congestive heart failure (n=26) and proteinuric nephropathies (n=36). Changes in serum creatinine (Scr), mean sUA levels and systolic (SBP) and diastolic (DBP) blood pressures (mmHg) were obtained from records before and 3, 1±0.2 months after RASb.

Results: Baseline eGFR (ml/min/1.73m²) was 43.6±2.81 and 64.4±8.89 in male and female patients, respectively. 55% male and 51% female patients increased Scr with RASb but only 8 male and 2 female patients increased baseline Scr more than 0.3mg/dl. RASb reduced significantly SBP (pre130±7.167 vs. post124.1±5.71, p=0.004) but not DBP. Reduction in eGFR was found in 87% of the patients in whom SBP was reduced by RASb. Reduction of SBP was unrelated to the increase in Scr. sUA (mg/dl) was 6.9±0.1 (males) and 6.1±0.2 (females) (p=0.09). In female there was no relation between UA levels and change in Scr. In male there was a direct relationship between changes in Scr (Scr/pre-Scr/Post) and the mean serum UA levels (sr=0.36, p=0.008) that was unrelated to SBP changes. Relationship was stronger in male patients with sUA ≥7.0 (f<0.051).

Conclusions: Since 14% of the male patients treated with RASb increased Scr more than 0.3 mg/dl and deterioration of kidney function was directly related to sUA levels, the potential benefit of reducing sUA in male patients treated with RASb should be investigated further.

PO0036 Seizure-Induced Hyperuricemia and Associated Urate Nephropathy: A Prospective Cohort Study

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Background: Urate nephropathy is an uncommon cause of acute kidney injury (AKI). Although most factors are associated with tumor lysis syndrome and rhabdomyolysis, occurrence following severe seizure has also been described. There are effective ways to prevent and treaturate-associated AKI, when adequately identified. However, uric acid measurement following convulsion episodes is rarely performed and therefore, the incidence of hyperuricemia in this context is unknown. Our objective was to quantify these metabolic disturbances following severe generalised tonic-clonic seizures (GTCS).

Methods: We prospectively recruited patients admitted in our hospital for severe GTCS (≥5 min or a series of seizures with an incomplete return to baseline) and described the kinetics of serum uric acid, creatinine, creatine kinase and lactate during a 72h follow-up. The creatine-urate ratio was used to monitor urate tubular toxicity.

Results: From August 2018 to September 2019, 13 patients with a median GTCS duration of 5.0 minutes (IQR 2.0-12.5) were included. The median serum uric acid was initially 346.0 µmol/L (IQR 155.0-377.5) and decreased to 178.0 µmol/L (IQR 140.0-297.5), while serum creatine passed from 73.0 µmol/L (IQR 151.0-80.0) to 57.0 µmol/L (IQR 44.0-70.0) over follow-up (Figure). AKI occurred in 4 patients (KDIGO Stage A1).

Conclusions: Serum uric acid levels increase acutely following a severe GTCS than return to baseline within 3 days. During that period, there is an increased risk of AKI that might be associated with urate nephropathy. To quickly identify and manage patients at risk of acute hyperuricemia, related complications, measurement of uric acid following a GTCS might be beneficial.

Funding: Clinical Revenue Support

PO0035 Relationship Between Serum Uric Acid Levels and Reduction in Kidney Function Associated With Blockade of the Renin-Angiotensin System

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Background: Renin-angiotensin system blockade (RASb) induced by treatment with angiotensin type 2 receptor antagonists and angiotensin converting enzyme inhibitors is frequently associated with a reduction in glomerular filtration rate (GFR). Experimental hyperuricemia is associated with dysregulation of renal hemodynamics and reduced GFR. We studied if serum uric acid (sUA) levels are related to the depression of renal function associated to RASb.
Late Presentations of Secondary Oxalate Nephropathy
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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.

Presentation and Outcome of Oxalate Nephropathy Without Known Genetic or Gastrointestinal Cause
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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
Incidence of AKI After IV Vitamin C Treatment for Septic Shock: A Cohort Analysis of Real-World Application

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Background: Septic shock patients exhibit a high prevalence of vitamin C deficiency, and intravenous vitamin C (IVC) may provide a survival advantage. Preliminary findings from early studies were promising, however, recent studies fail to show a benefit of vitamin C on mortality. Case reports observed that IVC may be related to acute kidney injury (AKI) through oxalate-nephropathy. While IVC in sepsis merits further research, clinicians at one institution began the use of IVC as additional treatment for septic shock.

Methods: This study is a retrospective analysis of real-world evidence to evaluate the effects of IVC on AKI in patients with septic shock.

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 IV-C 1500mg and were categorized as the IVC+ group; 1634 (79.1%) did not receive IVC. A chi-square analysis can be seen in Table 1.

Conclusions: This retrospective study EMR observed that IV-C 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 IVC and the Development of AKI among Inpatients with Septic Shock.

Note: A logistic regression revealed that the odds of AKI were 2.57 times higher for IVC patients compared to non-IVC patients (95% CI 2.053, 3.23).
PO0043
Zolpidem Mega Dose Resulting in Hemodialysis

Introduction: Depression and hyperventilation 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 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 prompt intervention, hemodynamic stability and full recovery were achieved.

Discussion: The ingestion of 90 Zolpidem pills is a dangerous scenario. In our case, within 4 days of ingestion, the patient presented with myalgias, rhabdomyolysis, acute kidney injury, metabolic acidosis, and respiratory failure. The patient was admitted to the ICU with a Glasgow Coma Scale of 3 and underwent 18 days of renal replacement therapy (RRT) with CVVH initially and then iHD.

PO0044
Severe Exertional Rhabdomyolysis with AKI Associated with Sickle Cell Trait
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Introduction: Exertional rhabdomyolysis (ER) is a pathological breakdown of muscle cells which can result in acute kidney injury (AKI) from multiple mechanisms including tubular toxicity from hemoglobin, pigment, cast formation, and volume depletion. ER has a host of etiologies including drugs, infections, infections, electrolyte abnormalities, trauma, venom, and metabolic disorders. Sickle Cell Trait (SCT), a generally asymptomatic condition, has been rarely associated with ER. We present a case of severe ER with AKI in a previously healthy patient who was determined to have SCT as the only risk factor.

Case Description: A 39 y/o previously healthy black police recruit on no medications presented with myalgias and dyspnea following a routine training regimen. He was found to have diffuse tenderness and weakness of arms and legs. Initial labs showed serum creatinine (sCr) 2.0 mg/dL, Na 148 mmol/L, CO2 <5 mmol/L, Creatine Kinase (CK) 1,516 U/L. A peripheral blood smear showed few sickle cells. His urine was dark tea-colored and on urinalysis had large blood and minimal RBCs. Illicit drug panel, autoimmune studies, myophosphorylase deficiency, and myostatin panel including anti-SSA, anti-PM/Scl, and anti-U1RNP were normal or negative. A hemoglobin electrophoresis demonstrated 35% Hgb S and 62% Hgb A consistent with SCT. He was oliguric and was started on renal replacement therapy (RRT) with CVVH initially and then iHD. His CK and sCr peaked at 565,000 U/L and 13.9 mg/dL respectively (figure 1). He required 18 days of RRT. His sCr after discharge improved to 1.4 mg/dL.

Discussion: SCT is normally a relatively benign condition as there is enough normal Hgb to prevent significant sickling. However, increased O2 demand with exertion may promote clinically significant sickling and lead to vaso-occlusion and hypoxic muscle injury. ER in SCT is rare and unpredictable and therefore specific recommendations for re-introduction of exercise are not available. However, guidelines for Exercise Collapse Associated with Sickle Cell Trait (ECAST) can be used to guide long term patient management.
Calcium oxalate crystals in tubules (PAS stain, polarized light)

**PO0046**

**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 Cleto-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 hydronephrosis & a heterogeneous pelvic mass. Further labs revealed anemia, low PT, normal complement levels, ASO & ANA titers. A LE Doppler study was negative for venous thrombosis. A non-contrast MRI revealed a pelvic mass & possible obstruction secondary to a tumor.

**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.**

**Discussion:** Our patient’s clinical presentation was atypical in that her initial US findings of mild hydronephrosis 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. Decompression 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.

**PO0047**

**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 obtained. A latent class growth model identified patient groups based on similar patterns of AKI.

**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 deployment of post AKI care.

Funding: Veterans Affairs Support, Private Foundation Support

**PO0048**

**Trends in Nephrology Follow-Up After an Episode of AKI in US Veterans**

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**Background:** KDIGO guidelines recommend evaluating patients following AKI for new onset or worsening CKD. Yet, historically nephrologist referral post-AKI has been low. We sought to determine recent trends in outpatient nephrologist follow-up after a hospitalization with AKI.

**Methods:** We assembled a national cohort of US veterans surviving 30-days post hospitalization with KDIGO creatinine-defined AKI from 2008 to 2017, excluding those with ESRD or kidney transplant, those requiring dialysis within 30 days of hospital discharge, or discharged to hospice. The primary outcome was the proportion of AKI survivors completing an outpatient visit with a nephrologist within 6 months of their AKI hospitalization. To assess trends, we assessed the association of year (as a continuous variable) with follow-up in a Cox proportional hazards model adjusting for age, race, sex, AKI stage, hypertension, diabetes, CKD, Charlson Comorbidity Index, ICU utilization, acute myocardial infarction, acute heart failure, and hospital admitting service.

**Results:** Of the 480,200 survivors of AKI, 12.2% had a visit with a nephrologist within 6 months. The proportion of patients with nephrology follow-up ranged from 10.0% in stage 1 AKI to 43.8% in patients with AKI requiring inpatient dialysis. The proportion of patients receiving post-AKI care increased across the study period, from 11.8% in 2008 to 15.4% in 2017 (figure). Upon adjusting for demographics, comorbid conditions, and hospitalization characteristics, year remained a significant predictor of increasing nephrology follow-up after AKI (per year HR 1.024, 95% CI 1.021-1.027, p<0.01).

**Conclusions:** From 2008 to 2017, there was a modest increase in post-AKI follow-up that persisted after accounting for changing demographic, comorbid conditions and hospitalization characteristics. However, most patients with severe AKI did not have an outpatient visit with a nephrologist at 6 months, highlighting opportunities to improve processes of post-AKI care.

Funding: Other U.S. Government Support
Elevated Serum Tenasin C Predicts All-Cause Mortality in Critically Ill Patients with Multiple Organ Dysfunction
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Background: Tenasin-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 predicting all-cause mortality in critical 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 enrollment 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 120 patients with median (quartile) age of 64 (53, 73) and male of 67% in validation cohort were enrolled. 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 that in healthy controls (median 80.9 ng/ml, n=46, p<0.01 for both). The TNC levels were associated with the critical illness scores such as SOFA, APACHE II and SPAS II, as well as 28-day death probability (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). 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 SPAS II (0.872 and 0.779).

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.
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).

Method: We conducted a prospective 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 sCr increase in serum 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 67% AKI, 7% on CKD 33% was ischemic ATI (47%), toxic ATI (9%), ischemic/toxic ATI (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 [62% (94/152), 75% (45/60), 81% (29/36) and 93% (13/14), for those with no WxC, any WxC, >10% WxCs and >50% WxCs, respectively; chi-square for trend, p=0.014].

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 recovery.

PO0054
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 recently expanded the therapeutic options.

Methods: Retrospective analysis of the use of caplacizumab in more than 60 patients with acute aTTP immediately. ADAMTS13 activity measurements are central for a rapid screening of timing and adjunct treatment modalities. Based on this real-world experience and in a sustained reduction of the vWF activity.

Results: 76 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 AKI-Persist [62% (94/152), 75% (45/60), 81% (29/36) and 93% (13/14), for those with no WxC, any WxC, >10% WxCs and >50% WxCs, respectively; chi-square for trend, p=0.014].

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 recovery.

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 (UFnet) among critical ill patients with acute kidney injury treated with kidney replacement therapy. We examined U.S. critical care practitioner attitudes toward UFnet 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.

Results: 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 (CKRT) in 20% (IQR 12-34%) of their patients with medians UFnet rate of 51 mL/h (IQR 25-100 mL/h) for hemodynamically unstable and a maximal rate of 285 mL/h (IQR 200 – 341 mL/h) for hemodynamically stable patients. 58.3% (range 28.7%-79.2%) of practitioners assessed net fluid balance hourly. Hemodynamic instability was reported in 25% (IQR, 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%), inability to achieve the target (17.3%), high mortality (13.8%) and availability of resources (13.1%).

Conclusions: This study provides new knowledge on UFnet 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 UFnet.

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 hemodynamic 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 (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 (RTK), AKI recovery, and chronic kidney disease (CKD) progression was then assessed.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
assessed. Receiver operating characteristic (ROC) analysis was performed to evaluate the diagnostic performance of CEUS.

**Results:**
- **Cortical RT (Odds ratio [OR] = 1.21) predicted the KDIGO stage 3 AKI.**
- **Cortical TMT (OR = 1.07) and RT (OR = 1.20) predicted the initiation of RRT.**
- **Cortical WS (OR = 76.23) and medullary PI (OR = 1.25) predicted AKI recovery.**
- Medullary PI (OR = 0.97) and AUC (OR = 1.00) predicted CKD progression. 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**

**Silvi Shah, Anthony C. Leonard, Kathleen Harrison, Karthikayan Meganathan, Annette Christianson, Samantha M. Kramer, Charusha V. Thakar, University of Cincinnati, Cincinnati, OH; Cincinnati VA Medical Center, Cincinnati, OH.**

**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-day 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 g/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 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**

**Nasha Elavag, Si Li, Ibithola Yusuf, Bojana Milekic. The Wright Center for Graduate Medical Education, Scranton, PA.**

**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 8.65; 95% CI 6.46-11.57), septic shock (aOR 9.53; 95% CI 6.42-14.16), rhodanomylsis (aOR 3.03; 95% CI 2.39-3.84), requiring intubation (aOR 5.57; 95% CI 4.61-7.64, p<0.001), a longer length of stay (1.8 days; 95% CI 1.52-2.08, p<0.001) and higher costs ($508.44; 95% CI $398.88-$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.

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**PO0060**

**Impact of Chloride-Rich Crystalloids on Sepsis-Associated Communi-
yty-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%) patients 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: 3.8; 8] vs. 3.8 [IQR: 2.1; 6.1], P <0.001]. 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, 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 morbidity and mortality. Implementation of a set of evidence-based AKI care bundles may have some benefits to patient 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). 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; I² = 20%; Fig 2) and rates of AKI severity (odds ratio, 0.52; 95% CI, 0.35–0.76; P = 0.001; I² = 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.

PO0062

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 3.6 and 4.6 week randomization blocks. The SCAMP provided recommendations 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 3.6 and 4.6 week randomization blocks. The SCAMP provided recommendations 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.

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.
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 peroperatively 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 inability 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 increase in renin and OR: 3.44, 95%CI: 1.08-11.02 when the highest tertile was compared 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 and OR: 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%-33%).

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 utility in risk-stratification should be further explored in this vulnerable population.

PO0065

Angiotensin 1-7 as a Novel Biomarker of AKI in Pediatric Kidney Transplant Recipients
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Background: While graft survival rates of pediatric kidney transplant recipients have improved dramatically, acute kidney injury (AKI) accounts for up to 21% of graft failure in pediatric patients and prompt diagnosis of AKI is difficult. AKI activates the renin-angiotensin system (RAS), leading to increased angiotensin (Ang) II-induced inflammation and fibrosis. The ACE2/Ang-(1-7) pathway mitigates these effects but may be downregulated in AKI. The objective was to investigate Ang II and Ang-(1-7) as biomarkers to predict AKI in pediatric kidney transplant recipients. We hypothesized that changes in Ang II and Ang-(1-7) over time would predict biopsy-proven AKI in the first 6 months post-transplant.

Methods: This was a prospective cohort study of children recruited from a kidney transplant evaluation clinic. Blood and urine were collected pre-transplant and post-transplant at several time points. Ang II and Ang-(1-7) were measured with radioimmunoassays. Participants underwent cause or surveillance biopsies and histologic findings were recorded. We applied directed acyclic graph-informed Cox proportional hazards regression analysis with robust standard errors adjusted for age to estimate the association of time-varying Ang II and Ang-(1-7) with AKI.

Results: Of the 27 participants, mean age was 11.7 ± 6.1 years, 63% were male, and 44% were Caucasian. The most common cause of kidney failure was congenital anomalies of the kidney and urinary tract (30%) and 74% received a deceased-donor transplant. Ten patients (37%) had AKI, most commonly due to tacrolimus toxicity (19%). In the urine, a 1-unit increase per day in Ang II (HR 0.97, 95% CI 0.93-1.0), Ang-(1-7) (0.99, 0.98-0.999), and Ang II/Ang-(1-7) (0.56, 0.28-1.11) over time predicted AKI, while blood levels did not.

Conclusions: Among pediatric kidney transplant recipients, changes in urinary Ang II and Ang-(1-7) over time predict biopsy-proven AKI in the first 6 months post-transplant. Conversely, our findings suggest that for every 1-unit per day decrease in urine Ang-(1-7)[AMSM]1, AKI risk increases by 16% (95% CI 1-33%). Our findings support the notion that both pathways of the renin-angiotensin system are involved in transplant AKI. Larger studies are needed to confirm the utility of measuring Ang II and Ang-(1-7) as biomarkers to detect transplant AKI and inform its pathophysiology.

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 cytoreistance 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 glycercol-induced rhabdomyolysis, maleate-induced hypoxic/ischemic renal injury, and ischemia reperfusion injury. RBT-1 is composed of proprietary formulations of stannous protoporphyrin (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: 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 photo sensitivity 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 (16.3% vs. 8.9%), black (45.6% vs. 33.3%), 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 $12485.6 more than in patients without AKI (95% CI 10655.1-14315.2, 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.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO0068
AKI After Lung Transplantation: A Retrospective Analysis from a Single Transplantation Center
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Background: Acute kidney injury (AKI) is a common and serious complication after lung transplantation (Ltx). No data from the Swedish Ltx program have been published, and thus we performed a retrospective analysis of AKI after Ltx at our unit.

Methods: After ethical board approval, all patients ≥18 years who underwent Ltx in Gothenburg, Sweden, between 2012-2016 were assessed. Exclusion criteria were: death within 48 hours, multiple organ transplantsations or pre-operative dialysis. AKI was defined according to the KDIGO creatinine criteria and the AKI group was compared to the patients without AKI using Mann-Whitney U-tests or Chi²-tests as appropriate. A multivariate logistic regression model for pre- and intraoperative predictors of AKI was built.

Results: In total, 211 patients were transplanted 2012–2016, and 197 patients were analyzed. Of these, 37% developed AKI within 1 week after Ltx (grade 1; 58%, grade 2; 12%, grade 3; 29%). AKI was associated with increased mortality at 30 days (5.5% vs. 0.8%, p=0.044) and at 1 year (26.0% vs. 8.9%, p<0.001). In the regression model, higher body mass index, diabetes mellitus, measured GFR < 60 ml/min, tricuspid regurgitation and the use of extra-coraporeal circulation during Ltx were independent predictors of postoperative AKI (p<0.001).

Conclusions: AKI affected more than 1/3 of the patients after Ltx, and was associated with increased time on mechanical ventilation, longer stay in the intensive care unit and increased mortality. The multivariate regression model had a modest predictive value, with increased time on mechanical ventilation, longer stay in the intensive care unit and thus we performed a retrospective analysis of AKI after Ltx at our unit.

AKI was associated with increased mortality at 30 days (5.5% vs. 3.5%, p<0.001). 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 day7 was 0.922 vs. 0.849, the sensitivity was 0.900 on day (when set the critical value for AKI as 25.19ng/ml), and the sensitivity on day 7 was 1(When the critical value was set 23.16ng/ml), and the specificity of urine cyst-C on day 1 vs. day7 was 0.795 and 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.

PO0070
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 and 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 16.0.

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. 31.1±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 7.94–18.34, p<0.001), a longer length of stay (2.6 days, 95% CI: 2.21–2.93 days, p<0.001), higher costs ($6707.2; 95% CI: $5812.6–$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.

Funding: Government Support - Non-U.S.
Patients on CRRT

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 untargeted 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.

Funding: Clinical Revenue 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 given high 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: Government Support - Non-U.S.
(10% Ca gluconate at fixed rate 5 ml/hour) was needed in 10/41 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

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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, 1573 (14.3%) with AKI and 9408 (85.7%) without AKI. Baseline demographics were significantly different between the two groups including age, race, length of hospital stay (>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 univariate 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 multivariate 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 medicine 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?

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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) 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 (4.9±8.75 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 0.7±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.

PO0077

Predicting Outcomes After AKI: Are You Better Than a Machine?

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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 (AUROC) at each time point.

Results: Data was captured from 56 patients with stage 2 AKI. Nephrology providers (n=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 research into this area and implement strategies to enhance prediction of recovery after AKI.

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PO0078

Short-Term Prognosis of Patients with Cardiorenal Syndrome Type 1-Induced AKI Requiring Continuous Renal Replacement Therapy

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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 (54.1%), 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), lesser respiratory variations in the IVC diameter (59.6% vs. 13.3%, p=0.002), lesser vasopressor requirement (96.5% vs. 31.9%, p=0.001), and lesser respirator 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.
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(55.2%), oxalate crystals in 10(33.3%), and hematuria in 9(30%). Median plasma oxalate at the time of biopsy was 18.3 [reference <2.0] μmol/L in 26 patients and median 24 hour urine oxalate excretion was 53 [reference [7.9-40.5]] 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 table 1. 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)

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: A total of 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 in the population of Chinese remains largely unknown.

Conclusions: The addition of IV contrast was not associated with an increased risk of Contrast-induced nephropathy (CIN) has been described as a significant cause of acute kidney injury (AKI). Although the nephrotoxic potential of vancomycin has widely been published, the contributory effect of these two agents towards AKI has not been fully elucidated. We sought to better define this interaction.

Methods: The primary objective of this retrospective cohort study was to compare the incidence of AKI among adult patients receiving vancomycin (VAN) and vancomycin plus IV contrast (VC) within 96 hours of administration. Secondary outcomes included time to AKI development, hospital length of stay (LOS), and 30-day, all-cause mortality. A logistic regression was performed to identify potential risk factors for AKI among vancomycin-treated patients.

Results: A total of 114 patients receiving 4 consecutive days of vancomycin were included, 50 receiving VAN and 64 receiving VC. An additional 50 patients who received IV contrast alone were independently assessed for CIN, of which only 3 (6%) developed AKI. In the unadjusted analysis, no statistically significant difference in the rate of AKI (10% vs 20.3%; p=0.13), days until AKI (6 days vs 5 days; p=0.37), highest vancomycin trough (16.7 vs 17.8; p=0.62), and hospital LOS (7.5 days vs 8 days; p=0.62) were found between VAN and VC patients. The addition of IV contrast to vancomycin was not an independent risk factor for AKI after adjusting for relevant confounders (aOR 1.65; 95% CI, 0.48-5.65; p=0.42).

Conclusions: The incidence of CIN was not associated with an increased risk of AKI in vancomycin-treated patients. The incidence of CIN was rare.
PO0082
Mortality Prediction of Serum Neutrophil Gelatinase-Associated Lipocalin in Patients Requiring Continuous Renal Replacement Therapy Byung ha Chung,1 Yohan Park,1 Hyung Duk Kim,1 Eun jeong Ko,1 Tae Hyun Ban,2 Cheol Whee Park,1 Chul Woo Yang.1 Seoul Saint Mary’s Hospital, Seoo-co-gu, Seoul, Republic of Korea; 2Eunpyeong Saint Mary’s Hospital, Eunpyeong-gu, Seoul, Republic of Korea.

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 for 28-day mortality (hazard ratio 2.405, 95% confidence interval 1.296-4.783, 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.

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Figure 1. Predictive value for 28-day mortality of serum NGAL level, APACHE-II score, and SOFA score in low APACHE-II score group

PO0084
Prevalence, Length of Stay, and Hospitalization of AKI in Patients with and Without Sjogren Syndrome Mohamedanwar M. Ghandour, Yahya M. Osman Malik. Wayne State University School of Medicine, Detroit, MI.

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 Christina J. Montogomerie,1 Jonas Spaak,1 Marie Evans,2 Stefan H. Jacobson.1 1Karolinska Institutet, Danderyd University Hospital, Department of Clinical Sciences, Division of Nephrology, Stockholm, Sweden; 2Karolinska University Hospital Huddinge Department of Renal Medicine, Stockholm, Sweden.

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 laboring optimal treatment strategies and optimal findings for patients outcomes in relation to cause of AKI in consecutive patients in a nephrology department.

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 ± 227.4 and 184.5 ± 184.5 μmol/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%), urina ry obstruction (11.2%) and renal that included sepsis (13.79%), cardio-renal syndrome (3.45%), drug induced nephrotoxicity (2.6%), other inclusion ATN (9.70%). Renal function recovery was complete in 44.8%, Partial in 22.4% whereas 32.8% did not have any recover. 6 (1.7%) 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 μmol/L while only 32% of the overall patients were alive at 12 months with s.creatinine (eGFR) (mean ± std dev) 161.8 ± 127.4L (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 convenience sample of 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.

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

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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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Background: Acute kidney injury (AKI) is a common and severe complication after left ventricular assist device (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 of renal function after RRT after LVAD can be expected in 50-55% of patients, although these estimates vary by LVAD type. Further studies are needed to understand the predictors of recovery after LVAD and its impact on patient survival.

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 RRT will be an important advance.

Methods: Our objective was to Identify which nephrologist intervention decrease the need of RRT. We analyze age, gender, comorbid conditions, cause of AKI, pharmacology therapy, cause of RRT, 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) (Figure 1). Only fluid adjustment decreases the risk of KRT (OR 0.74, 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) being fluid overload the main cause of KRT (IC 95% 0.76, 95% CI 0.65-0.89, p < 0.001). (Table 1)

Conclusions: In AKI, fluid adjustment was the most important nephrologist intervention to avoid KRT.
Usefulness of the Neutrophil-to-Lymphocyte and Platelet-to-Lymphocyte Ratios in Community-Acquired AKI

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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 73.22. Etiology of CA-AKI: prenephritic 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% of cases required hemodialysis and 12.5% died. Mean NLR was 9.14 ± 8.47. Mean PLR was 236.99 ± 228.41. NLR according to etiology was: prenephritic 8.55±6; renal 9.37±9.8; obstructive 13.99±14.82 (significant differences between obstructive and prenephritic). PLR according to etiology: prenephritic 228.31±216.34; renal 236.15±233.77; obstructive 320.37±304.89 (non-significant differences). Within the group prenephritic, 79 cases were complicated by acute tubular necrosis (ATN). These cases presented a higher NLR (10.7±8.47, 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 baseline (r=-0.237; p<0.001). The PLR also showed the same 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利亚lo 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 needed 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.

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 latest 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 obtained with the first analysis performed.

Conclusions: Tubular injury manifests with diverse histological changes. Efforts to establish protocols to harmonize biopsy practices, handle kidney biopsy and report results across clinical practice are needed to improve our understanding of this complex disease.

AKI and CKD Distribution in the Novel Clinical Phenotypes for Sepsis

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Background: Sepsis is the most common cause of Acute Kidney Injury (AKI) in critically ill patients. Four clinical phenotypes (alpha, beta, gamma, delta) of sepsis have been recently described. Our objective was to investigate which of these sepsis phenotypes were associated with severe AKI, chronic kidney disease (CKD), AKI with CKD, and acute kidney disease (AKD).

Methods: We examined the 4 phenotypes using patient data from a previously published multicenter sepsis trial. After excluding patients with end-stage kidney disease and missing data, we analyzed 1243 patients with septic shock. We described the prevalence of severe AKI within the first 24 hours defined as KDIGO stage 2 or 3 or stage 1 with [TIMP-2]/[IGF-BP7] at 6 hours >2.0. AKD was defined for patients with severe AKI as 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 (31.0%, overall p<0.0001). The delta was most common in the beta phenotype (52.8%, overall p<0.0001) while in the others was lower (31.4% in alpha, 28.6% in gamma, and 35.0% in delta). The highest prevalence of AKI with CKD was again in the beta phenotype (52.8%), 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 AKDI but these cases were less likely to progress to AKD.

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Day 1 biomarkers of GS-CSF, IL1, IL6, IL8, TNF-alpha, IL10, TNFR1, TNFR2, MIF, IGF 1, and IGF 2 were not statistically different between the two subgroups. However, patients in the Low HU subgroup had higher IL8, TNFR1, TNFR2, and DRS levels at day 8.

Conclusions: Using a person-centered analytic technique (i.e., LCA), we found two subgroups of patients with distinct health utility profiles with 90-day survival following acute kidney injury. Demographic, clinical, and biomarker characteristics associated with each subgroup may be used to identify patients at high risk of poor HRQOL.

Funding: NIDDK Support

PO0097

Safety and Efficacy of a New Simplified Regional Citrate Anticoagulation Protocol for Continuous Venovenous Hemodiﬁlration and Sustained Low-Efﬁciency Dialysis Focused on Acid-Base Balance Optimization and Prevention of Kidney Replacement Therapy-Induced Hypophosphatemia

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Background: Regional citrate anticoagulation (RCA) is the first-line anticoagulation strategy for Kidney Replacement Therapy (KRT) in Acute Kidney Injury (AKI). Hypophosphatemia is a common electrolyte disorder in the ICU, especially in course of prolonged and highly efﬁcient KRT. This pilot study is aimed at evaluating a simplified RCA protocol for Continuous Venovenous Hemodiﬁlration (CVVHDF) and Sustained Low Efﬁciency Dialysis (SLED), based on the combination of a low-concentration citrate solution with a phosphate-containing solution.

Methods: KRT was performed in ICU patients with AKI by the Prismax system (Baxter) and polyacrylonitrile AN69 filters (ST 150, 1.5 m2, Baxter), combining a 18 mmol/l pre-dilution trisodium citrate solution (Registoc 180, Baxter) with a phosphate-containing solution used as both dialysate and post-dilution replacement (TRALI 0, HPO 45, 1, Mg2+ 0.75, HCO3 - 22 mmol/l, Biphosphyl, Baxter). Calcium chloride (CaCl 10%) was infused in a central venous line to maintain the systemic Ca2+ within a normal range. In each patient three consecutive daily 8-h SLED sessions or 72-h CVVHDF were evaluated. Phosphorus (P) losses were replaced, when needed, with sodium glycophosphate pentahydrate (Glycophos® 20 mmol/20 ml, Fresenius Kabi Norge AS, Halden, Norway).

Results: 20 patients with AKI on SLED and 10 on CVVHDF were studied (mean APACHE II score 23.8). No premature interruptions for irreversible filter clotting occurred. Minimum dialyzed dosage was delivered in 95% of cases. No statistically signiﬁcant differences were observed between systemic ACT measured at KRT start and at different times during KRT. No major hemorrhagic events nor clinically relevant episodes of hypo- or hypercalcemia were observed. Acid-base status and serum phosphorus levels were effectively maintained.

Conclusions: Our simpliﬁed RCA protocol is safe and efficacious both for SLED and CVVHDF, allowing to optimize acid-base balance and to preventing KRT-related hypophosphatemia.

PO0098

Relationship Between the Presence of Infectious Disease and Clinical Outcomes of Patients with Cardiorenal Syndrome Type 1

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Background: Cardiorenal Syndrome type 1 (CRS-1) can be triggered by an infection. The pathophysiological basis is vascular congestion, which is why it has been treated with different strategies of diuretics, but in the presence of infection, the inflammatory, neurohumoral and hemodynamic effects can compromise the efficacy of the diuretic therapy and potentially worsen clinical evolution. Here we compare the clinical evolution during hospitalization of CRS-1 patients with and without infection.

Methods: This is a retrospective cohort study conducted in the Hospital Civil de Guadalajara “Fray Antonio Alcalde”, from January 2015 to September 2018. Conducted in CRS-1 patients, we showed the clinical evolution and diuretic strategies analyzed accounting for the presence or absence of infection.

Results: We identified 63 patients classified as having CRS-1, 28 (44.4%) were classified as having an infectious disease. The mean age was 62 years (±14.6) and 58 (±12.4) in the group with infection and no infection, respectively. There were no statistically signiﬁcant differences between the clinical outcomes of both groups. The median length of hospital stay was 8 days in the group with infection and 7 days in the group without infection (p=0.065). Three patients (10.7%) of the group with infection received renal replacement therapy and 1 patient (2.9%) in the group without infection (p=0.015). In the group with infection 31% of patients died (71%), whereas in the uninfected group there were no deaths (p=0.194). SCR values tend to diminish in a similar manner in both groups. We found that all patients received furosemide at least during the first five days of hospitalization and the strategy of the diuretic chosen was similar between groups. No statistical differences were observed in the clinical evolution of patients with CRS-1 is similar in the presence or absence of infection. We anticipate that this study may be a reason to expand knowledge in patients with CRS-1 and the presence of infection.
Design of START: A Phase 2 Study Evaluating the Safety and Efficacy of RBT-1 on Preconditioning Response Biomarkers in Subjects Undergoing Cardiac Surgery

Bluipinder Singh,1,2 Philip T. Lavin,1 Andreas Orfanos,3 Stacey Ruiz,2 Donald J. Keyser,2 Alvaro F. Guillen,2 Richard A. Zager,6,3 Navdeep Tangri,6 Jean-Claude Tardif,2 1University of California Irvine, University of California Irvine, Irvine, CA, US, Department of Medicine, Irvine, CA; 2Renibus Therapeutics, Southlake, TX; 3Montreal Health Innovations Coordinating Center, Montreal, QC, Canada; 4Fred Hutchinson Cancer Research Center, Seattle, WA; 5University of Washington Department of Medicine, Seattle, WA; 6University of Manitoba, University of Manitoba, Winnipeg, MB, CA, Winnipeg, MB, Canada; 7Institut De Cardiologie de Montreal, Montreal, QC, Canada; 8Boston 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.

Conclusions: The multinational START study will assess the cytoprotective preconditioning response to RBT-1 in subjects undergoing cardiac surgery.

Funding: Commercial Support - Renibus Therapeutics

PO0102
Use of Azathioprine in Treating Severe Corticosteroid-Resistant Acute Interstitial Nephritis
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Introduction: Acute interstitial nephritis (AIN) is a pattern of renal injury characterized by inflammatory infiltrate in renal interstitium leading to decline in renal function. It is commonly caused by drugs such as penicillin, diuretics and proton pump inhibitors. Other causes include autoimmune diseases or systemic infections. Treatment involves removing the offending agent and steroids in severe cases. We describe a case of drug induced severe AIN refractory to steroids that is treated with azathioprine, an immunosuppressant drug that inhibits purine synthesis.

Case Description: A 20 year old Caucasian female with past medical history of gastroesophageal reflux disease (GERD) presented to the emergency with severe nausea, vomiting and oliguria. She had been taking omeprazole for 2 weeks prior to presentation. Initial labs indicated eosinophilia, raised creatinine levels of 3.5 mg/dl and Blood Urea Nitrogen of 27 mg/dl. Renal biopsy was done which showed severe acute interstitial nephritis with raised eosinophils. The diagnosis of Acute Kidney Injury secondary to drug induced AIN was made and patient was given pulse dose steroids for 3 days. She was discharged on 60 mg of prednisolone daily. A month later, the patient’s creatinine improved to 1.75 from a peak of 6.27 mg/dl. The steroid dose was tapered to 40 mg. However, the creatinine raised to 2.7 mg/dl again due to which prednisolone dose was

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

Underline represents presenting author.
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 in future as an adjuvant or alternative first line 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.

PO0103
The Successful Treatment of Bile Cast Nephropathy with Plasma Exchange
Sweeth Reddy, Theresa Kinard, Margaret Ryan, Leslie F. Thomas. Mayo Clinic Arizona, Scottsdale, AZ.

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 Bile Cast Nephropathy with bile cast nephropathy using therapeutic plasma exchange (TPE).

Case Description: CASE 1: A 59 year old man with stage 3 colon carcinoma on Cepectabine developed chemotherapy-induced liver toxicity resulting in severe cholestasis and biopsy-proven bile cast nephropathy. He underwent TPE. CASE 2: A 69 year old man with colon cancer post remote ileocolic anastomosis and lower extremity edema 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 prior to and after TPE therapy is noted in Table 1.

Discussion: In 1970, TPE was introduced as a treatment modality for 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.

PO0104
An Unusual Case of IgA Nephropathy Associated with Parvovirus B19
Lalith S. Lakhanli, 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 hepatitis like glomerulonephritis with endocapillary proliferation. We describe a unique case of IgA Nephropathy (IgAN) in an African American patient associated with Parvovirus B19.

Case Description: A 23 year old African American female with a history of Hemoglobinopathies was diagnosed with 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 prior to and after TPE therapy is noted in Table 1.

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Renal Artery Thrombosis in a Patient Homozygous for Plasminogen Activator Inhibitor-1 4G Allele

American College of Physicians, Philadelphia, PA.

Introduction: Renal artery thrombosis is a serious, uncommon, and often undiagnosed condition. Physicians need to consider this diagnosis in unexplained flank pain, especially in the presence of risk factors. Plasminogen activator inhibitor-1 (PAI-1) is the major inhibitor of tissue-type plasminogen activator. Fibrinolysis is impaired due to increased plasma PAI-1 levels which play an important role in the pathogenesis of thrombotic disorders. Homozygous for the 4G allele had increased plasma PAI-1 concentrations.

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, glucose and blood. Creatinine was 1.6 and the baseline was unknown. CTA showed right renal artery occlusion. The patient was transferred to ICU and started on levodipine 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’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 settings. 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.

Ganja Kidney: Acute Tubular Injury Associated with Synthetic Marijuana, A Rising Incidence

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Introduction: Synthetic cannabinoids (SC), “Ganja”, have been used as recreational drugs producing a increasing popularity 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/min, 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. Interstitial hemorrhosis was identified but later discontinued after renal recovery. On discharge, serum creatinine was 1.2 mg/dl.

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 nephrotic agents.
PO0110
The Emerging Role of Bedside Doppler Ultrasound for Precise Assessment of Venous Congestion in Cardiorenal Syndrome
Abhilash Koralata,1 Saqib Mahmud,1 Olanrewaju A. Olayo,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.

PO0112
Hypothyroidism-Induced AKI: A Case Series
Soomathi Ramnieni, 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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PO0111
Furosemide: An Unusual Cause of Acute Interstitial Nephritis Requiring Hemodialysis: First Case Report
Hassan Alhalaibi. 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-GBM, and SPEP/UPEP. Urinalysis showed small blood, no protein, 12-15 RBC’s, 10 WBC’s. Renal ultrasound was normal. A kidney biopsy was performed which demonstrated interstitial edema with patchy inflammatory cell infiltrates with eosinophils. The tubules were dilated and showed significant degenerative changes in tubular epithelial cells. The patient was started on treatment for acute interstitial nephritis with oral prednisone 60 mg daily with a subsequent slow taper. Kidneys did not recover and he was placed on hemodialysis three times a week with close monitoring of kidney functions.

Discussion: Furosemide, a loop diuretic, is widely used for volume control. To our knowledge, this is the first report of AIN associated with loop diuretics that resulted in severe and requiring hemodialysis. Unfortunately, our patient did not respond to high dose steroids and he continued to require hemodialysis three times a week. Our report highlights the importance of close monitoring of any potential toxicities that may be associated with such medications.
Introduction: Renal cortical necrosis (RCN) is a rare cause of acute kidney injury (AKI) accounting for 1-2% of cases. It is most often associated with obstetric emergencies in developing countries. The most common non-obstetric etiology is hemolytic uremic syndrome, but it has also been described in renal allograft rejection, sepsis, and in rare cases pancreatitis where ten cases have been reported. We describe a case of severe renal cortical necrosis in a previously healthy young man with acute pancreatitis.

Case Description: A 29-year-old man with no significant medical history presented with severe epigastric pain and anuria for three days. He was diagnosed with alcohol-induced pancreatitis with a lipase level of 35,534U/L and AKI with a creatinine of 5.8mg/dL (baseline 1.2mg/dL). The anuria did not improve with fluid resuscitation, the AKI progressed and he 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 20ml/min/1.73m². 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, vasospasm and endothelial injury resulting in ischemia. 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.

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

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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 exploitation and antibiotic spacer placement initially presented to the ED with fever, rash, and pruritus. She was treated with cefepime and vancomycin for probable 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 daptomycin. 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.

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 [7.35x10^9/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 discharged on a higher dose of 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.

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 for 5 days. Preliminary results showed IgA nephropathy with oxford classification score 5.18mg/dL from 1.1mg/dL one month prior). The patient was recently started on rivaroxaban for 5 days. Preliminary results showed IgA nephropathy with oxford classification score 5. Prolonged corticosteroid treatment is often required as relapse after initial improvement is not uncommon.

Discussion: The use of novel oral anticoagulants (NOAC), has become prevalent in the medical community as a treatment strategy for various diseases. While previous cases have been mostly described in patients on warfarin, this case illustrates the importance of recognizing the new phenomenon of ARN as a risk factor for patients on NOACs. Due to limited data and no prospective studies, expert opinion has recommended switching one oral anticoagulant to another or reducing the dose of the offending agent. Further research is needed to understand this disease process to help design prevention and treatment strategies.

Gross Hematuria, Intense Interstitial Hemorrhages, Red Blood Cell Casts: An Atypical Triad of Amoxicillin-Clavulanate-Induced Acute Tubulointerstitial Nephritis
Ramzi A. Rahman, Farooq Ahmad, Mohammed Akhtar, Muhammad Asim. Hamad Medical Corporation, Doha, Qatar.

Introduction: Drug induced tubulointerstitial nephritis (TIN) usually presents with acute kidney injury, pyuria, white cell casts and micro-hematuria. We report this case to highlight a unique pattern of presentation.

Case Description: A 33-years-old man presented with gross hematuria and acute kidney injury three weeks after a throat infection treated with Amoxicillin-Clavulanate. He denied any previous episodes of hematuria, family history of renal disease or use of any other medication. Physical examination was normal other than mild cervical and axillary lymphadenopathy. Laboratory tests revealed serum Creatinine of 5.3mg/dL, hematuria, sterility pyuria and minimal proteinuria. Immunoregulation screen and renal ultrasound were normal. Peripheral blood smear demonstrated eosinophilia and 7% blast cells. Flow cytometry and bone marrow studies confirmed Acute T-cell Lymphoblastic Leukemia. Kidney biopsy showed acute interstitial nephritis but normal glomeruli. The most striking features were multifocal intense interstitial hemorrhages, abundant red blood cells casts (RBC) in several tubules and RBC casts in some. Direct immunofluorescence, SV40 staining and immunohistochemical studies for leukemia infiltration were negative. Treatment with systemic steroids was initiated. Serum creatinine started to decrease within 3 days. Steroids were continued as a part of induction chemotherapy instituted subsequently for leukemia. Renal function normalized and hematuria subsided within 2 months.

Discussion: Drug induced TIN can present with atypical features masquerading as glomerulonephritis, vasculitis or infectious interstitial nephritis. It is plausible that severe infection led to a major decrease in circulating interstitial vascular walls resulting in interstitial hemorrhages that extended into the tubules through ruptured basement membrane producing gross hematuria and RBC casts.
PO0123

IgG4-Related Disease with Renal Involvement in a Patient with HIV Infection
Karen Flores, Samir V. Parikh, Ganesh B. Shidham. The Ohio State University, Columbus, OH.

Introduction: Immunoglobulin G4-related disease (IgG4-RD) is a fibroinflammatory disease that can affect multiple organs. It is characterized by lymphadenopathy and diffuse enlargement of one or multiple organs. Pathologic features include tissue infiltration by IgG4-positive plasma cells, storiform fibrosis, and increased tissue eosinophils. Tubulointerstitial nephritis is the most common renal manifestation. We describe a case of IgG4-RD in a patient with co-existing HIV infection.

Case Description: A 60-year-old male with CKD 3, hypertension, hepatitis B, and HIV was hospitalized due to malaise and acute kidney injury with serum creatinine of 4.2 mg/dL and 1.5 g/dL proteinuria. HIV was controlled with undetectable viral load on treatment. Infectious work up was negative. CT scan showed diffuse retroperitoneal lymphadenopathy. PET scan showed diffuse lymphoproliferative disease and increased uptake in lymph nodes of the neck, axilla, and anterior and posterior mediastinum. Right inguinal lymph node biopsy showed dense interfollicular T-cell infiltrate and dense polytypic plasmacytic infiltrate with a kappa/lambda ratio of 3:1 by IGH. TCR gene rearrangement and IGH studies were negative for a monoclonal population. Testing for HIV and HBV was negative. SPEP showed a small Bence-Jones clone (0.3 g/dL). UPEP showed a small amount of lambda free light chains. Bone marrow biopsy showed no evidence of T cell lymphoma but revealed hypolamellar marrow. Total IgG (5048 mg/dL) and IgG (572 mg/dL) were elevated and both C3 and C4 were low. Kidney biopsy revealed dense interstitial infiltration of plasma cells strongly positive for IgG (>50/hpf) and no electron dense deposits. The patient was diagnosed with IgG4-RD with renal involvement. He was treated with high dose prednisone and mycophenolate mofetil. Renal function improved from 4.6 mg/dL to a 1.9mg/dL after 3 months of IgG4 levels improved 70mg/dL and C3/C4 normalized suggesting disease control had been achieved.

Discussion: We describe a case of IgG4-RD with renal involvement in a patient with HIV infection. There are only a few reports in the literature. Differential diagnosis of kidney disease during HIV infection is broad. IgG4-RD is a severe systemic disorder that can be mistaken for infection or malignancy. IgG4-RD should be considered in the differential for acute kidney injury in the setting of HIV.

PO0124

Renal Replacement Therapy in Pheochromocytoma
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Introduction: Pheochromocytoma is a rare tumor derived from chromaffin cells of the sympathetic nervous system. The triad of headache, palpitations and diaphoresis is often present, but catecholamine excess can present in various contexts. Tumors secreting epinephrine can present with episodic hypotension; rapid cycling fluctuations of hypotension and hypertension also occur. Most acute kidney injury (AKI) in the setting of pheochromocytoma crisis is due to ischemic acute tubular necrosis (ATN). For cases requiring renal replacement therapy, there are no studies supporting one form over another. We describe a patient with Pheochromocytoma who developed AKI requiring renal replacement therapy (RRT).

Case Description: 29 year old woman with history of migraines presented to outside hospital with headache and chest pain, and found to be in hypertensive emergency with mild elevation of troponins. Patient was transferred to our hospital for evaluation of possible myocardial infarction. Cardiac catheterization showed clear coronaries. Patient became hypotensive during the procedure and Intra-Aortic Balloon Pump was placed. Imaging showed high density mass in the left adrenal gland. Patient was started on Phenoxybenzamine. Biochemical tests confirmed Pheochromocytoma. Labs showed creatinine of 5.38. Patient became amric and RRT was initiated with intermittent hemodialysis (iHD). Due to the acute dialysis need, high dose hydroxyurea and mycophenolate mofetil had good pressure fluctuations and became hypotensive with decreased responsiveness. Imaging was negative for acute bleed but concerning for cerebral edema. RRT was switched to continuous renal replacement therapy (CRRT) which was better tolerated.

Discussion: 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 cardio toxicity which in turn leads to ischemic ATN. Patient was able to tolerate iHD 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...
cerebral edema in the setting of Pneumocystis jirovecii, 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 neurotropic ophthalmia in patients with HIV infection. Nephrotoxicity 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 57-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 neurotropic ophthalmia. 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 alkalize her urine but Scr remained 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 nephrotoxicity is a very rare occurrence in clinical practice. Hence, clinicians 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 pneumonia 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 progressively increased 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. Admission and COVID-19 PCR was positive. Other labs included: peak AST 1692 U/L and ALT 291U/L, ferritin 1436 ng/ml, 4.86fmg/dL, D-Dimer 2330 2Dd, 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 kidney injury due to rhabdomyolysis. He was treated initially for 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 pre-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 included 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 (~15 cm each) with irregular outlines and multiple parenchymal hypoechogenic to heterogeneous 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-reticular 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 the 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. Hydronephrosis may be noted on RUS if there is compression of the renal hilum or ureters by the lymphomatous tissue. Nephrologists performing point of care ultrasonography should 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
Yuko Shibata, Kazuhiro Fukuoka, Shinya Kaname. Kyorin university school of medicine Kyorin Daigaku, Mitaka, Japan.

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 depositions 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 readmitted 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 completed remission was achieved a few weeks later. Electron microscopy of the 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 might have been precipitated by influenza infection or some unknown factor.

PO0129
Thrombotic Microangiopathy with Acute Interstitial Nephritis

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 generalized edema and decreased bilateral lower extremity pulses. The patient was started on hemodialysis and his renal function improved and he was discharged from dialysis. However, he was rehospitalized two weeks later due to return of bilateral lower extremity edema. Additional symptoms included one week of general malaise, persistent cough, and left lower quadrant pain. The patient was 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 heterogeneous 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-reticular 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 the 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. Hydronephrosis may be noted on RUS if there is compression of the renal hilum or ureters by the lymphomatous tissue. Nephrologists performing point of care ultrasonography should 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.
examination revealed an obese man with bilateral lower extremity edema, eczematous rash, and mottled discoloration 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 infectious, and connective tissue diseases was ordered and results were unrevealing. ADAMTS13 activity was decreased at 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:** Thrombocytopenia is characterized by endothelial damage causing microangiopathic hemolytic anemia, thrombocytopenia, and end-organ damage. TMA can be attributed to genetic or acquired autoimmunity, 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**

Zhubiz Solhjou,2 Ignacio A. Portales Castillo,2 Bassem Mikhail,2 Nicholas Chedid,1 Ebrahim Barkoudah,1 Alice M. Sheridan.2 Brigham and Women’s Hospital, Department of Medicine, Boston, MA; 2Brigham and Women’s Hospital, Renal Division, Boston, MA.

**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. Despite the viral injury to tubular epithelial cells and podocytes, rhabdomyolysis has also been described. Rhabdomyolysis has been reported in infection with SARS-CoV-2, Respiratory Syncytial Virus and Influenza A. Although mild CK elevation was reported in cohorts of patients with COVID-19 and there is a single case report of late onset rhabdomyolysis, overt rhabdomyolysis in SARS-CoV-2 infection 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 4 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 mild tachypnea, but no hypoxia. Lungs were clear and all muscle groups were soft and non-tender. Pneumocystis carinii pneumonia was by 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+ RBC by 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 mcg/L respectively on day 5. He received isotonic intravascular (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, dictship 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 especially 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.
fear and eosinophilia, and is usually a diagnosis of exclusion. On renal biopsy (Bx), DI-AIN usually presents with interstitial inflammation rich with eosinophils and plasma cells and, in rare occasions, with neutrophils. Here, we report a Zosyn induce neutrophil-rich AIN case.

**Case Description:** A 40-year-old female with medical history breast cancer came with fever, pain and induration over her left breast. On admission she got Zosyn for suspected breast abscess. Next day, AKI noted, creatinine (Cr) increased from 0.6 to 3.3mg/dL. She remained hemodynamically stable. Laboratory showed no anemia, leukocytosis or peripheral eosinophilia. BUN/Cr of 38/4.7. Urinalysis negative for protein, blood, crystals, casts, white blood cells, red blood cells, nitrites, uric acid, and chloride <20mmol/L, positive urine eosinophils. Negative autoimmune and hepatitis B/C work up. Blood and urine cultures were negative. Renal bladder ultrasound (US) showed normal kidney size with no sign of infection. Breast US findings were concerning for neoplasm. Zosyn was held and prednisone (1mg/kg) was given for suspicious of DI-AIN. Renal Bx was done showing interstitial inflammation rich with neutrophils and neutrophilic 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 of 2.36. 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 AIN as repeated 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 initiation of steroid can prevent further kidney injury or potential chronic kidney disease.

**PO0134**

A Case of BK Polyomavirus-Associated Nephropathy of Native Kidneys in a 19-Year-Old Woman with a History of Orthotopic Cardiac Allotransplantation

**Introduction:** BK polyoma virus associated nephropathy (BKPvAN) is common among kidney transplant recipients. Approximately one to ten percent of kidney transplant recipients will develop BKPvAN. BKPvAN can lead to failure of the transplanted kidney allograft.

**Case Description:** A 20-year-old woman who had orthotopic cardiac allotransplantation in November of 2016 presented to the hospital in January of 2020 with upper respiratory tract infection like symptoms. Her baseline serum creatinine was 1.4 mg/dL three months prior to presentation. Her maintenance immunosuppression included tacrolimus and sirolimus. On admission her serum creatinine was 4.4 mg/dL.

**Discussion:** BK polyoma virus associated nephropathy of native kidneys is relatively rare. Upon our research we have only found a few case reports.
Urinary abnormalities in 20 patients with EVALI

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PO0138

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 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

Figure 1. Kidney Biomarker Trends from Time 1 (24-48 hours) to Time 2 (5-7 Days)

Figure 2. Receiver operating characteristic curves for MAKE-Discharge

PO0139

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 chemoattractant 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

PO0140

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 < 0.0001) 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.

Figure 1. Risk of 28-day mortality by Day 0 KIM-1 level

Table 1: Risk of 28-day mortality by Day 0 KIM-1 level

<table>
<thead>
<tr>
<th>Day 0 KIM-1 (log 10% SD)</th>
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<th>Adjusted HR for Urine Creatinine (95% CI)</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.
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 diuresis. The imperfections of Scr or Cys to estimate GFR in non-steady state could contribute to misinformation of kidney function 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 Scr, CKD EPI Cys, CKD EPI Cr, 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 Scr, r=0.81; CKD EPI Cys, r=0.81; CKD EPI Cr, r=0.84; sMDRD, r=0.81; kGFR, r=0.81, p=0.0001). CKD EPI Cr 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. KIDGO Scr-based AKI criteria frequently failed to detect relevant decreases of mGFR (Sensitivity 55%).

Conclusions: In patients hospitalized for ADHF undergoing decongestion, 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. KIDGO 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.

Funding: Commercial Support - FAST Biomedical

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 beneficial 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-hydroxynoneal and neutrophils, respectively. Anti-inflammatory cytokine levels were measured by enzyme-linked immunosassay.

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.

Funding: Private Foundation Support

PO0143

Although Human Mesenchymal Stem Cells Effectively Treat AKI in Rats, They Elicit an Immune Response, Abolishing Their Subsequent Protective Activity
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Background: Preclinical and clinical studies have shown reprotective effects of allogeneic Mesenchymal Stem Cell Therapy (MSC) in preventing AKI, obtained without eliciting an antibody response, confirming MSCs’ immune privileged/immune-modulating properties. Many groups have attempted to enhance MSCs’ potency by introducing beneficial genes via xenogeneic expression vectors. Whether such alterations conserve MSCs’ immune privileged characteristics is unknown. We here tested whether (1) the expression of human antigens by MSCs from Fischer344 (F344) rats transgenic for human Alkaline Phosphatase (hPAP) in human MSCs (hMSC) or human Adipose-derived Stem Cells (hASC) alters the cells’ reprotective function in female F344 rats with IRI-induced AKI; (2) whether the administration of these cells elicits an antibody response; (3) whether such a response affects the re-protective efficacy of the cells in subsequent treatments.

Methods: RBC AKI (42 min. bilateral pedicle clamp) was induced (n=6/group). Post reflow, groups were infused with the suprarenal aorta (s.a.) with hPAP+MSC, hASCs or hMSC, 0.5-2x10^6 cells), or vehicle. Ten days post-AKI, serum samples were obtained and analyzed by FACS to assess for antigenic responses (IgG antibodies to (1) MSC-specific genes, or (2) hPAP. Two more groups of F344 rats (n=6 each) were inoculated i.p. with hASC (5x10^5). Immune response to hASCs was assessed 14 days post inoculation, and RBC AKI was induced as above, followed upon reflow by an identical s.a. infusion of hASCs or vehicle.
Results: Versus controls, all 3 cell types significantly protected renal function and hastened AKI recovery (p<0.05). Autologous marrow or allogeneic exosomes 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 xenogeneic expression vectors for genes meant to enhance MSCs' clinical efficacy. (Not U of Utah work)

Funding: Commercial Support - SymbioCellTech, LLC

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, 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 harvested 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 5 groups of male F344 rats (~200 g wt.; n=7 each). Upon reflow, groups were infused (suprarenal aorta) with either (1) 1x10^6 ASCs, (2) 1x10^6 autologous SVF cells, (3) 1x10^6 syngeneic, cultured MSCs, (4) and (5) vehicle in animals with or without fat harvest.

Results: Outcome were compared to those of sham treated animals (n=7). Renal failure 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 liposaprate, 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 insult 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' reperfusion 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 (nanosight), protein and gene expression of relevant markers. I/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 administered via left carotid artery either 1 ml of Vehicle (PBS; n=8), Exosomes (200μg protein equivalent; ~4x10e10 exosomes; n=6), or MSCs (2x10e6; n=6) on Day 3.

Results: 1x10e6 MSCs secrete ~ 4.9x10e10 exosomes and other microvesicles (mode 1.36; median 0.87 x10e10) and they express CD44 and CD29, and carry mRNAs of renoprotective genes expressed in MSCs. While both MSC and exosome administration improved survival over PBS, renal function only showed significant and sustained improvement in exosome-treated rats.

Conclusions: MSC-derived exosome therapy days 3 post progressive AKI, when renal blood flow is significantly impaired and when most clinical AKI is diagnosed, is superior to MSC therapy, likely due to their ability to deliver their renoprotective cargo into the compromised renal microcirculation. These data have, we posit, significant translational promise for the development of an effective rescue therapy for advanced AKI. (No University of Utah resources were used for this work.)

Funding: Commercial Support - SymbioCellTech, LLC

PO0146

Microparticles Released in Response to AKI May Influence Glucose and Salt Metabolism

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Background: Renal epithelial injury due to ischemia or toxic/inflammatory insults is the primary cause of acute kidney injury (AKI). Due to their high metabolic activity renal tubular epithelial cells (RPTEC) are especially vulnerable to damage leading to a clinical syndrome of disruption in salt, water and glucose homeostasis. 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 the release of MP carrying SGLT2, and SL12123 (NCC) in response to kidney injury. Immortalized RPTEC lines were treated with Oxidative stress (H2O2) or inflammatory stress (TNFα) agents by the validated methodology to study in vitro models of AKI. 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 SGLT2, and SL12123 (NCC). FlowJo software was used for analysis. Mann-Whitney test was used for comparisons.

Results: RPTEC models of injury (H2O2) resulted in a significant increase in the release of MP positive for SGLT2 MP 5.49 X 10^10/ml vs 0.41 X 10^10/ml for control cells (p=0.05) and NCC (SL12123) 4.2 x 10^6 vs 0.63 X 10^6 for control cells (p=0.05). Similar changes were observed when cells were treated with TNFα (p=0.05) for SGLT2 and NCC. We also confirmed the presence of MP containing SGLT2 and NCC in AKI (104.60 X10^10/ml and 1.77 X 10^10/ml, respectively). However, when compared to controls, the difference was statistically similar.

Conclusions: This is one of the first reports to confirm that key transporters from renal epithelium can be released and detected as MP in both in vitro and clinical settings of AKI. These findings may provide novel insights into the mechanisms of glucose, salt and water dysregulation during kidney injury and repair.

PO0147

Sex as a Biological Variable in Cardiac Outcomes after AKI in Mice

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Background: Acute kidney injury (AKI) is common in patients, and predisposes patients to cardiovascular disease. Estrogen is known to protect against ischemic AKI, however it is unknown whether it also protects against the cardiac sequelae of AKI. We report a 1 year study evaluating the cardiac and metabolic effects of bilateral renal ischemia-reperfusion injury in male and female C57BL/6 mice.

Methods: Males received 25 minutes of ischemia, while females received 34 minutes. Serial glomerular filtration rate (GFR), echocardiograms and blood pressure assessments were performed with sacrifice at 1 year. Plasma and cardiac metabolites were measured. Mead's resource calculation was utilized to calculate sample size of n = 5-11. Comparison between two groups was performed using unpaired t tests assuming Gaussian distribution with Welch's correction, P < 0.05 for statistical significance.

Results: Serial measurements of GFR showed that the AKI model was matched with Welch's correction, P < 0.05 for statistical significance.

Conclusions: This is the first study to show chronic diastolic dysfunction after AKI and variations in cardiorenal outcomes with regards to sex. Diminished cardiac ATP is a potential cause of cardiac dysfunction.

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 report that all 3 variants had altered cell surface KIM-1 expression compared to wild-type. Importantly, the phagocytes phenotype of apoptosis was significantly reduced in HEK-293 cells expressing each of the KIM-1 variants compared to those expressing wild-type KIM-1, indicating that mutations in these coding regions contribute to a functional impairment of KIM-1 activity.

Conclusions: This is the first study suggesting that human polymorphic variants in HAVCR1 may have consequences on the functional role of the KIM-1 protein in the kidney. This work strengthens the plausibility of a biological role for KIM-1 during AKI.

Funding: Government Support - Non-U.S.

PO0150

Sympathetic Signaling in Macrophages Mitigates Systemic Inflammatory Response and Renal Ischemia-Reperfusion Injury

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Background: The sympathetic nervous system is known to control immune cell dynamics. However, the detailed role of sympathetic signaling in inflammatory diseases is still unclear. Here, we focused on sympathetic signaling in macrophages and aimed to determine whether its activation attenuates lipopolysaccharide (LPS)-induced sepsis and renal ischemia/reperfusion injury (rIRI).

Methods: In vivo Three types of macrophages (RAW 264.7 cells [murine macrophage cell line], murine peritoneal cells, and differentiated U937 cells [human monocyte cell line]) were used to determine the effects of sympathetic signaling, especially β, adrenergic receptor (ADRB2) signaling, on LPS-induced proinflammatory cytokine (TNF-α) production. In vivo: We examined the effects of salbutamol (β2-selective agonist) on LPS-induced sepsis and rIRI models. Macrophage-specific ADRB2 conditional knockout (ADRB2 cKO) mice were used to elucidate the contribution of ADRB2 signaling in macrophages.

Results: In vivo Norepinephrine, a main sympathetic neurotransmitter, reduced LPS-induced TNF-α production in the three types of macrophages. This anti-inflammatory effect was also induced by salbutamol and reversed by butoxamine (β, selective antagonist) in a dose-dependent manner, indicating the importance of ADRB2 in this process. Furthermore, T-cell immunoglobulin and mucin-3 (TIM-3) expression was upregulated in macrophages by ADRB2 signaling and partially mediated the anti-inflammatory phenotype. In vitro: Salbutamol administration immediately before LPS treatment significantly reduced plasma TNF-α levels in mice, which was mitigated in macrophage-specific ADRB2 cKO mice. Salbutamol administration 24 h before rIRI also attenuated acute kidney injury, which was relieved in macrophage-specific ADRB2 cKO mice. The protection against rIRI was abolished in the mice in which splenectomy was performed 10 days before salbutamol administration, which suggests the contribution of splenic macrophages to the protective effects. In fact, adoptive transfer of salbutamol-treated splenic macrophages conferred protection to the recipient mice subjected to rIRI.

Conclusions: Sympathetic signaling via ADRB2 in macrophages attenuates systemic inflammatory response and rIRI. Phenotypic alterations in splenic macrophages might play critical roles in the protection against rIRI.

Funding: Government Support - Non-U.S.

PO0148

Glomerular Filtration Fails to Increase During Pregnancy After Cardiac ATP whereas Females did not.

AKI Mechanisms - 1

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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 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 demise, and mild uremia in the dams. In the current study, we hypothesized that glomerular filtration failure to increase during pregnancy in these dams after recovery from IR.

Methods: Female Sprague Dawley rats (10 weeks of age, n=3) were implanted with telemeters into the femoral artery for continuous BP measurements. Following 10 days of recovery, rats were randomized to receive either 45 minutes of warm, bilateral renal ischemia or sham surgery. Rats were then given 1 month to recover. Full recovery from IR was confirmed by return of plasma creatinine and urine protein excretion to baseline prior to mating. Vaginal smears were performed daily once mating began, to identify gestational day 1. 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 area under the curve analysis (2080±33 vs 2184±16, p<0.05, t-test). Glomerular filtration rate was significantly higher in control vs 1.2mmHg in IR dams (3.1±0.7ml/min vs 1.6±0.1ml/min, p<0.05).

Conclusions: These data suggest that after recovery from IR, the kidneys are unable to appropriately increase glomerular filtration rate during pregnancy. Ongoing studies in the laboratory are focused on alterations in plasma volume expansion during pregnancy after IR. We propose that plasma volume expansion, characteristic of normal pregnancy, is essential to maintain renal perfusion and prevent fetal growth.

Funding: Other NIH Support - NHLBI K9 H150281 and NHLBI P01 HL134604

PO0149

Polymorphisms in HAVCR1 Alter KIM-1-Mediated Phagocytosis

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Background: Renal ischemia reperfusion injury (IRI), necrotic cells, and apoptotic tubular epithelial cells (TECs) undergoing secondary necrosis, release their immunogenic contents into the extracellular milieu, exacerbating inflammation. Kidney Injury Molecule-1 (KIM-1) is a cell-surface glycoprotein upregulated on TECs during acute kidney injury (AKI). We previously uncovered that KIM-1 protects against renal IRI by enabling TECs to bind and engulf dying neighbouring cells, limiting inflammation and tissue damage. The gene encoding KIM-1 (HAVCR1) and tissue damage. The gene encoding KIM-1 hypothesized that the relevance of human KIM-1 polymorphisms in renal IRI has not been studied. We assessed the in vitro activity of HAVCR1 in immortalized cell lines and tissue samples. HAVCR1 expression in immortalized renal cell lines was significantly reduced in HEK-293 cells expressing each of the KIM-1 variants compared to those expressing wild-type KIM-1, indicating that mutations in these coding regions contribute to a functional impairment of KIM-1 activity.

Methods: Using site-directed mutagenesis, we generated constructs for 3 high-frequency HAVCR1 coding variants in addition to an expression plasmid encoding wild-type KIM-1 (pcDNA3-KIM-1). We then expressed the pcDNA3 vector, or HAVCR1 variants in HEK-293 cells using stable transfection.

Conclusions: While serum creatinine and GFR were significantly reduced in HEK-293 cells expressing each of the KIM-1 variants compared to those expressing wild-type KIM-1, indicating that mutations in these coding regions contribute to a functional impairment of KIM-1 activity.

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

PO0151

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 reperfusion injury. 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, BALB/c mice were perfused with radiolabeled [3H]LDHA-labeled macrophages (BDMD) from wild-type and LysM-Cre LDHA knockout (LDHA KO) mice grown in M-CSF for 7 days and then polarized with IFN-γ for 24 h. To test the effect of myeloid deletion on AKI, in vivo studies were performed using wild-type and LDHA KO mice using a bilateral IR model. In vivo LDHA KO mice had a significant decrease in essential glycolytic switch machinery in addition to the decrease in the efficiency of oxidative phosphorylation. As a result, LDHA deficient BDMD showed a diminished proinflammatory and fibrotic profile ensuing lesser renal fibrosis despite similar functional injury in both genotypes. These results suggest that LDHA is a potential target to manipulate immunometabolism in the pathogenesis of AKI.

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

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Underlines represent presenting author.
**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 NGAL mRNA expression levels. Histological damage was assessed by light microscopic analysis of H&E stained kidney sections. In different sets 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 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 with PD-1−/−, 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 cytoskeleton rearrangement and microtubule movement related to cell motility, granule release and cell division.

**Funding:** NIDDK Support

**PO0153**

**ST2/IL33 Signaling Axis in Tregs Critical for Restoring Kidney Tissues Homeostasis on Injury**

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**Background:** Renal diseases are a major cause of morbidity and mortality worldwide. Thus, leading to a great financial burden on health care systems. Inflammation elicited by a variety of cytokines and chemokines is a major player in the initiation and progression of the disease. Interleukin 33 (IL-33) acts as an ‘alarm’ that regulates the immune response during injury. IL-33 acts in an autocrine/paracrine manner through membrane receptor (ST2) aka IL33R or IL-1 receptor-like 1 (IL1RL1), triggering an innate and adaptive immune response. There is no evidence determining the importance of the ST2/IL33 axis in Tregs during kidney injury. In this study, we attempt to delineate the role of the ST2/IL33 pathway in Tregs cells using murine renal injury models and kidney organoids.

**Methods:** Murine ischemia-reperfusion injury (IRI) model was used to investigate the importance of cell-specific ST2/IL33 signaling using IL1RL1+/+ and Foxp3-cre mice to delete ST2 expression in Tregs. RNA sequencing analysis, flow cytometry, histology, immunohistochemistry, quantitative gene expression, and biochemical analysis were applied to dissect the role of ST2/IL33 signaling. Kidney organoid based 3D cell culture platform was used to setup co-culture experiments with ST2+/− and ST2+/+ Tregs for invitro evaluation.

**Results:** The RNA sequencing analysis of ST2-High Tregs indicated higher expression of regenerative factors such as angiopoietin (AREG) and Growth/differentiation factor 15 (GDF15). The in vitro renal injury experimental data indicated that elimination of ST2/IL33 axis was critical in exacerbation of renal injury leading to worsening of renal function as determined by plasma creatinine, blood urea nitrogen, kidney injury markers (Kim) and NGal) and fibrosis markers (Coll1α, Col3α1, SMA, and vimentin). Co-culture of kidney organoids with ST2+/+ expressing Tregs protected organoids from cellular apoptosis under invitro ischemia-reoxygenation conditions compared to ST2−/− Tregs.

**Conclusions:** Impairment of ST2/IL33 signaling in Tregs leads to worsening of renal function following ischemic injury. This indicating that activation of ST2/IL33 signaling in Tregs is critical in the regulation of inflammation, apoptosis, and repair in renal tissue during inflammation and injury.

**Funding:** NIDDK Support, Other NIH Support - 1R01 AI116725

**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 persuing better therapeutic options.

**Methods:** We subjected C57BL/6 mice to 25 minutes of renal pedicle clamping followed an intraperitoneal injection of TLR inhibitor 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.

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

**PO0155**

**Six1 Activation Is Involved in Cell Proliferation and Migration and Anti-Inflammation of Acute Ischemia-Reperfusion Injury in Mice**

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**Background:** Nephrogenic proteins are re-expressed during the regeneration process after ischemia reperfusion (IR) injury, while the role of these proteins in the repair of kidney injury is still unknown. We found that Six1, a developmentally regulated homeoprotein is reactivated in tubular epithelial cells (TECs) after IR injury.

**Methods:** We established Six1 overexpression cell lines to confirm its effect on kidney repair in vitro. Cell proliferation and cell migration was detected by flow cytometry and wound healing assays respectively. In different set of experiment, to detect the anti-inflammation capacity of Six1 overexpressing cells, and chromatin immunoprecipitation (ChIP)-qPCR was used to analyze Six1 protein occupancy of the indicated genes. In vivo,
we injected adeno-associated viral vector serotype 9 (AAV9)-Six1 into uninjured renal pelvis before IR injury, then assessed morphologic and functional parameters and gene expression in IR injury.

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 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 C57BL/6J. Knees, lymph nodes and spleens were collected on D1, D3 and D7. MRCs were identified by Flow cytometry. Expression of IRF8 and MHC II were quantified by IHC. Six1 could suppress inflammation through NF-κB-mediated pathway. Six1 target the phenotype of DC. 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.

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Methods: To determine the function of Pax2 reactivation in mouse proximal tubules, we generated kidney proximal tubule-specific Pax2 conditional knockout (KO) mice. The conditional KO mice were established by KAP (kidney androgen regulated protein) Cre mice and Pax2 flox mice. Six to eight-week-old male mice were used for ischemia-reperfusion (IR) injury (left kidney, 60 minutes). The intensity of cell proliferation and fibrosis of injured kidney was evaluated. A Pax2 inhibitor (EG1) was used to evaluate the roles of Pax2 in the hypoxia condition of cultured tubular epithelial cells (0, 5%, 24 hour).

Results: The number of Pax2-positive cells and Pax2 mRNA increased after IR injury. However, the reactivation of Pax2 was significantly suppressed in conditional KO mice (p<0.05). In vitro study revealed that hypoxia condition of cultured tubular epithelial cells (0, 5%, 24 hour).

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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

Yujia Wang, Chuan-Ming Hao. Huashan Hospital Fudan University, Shanghai, China.

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 methotrexate (HDMTX) 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 HDMTX 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 HDMTX/LT was analyzed.

Results: Enzymes of de novo NAD+ synthesis pathway including KMO, KYNU, HAAO, QPRT, 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 HDMTX treatments were included in the discovery cohort and AKI developed after 35 HDMTX treatments (18.3%). In those who developed AKI, the urinary 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 = 0.023; 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 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.

Sphingolipid Transporter 2 (Spsn2) Expression, Localization, and Role in AKI

Nataliya Skrypnik,1 Shuaiqun Zheng,1 Sylvia Checova,1 Nabin Poudel,1 Kevin Lynch,1 Mark D. Okusa.1 Division of Nephrology and Center for Immunity, Inflammation, and Regenerative Medicine, University of Virginia, Charlottesville, VA; 2Department of Pharmacology, University of Virginia, Charlottesville, VA.

Background: The sphingosine 1-phosphate (S1P) transporter Spns2 exports S1P and its role in kidney function was evaluated by measurement of plasma creatinine. Spns2 localization and its expression was validated by western blot (WB), quantitative real time PCR and IF.

Methods: We generated clone with the highest expression by the method of limited dilutions in TKPTS; Spns2 expression was assessed by western blot (WB) of membrane-enriched fractions of kidney. Renal activation of S1P receptors can protect kidneys from acute injury, but little is known of the role of Spns2 in kidney. In these studies, we investigated the expression, localization, and role of Spns2 in the kidney after ischemia-reperfusion injury (IRI).

Results: Spns2 is expressed in high abundance in kidney and is localized to the brush border of S1–S3 segment of proximal tubules (PT) and wheat germ agglutinin a marker of parasympathetic ganglionic blocker hexamethonium. Moreover, ablation of the splenic nerve abolished the renal protection elicited by vagal sensory afferent stimulation (afferent VNS). The protective effect of afferent VNS persisted after blocking the rise in corticosterone with mifepristone or after subdiaphragmatic vagotomy, but was abolished by the sympathetic/parasympathetic ganglion blocker hexamethonium. Moreover, ablation of the spleen (predominantly sympathetic nerve) and splenectomy abolished the protective effect of afferent VNS. Finally, adoptive transfer of splenocytes from mice subjected to IRI but not to sham stimulation, protected recipient mice from kidney IRI, suggesting that splenocytes activated through the splenic nerve mediate the kidney protection.

Conclusions: Spns2 is expressed in high abundance in kidney and is localized to the brush border of S1–S2 segments of the PT. Following IRI, PT Spns2 expression is reduced and appears in the urine. Spns2 can serve as a potential target to prevent AKI, however further studies are needed to determine whether the protective effect of Spns2 inhibitor was due to lymphopenia or to a direct effect of Spns2 expressed in PT.

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 diet-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 diet-fed rats. 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 and the fatty acid composition of membrane phospholipids, but was not enough to improve renal insufficiency or histological damage.

A Vago-Sympathetic Reflex Mediates Kidney Protection from Ischemia-Reperfusion Injury

Shinji Tanaka,1 Chikara Abe,1,2 Shujiu Zheng,1 Yusuke Yamaoka,1,3 Jonathan E. Lipsey,1 Nataliya Skrypnik,1 Junlan Yao,2 Tsuyoshi Inoue,3 Daniel S. Stornetta,2 Stephen Abbott,2 Diane L. Rosin,2 Ruth Stornetta,2 Patrice G. Guyenet,1 Mark D. Okusa.1 Division of Nephrology and Center for Immunity, Inflammation, and Regenerative Medicine, University of Virginia, Charlottesville, VA; 2Department of Pharmacology, University of Virginia, Charlottesville, VA; 3Department of Physiology, Gifu University Graduate School of Medicine, Gifu, Japan; 4Division of CKD Pathophysiology, The University of Tokyo Graduate School of Medicine, Tokyo, Japan.

Background: We recently showed that electrical stimulation of the cervical vagus nerve (VNS) protected mouse kidneys from ischemia-reperfusion injury (IRI) by activating the cholinergic anti-inflammatory pathway (PMID: 27088005). Whether the protection is caused by the activation of vagal efferent or afferent fibers needs clarification.

Methods: We generated choline acetyltransferase-channelrhodopsin-2 (Chat-ChR2) mice and vesicular glutamate transporter 2 (Vglut2-ChR2) mice, which express ChR2 in vagal efferent and afferent neurons, respectively. Selective optogenetic stimulation of vagal sensory afferent fibers (Vglut2-ChR2 mice) or efferent fibers (Chat-ChR2 mice) was performed 24 h before bilateral renal IRI, and mice were euthanized 24 h after IRI.

Results: Optogenetic VNS protected kidneys from IRI in both Chat-ChR2 and Vglut2-ChR2 mice as shown by decreased plasma creatinine, reduced renal Kim-1 expression and improved kidney histology. Next, we sought to identify the circuitry responsible for the renal protection elicited by vagal sensory afferent stimulation (afferent VNS). The protective effect of afferent VNS persisted after blocking the rise in corticosterone with mifepristone or after subdiaphragmatic vagotomy, but was abolished by the sympathetic/parasympathetic ganglion blocker hexamethonium. Moreover, ablation of the splenic nerve (predominantly sympathetic nerve) and splenectomy abolished the protective effect of afferent VNS. Finally, adoptive transfer of splenocytes from mice subjected to IRI but not to sham stimulation, protected recipient mice from kidney IRI, suggesting that splenocytes activated through the splenic nerve mediate the kidney protection.

Conclusions: Stimulation of either vagal efferent or afferent neurons protected the kidneys from IRI. The beneficial effect of afferent VNS requires the spleen and is mediated via a vago-sympathetic reflex.

Funding: NIDDK Support
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 (pO2) were continuously measured via Laser Doppler Flowmetry. In a second setting, kidney function parameters 24 h post I/RI as compared to placebo treated rats.

Results: Unilateral clamping resulted in an immediate drop of RBF and pO2 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 pO2 during reperfusion (figure). In the second setting, preventive treatment with BAY 2327949 resulted in dose-dependent, significant improvements of kidney function parameters 24 h 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.

Funding: Commercial Support - Bayer AG

PO0165
Augmenter of Liver Regeneration Protects Kidney from Ischemia-Reperfusion Injury via Regulation of TLR4/MAPKs 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; 1/R group; 1/R+rhALR1 group; 1/R+rhALR2 group. TLR4, neutrophils and macrophages were detected by immunochemistry. 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 fibrosis by neutrophils (24 h) and macrophages (72 h), as well as lower levels of inflammatory cytokines compared to the untreated control rats. Furthermore, rhALR downregulate 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

PO0166
DPP-4 Inhibitor Attenuated Renal Vasocostriction 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 dipetidyl 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.
Mediated Apoptosis
PTEN Protects Against Ischemia Reperfusion-Induced AKI via Concentration-response curves to ET-1 in perfused kidneys of SHAM (A) and BDL (B) rats.

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whether PTEN involves in acute kidney injury (AKI) remains unclear. α

induced injury possibly via regulating cytoskeleton and TNF-α biomarker for early prediction and evaluation of AKI. PTEN protected HK-2 from IR-induced injury in IRI-AKI mice, suggesting that PTEN is promising to be a serum marker for evaluating renal injury in IRI-AKI mice. 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 6-hour post-reperfusion vs. control (p<0.05) relative to control, determined by TUNEL assay. Mitochondrial DNA (mtDNA) content was reduced by 23% in I/R-placebo group (p=0.067) from control, starting by 1-hour post-reperfusion. In contrast, treprostinil preserved mtDNA content to control levels (p<0.001) relative to control, determined by TUNEL assay. Treprostinil also prevented I/R-mediated apoptosis at 24-hour post-reperfusion. Treprostinil 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 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 by 1-hour post-reperfusion. In contrast, treprostinil preserved mtDNA content to control levels (p<0.01). In addition, placebo increased cytotoxicity release into cytotox 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 show 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 cytotoxicity 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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Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only

Underline represents presenting author.
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 underlying mechanisms of the pre-conditioning effect have not been elucidated. We have recently discovered that DNA double strand break (DSB) DNA 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 Antimycin 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 adenosine, 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 was observed 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 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.
of urine NGAL is from the plasma, our next step was to examine the renal handling of plasma NGAL.

**Methods:** Mice: C57Bl/6. Interventions: bilateral kidney ischemia reperfusion (IR) - 27 minutes; maleic acid (MA) (400mg/kg pH 7.4 in saline, IP); furosemide (4mg, IP); unjured vehicle animals served as a control. Recombinant human (rh) NGAL (5ug, IV) was injected to dissect the fate of circulating NGAL. Measurements: transcutaneous 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) = [(urine rhNGAL) / x plasma creatinine])/[(plasma [rhNGAL] x urine creatinine)] x 100.

**Results:** Unjured 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 rNGAL in both models. Furosemide (PT injury model): GFR ~ 30%, plasma and urine rhNGAL was slightly elevated, urine rNGAL 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 treated mice. Megalin is expressed on the brush border of proximal tubular cells in the mouse kidney. To link the PT function with plasma and urine NGAL concentrations, we performed microarray analysis of plasma and urine NGAL concentrations in the mouse kidney. Megalin expression was increased in the kidney of mice with high ngAL plasma concentrations.

**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.

**Funding:** Veterans Affairs Support

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**Case Description:** A 40-year-old man with hypertension and tobacco use presented with bilateral flank pain and gross hematuria. 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 TTH polyps and interstitial non-caseating granulomas. Immunohistochemistry assay showed TTH polyps within markedly dilated renal tubules, consistent with obstructive nephropathy. Nephrology and urology consultation was requested for evaluation of obstruction. 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 100mg/d and resolution of hydronephrosis.

**Discussion:** We encountered a rare presentation of acquired hemophilia with macroscopic hematuria and AKI. We suspect that bladder clots and associated intraluminal clots resulted in increased tubular pressures causing obstructive nephropathy and the formation of intratubular TTH polyps. Administration of immunosuppressive therapy has been used to treat TTH polyps, and there is evidence that 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.
Case Description: 39-year-old man with no past medical history referred from another institution with COVID-19 pneumonia, for which he completed 4 days of hydroxychloroquine. On admission, patient was found to have SCr of 2.0 mg/dL, which increased to 10.8 mg/dL during a 3-day period. Urinalysis showed dysmorphic RBCs but no casts. Total albumin/creatinine ratio in urine was 3.2 mg/g and FeNa >1%. Renal ultrasound showed no obstruction or masses. Other laboratory results showed methemoglobinemia (14 mg/dL), acute liver failure, schistocytes in the peripheral smear and a G6PD assay with marked deficiency. Other serologies were negative. Patient reported prior ingestion of 1 gr acetaminophen (APAP) every 4 hrs for several days; treated with 48 hrs of N-acetylcysteine infusion. The AKI was complicated by hyperkalemia, severe anion gap metabolic acidosis and volume overload requiring long term renal replacement therapy after failure of resuscitation with crystalloid, albumin, and vasopressors.

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 role of COVID-19 as a cause of our patient’s AKI. COVID-19 has been associated with acute kidney injury, increased inflammation, and toxicity to multiple organs. In previous reports, patients with severe COVID-19 pneumonia have experienced elevated levels of inflammatory cytokines (i.e., IL-6, IL-10, TNF-α) and increased kidney injury biomarkers (i.e., NGAL, IL-18). The similarity of these findings to our patient’s case is striking. Our 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.

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. The detection of C5b-9 on endothelial cells may help determine the timing and selection of treatment to break the vicious cycle of malignant hypertension and worsening renal TMA.

Case Description: 54-year-old woman with a history of gestational hypertension, presented to the ED with complaints of headache and visual changes. She was found to be in an hypertensive emergency with an SBP in the 200s. 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 TMA with global granular mesangial and basement membrane staining for IgG, IgA, IgM, C1q, C3, free kappa and lambda light chains of <5 RBC/HPF. Her urine toxicology screen was positive for opiates and cannabinoids. Renal biopsy revealed widespread edema of the interstitium and a mild to focally moderate inflammatory infiltrate involving approximately 80% of the cortical area. Tubular dilation, cytoplasmic vacuolization, and rare mitoses were seen in the tubules. He reported 2 sessions of hemodialysis, but he had a rapid resolution of his kidney failure with steroid initiation. A repeat chest CT showed resolution of bibasilar opacities, although with persistent upper lobe ground glass opacities consistent with smoking and vaping-related injury.

Discussion: Synthetic cannabinoids use should be considered in young healthy patients who present with unexplained AKI, as there are more case reports suggesting its direct nephrotoxicity. The etiology of tubulointerstitial injury from synthetic cannabinoids remains elusive, but a dysregulation of the endocannabinoid system in kidneys via endogenous cannabinoid receptors, CB1 and CB2, may be part of the mechanisms of injury. The cannabinoid receptors are now recognized to play potential roles in diabetic nephropathy and chronic kidney disease progression, and our future research may shed light on their possible role in immune activation.

PO0180
Acute Interstitial Nephritis and Diffuse Pulmonary Infiltrates in Recreational Drug User
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Introduction: Synthetic cannabinoids are designer drugs smoked as an alternative to marijuana with lower cost and greater potency. Here we describe a patient who presented with acute kidney injury and diffuse pulmonary infiltrates with recent inhaled synthetic cannabinoids use.

Case Description: A 26-year-old man with history of alcohol and recreational drug abuse including marijuana, tobacco and vaping, presented with acute kidney injury and diffuse pulmonary infiltrates. He recalled attending a party a week ago where he smoked someone else’s marijuana. On presentation, he was hypertensive to 170/115 mmHg with benign physical examination. Laboratory values were significant for serum creatinine of 17 mg/dL and BUN of 162 mg/dL. Urine sediment showed no cellular casts, but some monomorphologic red blood cells, rare dysmorphic red blood cells and white blood cells. He had a spot protein/creatinine ratio of 230 mg/g. Chest X-ray showed bilateral pulmonary infiltrates. Renal ultrasound showed normal kidneys. Laboratory studies were all negative including CK, ANCA, anti-GBM, ANA, dsDNA, SFP and legionella urinary antigen. His urine toxicology screen was positive for opiates and cannabinoids. Renal biopsy revealed widespread edema of the interstitium and a mild to focally moderate inflammatory infiltrate involving approximately 80% of the cortical area. Tubular dilation, cytoplasmic vacuolization, and rare mitoses were seen in the tubules. He reported 2 sessions of hemodialysis, but he had a rapid resolution of his kidney failure with steroid initiation. A repeat chest CT showed resolution of bibasilar opacities, although with persistent upper lobe ground glass opacities consistent with smoking and vaping-related injury.

Discussion: Synthetic cannabinoids use should be considered in young healthy patients who present with unexplained AKI, as there are more case reports suggesting its direct nephrotoxicity. The etiology of tubulointerstitial injury from synthetic cannabinoids remains elusive, but a dysregulation of the endocannabinoid system in kidneys via endogenous cannabinoid receptors, CB1 and CB2, may be part of the mechanisms of injury. The cannabinoid receptors are now recognized to play potential roles in diabetic nephropathy and chronic kidney disease progression, and our future research may shed light on their possible role in immune activation.
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.

Results: Serum troponin-I was 0.02 ng/mL with negative immune-florescence (IF), minimal interstitial fibrosis/tubular atrophy, no schistocytes. She was started on pulse steroids for clinical suspicion of eclampsia. Result of RF 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 related TMA. While awaiting biopsy therapeutic plasma exchange (TPE) was initiated, it was stopped after 3 sessions. Kidney biopsy on day 12 of delivery showed TMA, with negative immune-flourescence (IF), minimal interstitial fibrosis/ubular atrophy, focal 2/15 glomerular crescents and minimal arterial intimal thickening. Patient became progressively oliguric, requiring hemodialysis. At the time of writing this report, there has been no recovery at 4 weeks as patient remains oliguric on thrice weekly dialysis.

Discussion: Peri-partum care is crucial in early detection and prompt management of TMA in patients with pre-eclampsia/Eclampsia. Benefit of TPE in post-partum period is not well established. A kidney biopsy was obtained but the diagnosis remained elusive with negative IF in setting of reduced complement levels. Further studies should evaluate treatment strategies in the late-presenting patient to avoid irreversible kidney injury.

Thrombotic Microangiopathy as a Complication of Malignant Hypertension

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Introduction: Thrombotic microangiopathies (TMA) are defined as disorders characterized by the presence of microangiopathic hemolytic anemia (MAHA), thrombocytopenia, and microthrombi. Of all the known causes of TMAs, malignant hypertension is one of the most underreported ones.

Case Description: A 23-year-old African American male patient presented to the emergency department with a 2-week history of nausea, vomiting, diarrhea, and abdominal pain. His past medical history is significant for hypertension treated with lisinopril, but the patient is noncompliant with his medication. He had a blood pressure of 245/176 mmHg. Laboratory tests revealed hemoglobin of 10.7g/dl, platelet count of 88,000/microliter, white blood count of 14,300/microliter, blood urea nitrogen of 29 mg/dl, creatinine of 4.7 mg/dl (unknown prior creatinine levels), lactate dehydrogenase of 900 units/l, low haptoglobin, serum potassium of 2.1mg/dl and normal coagulation profile. With control of blood pressure, the platelet counts improved. ADAMTS13 test and stool Shiga toxin were negative. Peripheral blood smear showed schistocytes. Workup for secondary hypertension were all negative. A diagnostic CT guided left kidney biopsy revealed active and chronic TMA.

Discussion: In our patient presenting with renal TMA and severe hypertension, TTP was thought to be less likely as the patient did not have the classical presentation of fever and neurological symptoms. In addition, thrombocytopenia and LDH levels normalized with aggressive control of blood pressure. Hence, plasma exchange was deferred. Since the patient presented with diarrhea, HUS was high on the differential, but a negative Shiga toxin PCR ruled out the possibility. Renal biopsy revealed acute and chronic TMA in renal blood vessels with focal severe arteriolarocclusion, fibrin, and onion skinning of arteries supporting the diagnosis of malignant nephroclerosis as the cause of TMA.

Drug-Induced Thrombotic Microangiopathy from Trimethoprim-Sulfamethoxazole

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Introduction: Thrombotic microangiopathy (TMA) is a common condition manifesting with microangiopathic hemolytic anemia, thrombocytopenia and end-organ damage including, acute kidney injury. TMA can be associated with many clinical syndromes and is most often due to malignant hypertension, malignancy or complement dysregulation but can also be triggered by medications. Here we describe a rare case of TMA caused by trimethoprim-sulfamethoxazole (TMP-SMX).

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, profuse diarrhea 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 G157H 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 TMAs 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 hemoglobin cast nephropathy.

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 6.6 mg/dL, BUN 66 mg/dL, hemoglobin 11.1 g/dL and platelets 9,000/uL. 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.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
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 isomorphic 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 ascpites-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 extraperitoneal and all intraperitoneal bladder injuries require surgical repair.
glomerulosclerosis (FSGS). Anabolic steroids are directly toxic to renal glomeruli. Chronic and interstitial fibrosis, severe interstitial fibrosis, and glomerular sclerosis and focal remodeling of the glomerular basement membranes consistent with 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.

Anabolic steroids bind to podocyte androgen receptors resulting in the apoptotic destruction of podocytes. The patient’s clinical course highlights 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.

**PO0189**

Triptan-Induced Vascular CKD, the Importance of a Differential Diagnosis

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Introduction: Triptans are selective (5-HT) receptor agonists resulting in vasoconstriction reversing the vasodilatory mechanisms of migraine headaches. Animal studies have shown 5-HT2 receptors in the renal arteries and intense vasoconstrictive effect of 5-HT on the renal arteries. We describe a case of progressive CKD with biopsy proven vascular injury due to sumatriptan use.

Case Description: A 52-year-old male with history of CKD stage 3, migraine headaches, and hyperlipidemia presented to nephrology clinic for evaluation of CKD. Review of records revealed a rise in sCr from 1.2 to 2.8 mg/dl over the preceeding 4 years. Urinalysis was negative for hematuria, proteinuria, and pyuria. CT revealed symmetric kidneys without dilation. A kidney biopsy was performed and showed patchy cortical atrophy and interstitial fibrosis with moderate vascular sclerosis and focal remodeling of the glomerular basement membranes consistent with prior vascular injury as well as acute tubular injury. A hematologic evaluation did not reveal an etiology and further history revealed use of sumatriptan 8-10 times per month. After discontinuation of sumatriptan the creatinine improved in spite of increased NSAID use. Currently botulinum injections are being used as migraine prophylaxis. This case highlights the importance of a review of all medications and for potential nephrotoxicity.

**PO0190**

Roid Renal Failure

Margaret Mallari, Priyesh T. Thakkar. AtlantiCare Regional Medical Center, Atlantic City, NJ.

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 Exel, an over-the-counter potassium-sparring 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 (1.0-1.2), CPK 2630 U/L (26-308). Chest X-ray showed right lower lobe pneumonia. Urinalysis showed proteinuria. Renal ultrasound revealed cortical echogenicity with no dilation. A kidney biopsy was performed to evaluate for CKD.

Discussion: This case highlight the broad differential diagnosis of acute and chronic kidney injury. The biopsy findings of primarily vascular injury were initially felt to be cryptogenic, but further review revealed the etiology to most likely be triptan induced. After discontinuation of sumatriptan the creatinine improved in spite of increased NSAID use. Currently botulinum injections are being used as migraine prophylaxis. This case highlights the importance of a review of all medications and for potential nephrotoxicity.

**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 and CD11b, kidney MNPs were phenotypically divided into five distinct subsets, which were further subdivided into functional subsets of proinflammatory M1-like (CD16+/MHCII+CD206-), and regulatory M2-like (CD206+). 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 multimodality regarding for example in vitro phagocytosis. The F4/80+ 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.

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 multimodality regarding for example in vitro phagocytosis. The F4/80+ 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 subtypes and identifies new therapeutic targets 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. Funding: Commercial Support - Bayer AG

PO0193
Microparticles Containing M2 Monocyte 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. Monocyte phenotypes (M1 = CD14+/CD16−; M2 = CD14+/CD16+) are associated with various acute and chronic renal injury states. While it is known that MP are released in the early phase of AKI, which can influence tissue modelling and repair.

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 albumin creatinine was 1.8 mg/dL and the time between admission and sample collection was 3-4 days. MP containing M2 Monocyte markers were significantly higher in AKI patients compared to controls (347.03 vs 27.14 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), coxinophilins (CD66b, p = 0.0001), and also in platelets (CD42b, p = 0.05).

Conclusions: MP containing monocyte/macrophages 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.

PO0194
Novel Immune Defense Cells of the Kidney Epithelia
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Background: Urinary tract infections (UTIs) are one of the most common bacterial infections worldwide, affecting infant boys, older men, and most prominently, women of all ages. It is predominately caused by uropathogenic E. coli and can lead to urethritis and kidney failure if untreated. We have found a major role for kidney epithelia, specifically the intercalated cells (IC), that are activated in defense against bacteria. Given the heterogeneity of kidney cell types, we hypothesized that there could be other cells that respond to a UTI.

Methods: We performed 10x Genomics single cell RNA-seq (scRNAseq) of whole kidneys from mice with UTI at 12 hrs and from mice without infection. We also performed scRNAseq of IC from lipopolysaccharide (LPS)-induced mice at 0, 8, and 24 hrs using a novel mRNA profiling method, pooled library amplification for transcriptome expression (PLATE)-seq. We used ROSA26-nT-nG mice, known to have immune properties, to dissect the LPS-induced IC. After LPS induction (525 cells) further revealed time-dependent activation of immune responses. We found that these IC/DP cells increased Umod expression in both UTI (1.6 fold change; padj=1E-2) and LPS (1.7 fold change; padj=1E-6) analyses. Umod, known to have immune properties, is commonly expressed in the loops of Henle and distal tubule, but may be a novel bacterial defense role in the IC/DP cells.

Conclusions: We found a novel immune defense role of the double positive collecting duct cells in response to UTI. These transectually active cells induce genes involved in cytokine and innate immunity and can provide new insights into the epithelial defense of the kidney.

Funding: NIDDK Support

PO0195
Role of Glomerular Filtration Rate (GFR)-Modifying Drugs in Prevention of Anticoagulant-Related Nephropathy (ARN)
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Background: Acute kidney injury (AKI) with red blood cell (RBC) tubular casts secondary to different anticoagulants has been recognized as ARN. ARN is seen in patients with underlying kidney diseases. 5/6 nephrectomy (5/6NE) animal model reproduces morphologic features of ARN. One of the possible pathogenetic mechanisms of ARN proposed to be increased GFR. Aim of the current study was to investigate the role of GFR-modifying drugs in prevention of ARN.

Methods: 5/6NE rats 3 weeks after the surgery were treated with direct thrombin inhibitor dabigatran (150mg/kg/day) and with GFR-reducing Enalapril (1.5 mg/kg/d) or GFR-increasing Albuterol (4 mg/kg/day) for 7 days. Daily monitoring of serum creatinine (Scr), blood pressure and hematuria was performed. Morphology of the kidney was evaluated at day 7 after animals were euthanized.

Results: Dabigatran resulted in gradual increase in Scr (Fig 1), hematuria, acute tubular necrosis (ATN) and RBC tubular casts in all treatment groups. Neither of GFR-modifying drugs significantly changed there parameters. ATN was 0.75 ± 0.27, 0.67 ± 0.25 and 0.70 ± 0.27 in Dabigatran, Dabigatran + Enalapril and Dabigatran + Albuterol treatment groups, respectively. Systolic blood pressure was reduced with Enalaprilbut did not change significantly with Albuterol. Diastolic blood pressure was not changed significantly with either treatment.

Conclusions: Our data indicate that GFR-modifying drugs do not prevent or aggravate ARN at least secondary to direct thrombin inhibitor.

Funding: NIDDK Support

PO0196
Tubular β-Catenin Ameliorates AKI by Regulating Apoptosis and Necroptosis
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Background: Renal tubular β-catenin signaling plays a protective role in acute kidney injury (AKI) but the underlying mechanisms remain debatable. Apoptosis and necroptosis of tubular cells are responsible for the renal dysfunction in AKI. This study aims to investigate the role of β-catenin activation in tubular cell death upon AKI and its underlying mechanism.

Methods: Transgenic ‘Tubcat’ mice conditionally expressing stabilized β-catenin in renal tubules following tamoxifen administration were used to establish septic LPS (induced) and non-septic (ischemia-reperfusion injury or IRI-induced) AKI models. Tubcat mice and their littermate controls were divided into the LPS and IRI groups. LPS mice received intraperitoneal injection of LPS (20 mg/kg). IRI mice received bilateral ischemia for 28 minutes, followed by 24 hours of reperfusion. All the mice were sacrificed at 24 hours. Apoptosis and necroptosis were evaluated by real-time quantitative PCR, western blot and TUNEL assay. Signaling cascade was examined by western blot.

Results: Compared to the controls, Tubcat mice under septice and non-septic AKI showed significantly delayed renal functional changes (lower serum creatinine levels) and reduction of (i) tubular injury score; (ii) apoptosis (Bax:Bcl2 ratio and number of renal TUNEL-positive apoptotic cells); (iii) necroptosis (expression of RIP1, p-RIP3 and p-MLK1); and (iv) renal expression of phospho-p53. Renal expression of phosphorylated Akt was increased significantly.

Funding: NIDDK Support
PO0197
Pulsed Ultrasound Improves Dysregulated Oxygen Metabolism and Reduces Tissue Injury in Sepsis-Associated AKI

Background: Sepsis associated-acute kidney injury (SA-AKI) results in part from oxygenation in septic and non-septic AKI. Tubular β-catenin might play a critical role in AKI by regulating cell death via modulating the p53/Akt signaling pathway. Fundings: General Research Fund (HKU 17119818), RGC Collaborative Research Fund (Ref: C7018-16G) and Hong Kong Society of Nephrology Research Grant (2019).

Funding: Government Support - Non-U.S.

PO0198
Reduces Tissue Injury in Sepsis-Associated AKI Mechanisms - 2
J Am Soc Nephrol 31: 2020
AKI Mechanisms - 2

PO0199
STC1 Prevents Lipopolysaccharide-Induced AKI via TGF-β
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Background: Lipopolysaccharide (LPS)-induced epithelial injury plays a critical role in the pathogenesis of acute kidney injury (AKI). Stanniocalcin-1 (STC1), a pleiotropic glycoprotein, has been reported to protect ischemic renal injury by reducing renal oxygen species, modulating inflammatory release, and inhibiting cell apoptosis. However, regulators of STC1 expression as well as its physiologic function in kidneys were unknown. We sought to elucidate the relationship between TGF β and STC1 in LPS-induced kidney injury in vitro and in vivo and to define the functional role of STC1 expression in renal tubular epithelium.

Methods: C57BL/6 J mice, STC1-/- (C57BL/6 J background) mice were randomly divided into blank control group, experimental control group and a mouse model of AKI was established. Primary mouse renal tubular epithelial cells isolated from wide type mice and STC1-/- mice were cultured. We detected changes in serum creatinine (Scr) and blood urea nitrogen (BUN) before and after model establishment, observed and scored renal tubular injury, and measure the expression of signal pathway proteins and downstream inflammatory factors.

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 STC1 (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.

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, NEAT1 is an enhancer of activated B cells (NF-κB) signaling and NEAT1 is implicated 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: In LPS-induced AKI, NEAT1 expression was upregulated in tubular cells, accompanied by elevated TLR4/NF-κB signaling. In vitro, tubular cells treated with LPS also showed increase in NEAT1, prior to the production of proinflammatory factors.
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 inflammation-related renal diseases. 

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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 Ang1 (1-7), Mas receptors (Ang1 (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 24 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. 33% of mice died by 48hrs, 30% were euthanized before full bleeding. Decreased AT1R in arterioles, 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 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 biomarkers that are these are significant markers of CLP are consistent with a severe AKI from the classical response. 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.

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 H3K4me3 and H3K27me3 marks and the presence of these two marks has been shown to affect gene regulation and transcription. In vitro models of AKI in HK-2 cells have demonstrated an increase in bivalent genes in AKI conditions.

Methods: 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 were activated bivalent genes are associated with upregulation of genes that drive the response to unilateral ureteric obstruction (UUO) in the mouse.

Conclusions: In conclusion, derepression of CLP-induced AKI and mitochondrial damage. Over-expression of FOXO1 could improve renal function and mitochondrial dysfunction, at least partly via PGC1-α and mitochondrial morphology and structure. Compared with LPS group, HNG reduced the renal expression of IL-1α, IL-6 and HMGB1 and significantly increased the expression of PGC1-α and TFAM in the kidney.

Conclusions: In conclusion, derepression of FOXO1-mediated gene expression following AKI and mitochondrial damage. Over-expression of FOXO1 could improve renal function and mitochondrial dysfunction, at least partly via PGC1-α and mitochondrial morphology and structure. Compared with LPS group, HNG reduced the renal expression of IL-1α, IL-6 and HMGB1 and significantly increased the expression of PGC1-α and TFAM in the kidney.
PO0205
The Effect of Overexpression of Intestinal Alkaline Phosphatase (IAP) on Intestinal Permeability and Renal Failure in Lipopolysaccharide (LPS) Treated IAP Transgenic (IAPtg) Mice
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Background: LPS associated sepsis is known to cause intestinal dysfunction in septic AKI. IAP is known to dephosphorylate LPS and render it inactive. We generated IAPtg mice who overexpress human IAP. We hypothesized that if IAPtg mice were subjected to septic AKI their kidney function and intestinal barrier permeability will be better preserved than non-transgenic mice.

Methods: IAPtg mice were developed in C57Bl6 background using human chimeric IAP under the control of villin promoter making them intestine and kidney specific overexpressing IAP. LPS (10 mg/Kg) was given to IAPtg (IAPtg+LPS) and C57Bl6 (C5LPS) to induce septic AKI. The control IAPtg (IAPtg-LPS) and C5Bl6 (C5-LPS) received saline. FITC-Dextran (FD) was gavaged 2 hours before sacrifice to measure intestinal permeability. Blood, intestine (duodenum, jejunum, ileum), and colon were harvested for biochemistry and immunoblot analysis.

Results: Serum urea and creatinine of IAPtg mice were 0.6 mg/dl and 65 mg/dl respectively which were 2 and 1.5 fold lower than C5-LPS mice (p<0.05). Serum FD levels of IAPtg>LPS (1.2± 0.1 ng/ml) were 2.5 fold lower than C5-LPS (p<0.05) suggesting improved intestinal integrity. Expression of tight junction protein (ZO-1), pro-apoptotic proteins (Caspase3, Bax), antiapoptotic protein Bcl2 in the colon, and intestine was measured by immunoblot. ZO-1 expression in the intestine and colon of C5-LPS was significantly higher than IAPtg-LPS (p<0.05). The expression of intestinal and colon caspase 3 in the IAPtg was 4 fold lower than C5-LPS (p<0.01). Intestinal and colon Bax of IAPtg/LPS were lower and Bcl2 higher than C5-LPS (p<0.05). Apoptotic markers of IAPtg+LPS were not significantly different from the control suggesting lower apoptosis 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 C5-LPS (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 endotoxic insult. 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

PO0206
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 glutamate, 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 of 0.8 g/kg NH4Cl).

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+, which is required for ammoniagenesis. PTs in acidic animals displayed intense Oil Red O staining and large multi-lamellar bodies (MLBs), consistent with a major decrease in lipid metabolism. Supplementing or reducing NAD (with lactate) and increasing pH back to 7.4 inhibited/reversed the appearance of MLBs, implying that changes in NAD and lipid metabolism are linked. Histological analysis of acidic animals showed thinning of PTs and shedding of debris, indicative of AKI. Intravital imaging revealed that mitochondria remained energized, but endocytosis of fluorescently labeled dextrans was markedly decreased, confirming a severe functional defect in solute transport. Partially reversing MA with intravenous injection of bicarbonate (0.42 g/kg) or supplementing NAD with nicotinamide (0.4 g/kg, prior to MA induction) both substantially improved dextran uptake.

Conclusions: MA induces major changes in PT NAD and lipid metabolism that result in a functional AKI state, which can be reversed or prevented. These findings might also help to explain why MA accelerates decline in function in chronic kidney disease.

PO0207
Loss of HDAC8 Leads to h2AX-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-lav larval zebrafish model of AKI improved survival and increased repair and proliferation after AKI. However, these mechanisms 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(lav/lav) and hdac8(lav/+)+tupant 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. Results were validated by qPCR on RTEC. h2ax−/− mice were used to examine AKI in WT and hdac8−/− zebrafish with and without AKI. There were a greater number γH2AX foci in RTEC of the h2ax−/− larvae with AKI than in either the uninjured h2ax−/− or WT AKI larvae. h2ax−/− mice exhibited less apoptosis compared to WT zebrafish with AKI, and as expected there were undetectable levels of TunNEL positive cells in WT and h2ax−/− uninjured tubules. We observed more Paxa2 positive cells in h2ax−/− larvae with AKI than WT larvae with AKI. Immunohistochemical analysis of Na/K-ATPase, a marker for epithelial polarization, in h2ax−/− zebrafish tubules maintain partial to full polarization during AKI, whereas WT larvae with AKI had complete mis-polarization of RTEC. RNA-Seq data analysis confirmed the epithelial polarization data demonstrating increased expression of mesenchymal genes and decreased epithelial gene expression in WT tubules with AKI compared to h2ax−/− in AKI injured zebrafish.

Conclusions: This study suggests a mechanism of repair and recovery after AKI in h2ax−/− zebrafish is mediated through increased γH2AX at sites of DNA damage. h2ax−/− mutant zebrafish preferentially uses mechanism of DDR for repair and proliferation, as opposed to apoptosis. The absence of apoptosis in h2ax−/− tubules can prevent complete depolarization and maintain membrane and maintain their epithelial gene signature, 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.

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PO0208
Protein Phosphatase 2A 2C Regprograms Cellular Energy Metabolism to Promote Tubular Cell Death and 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 PP2Aца 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 (Cot) protein in tubular cells was significantly upregulated in both patients and animal models with acute and chronic kidney injury. Ablation of PP2Aца in tubular cells alleviated cisplatin-induced acute kidney injury and unilateral ureteral obstruction-induced kidney fibrosis in mice. In cultured tubular cells, ablation of PP2Aczę promotes oxidative phosphorylation of fatty acids by increasing p-ACC levels and thus protects against cisplatin-induced cell death and TGFβ1-induced fibroblast production.

Conclusions: This study reveals the essential role for PP2Aczę in regulating tubular cell energy metabolism and survival, which may shed light on treating patients with kidney injury.

PO0209
In Vitro Inhibition of Renal OCT2 and MATE1 Secretion by Antiemetic 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 entecavir. Studies suggest that ondansetron, an antiemetic drug and 5-HT 3 receptor antagonist, has unknown effects on OCT2 and MATE1.

Methods: Transport of the fluorescent prototypical cation ASP (25 μM) was assessed in the presence and absence of 5-HT 3 antagonists (0.5-20 nM) using two in vitro models: 1) HEK293 kidney expressing human OCT2 or MATE1 and 2) double-transfected hOCT2-MATE1 MDCK cells. Cimetidine (50 μM) was used as a positive control.

Results: The relative order of potency for inhibition of ASP uptake by OCT2 was palonosetron > ondansetron > tropisetron > granisetron and in MATE1 was ondansetron > palonosetron > tropisetron > granisetron > dolasetron. In hOCT2-MATE1
Inhibition of OCT2-MATE1 Secretion of ASP by Ondansetron in MDCK Cells

PO0210
Klotho Deficiency Intensifies Hypoxia-Induced Expression of INF-α/β Through Upregulation of Rig-I
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Background: Hypoxia is a common pathway to progression of end-stage kidney disease. Although numerous studies have provided evidence that inflammation plays a major role in this process, the mechanism by which hypoxia induces inflammatory responses remains unknown. Retinoic acid-inducible gene-1 (RIG-I) encodes an RNA helicase that recognizes viruses including SARS-CoV2, which is responsible for production of interferon (IFN)-α/β to prevent the spread of a viral infection. Recently, RIG-I activation has been found under hypoxic conditions, and klotho deficiency intensified the activation of RIG-I in mouse brains. However, the roles of these functions in renal inflammation remain elusive.

Methods: In vitro, expression of RIG-I and INF-α/β was examined in normal rat kidney (NRK)-52E cells incubated under hypoxic conditions (1% O₂) for 30, 60, 90, and 120 min. Next, siRNA targeting RIG-I or scramble siRNA was transfected into NK52E cells to examine expression of RIG-I and INF-α/β under hypoxic conditions. In vivo, we induced renal hypoxia by clamping the renal artery for 10 min in wildtype mice (hypoxic WT mice) and Klotho knockout mice (hypoxic KI’ mice). Lastly, we investigated the expression levels of RIG-I and INF-α/β in 33 human kidney biopsy samples diagnosed with IgA nephropathy.

Results: In vitro, the expression levels of RIG-I and INF-α/β were increased significantly under hypoxic conditions. In vivo, we observed increased expression of RIG-I and INF-α/β in Klotho knockout mice compared to wildtype mice under hypoxic conditions. In human kidney biopsy samples, the expression levels of RIG-I and INF-α/β were significantly higher in IgA nephropathy compared to normal kidney tissues.

Conclusions: These findings suggest that hypoxia induces expression of INF-α/β through upregulation of RIG-I, and that klotho deficiency intensifies this hypoxia-induced expression.
Using a Kidney Microphysiological Device

Associated Nephrotoxicity from Polymyxin and Tobramycin Antibiotics

PO0213

and pathologic mitochondrial changes. Transmission electron microscopy, renal proximal

Systemic Gd treatment induced lipid-laden vacuoles with electron-dense material

AKI Mechanisms - 2

PO0214

and tobramycin exposure, no genes were differentially regulated compared

to controls. However, the use of these antibiotics is limited due to concerns of acute kidney

PO0215

polymyxin and aminoglycoside antibiotics are ever more important for effective bacterial

injury (AKI). We have employed a kidney microphysiological device system (MPS) with

cultured human primary proximal tubule epithelial cells (PTECs) to identify potential

injury. sFas and 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.

Conclusions: We found that different biomarkers have variable kinetics after PTEC

injury. SAS and 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.

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 splenic 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 crossbreeding 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 lipopolysaccharide (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 porcine macrophages from either WT or α7nAChR-deficient mice were used. These cells were stimulated with LPS after nicotine (pan nicotinic acetylcholine receptor agonist) or GTS-21 was administered, 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. Interestingly 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 in RAW264.7 cells or porcine 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.

Platelets vs. Neutrophils as Therapeutic Targets in Cholesterol Embolism-Related Arterial Occlusion, Kidney Infarction, and AKI

PO0215

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Background: Cholesterol crystal embolism (CCE), a life-threatening complication, is a consequence of the rupture of atherosclerotic plaques in patients with advanced atherosclerosis. CCE: often missed as a cause of AKI. CCE 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. In vitro studies CC with neutrophils, platelets, endothelial cells.

Results: At 24h, MRI and μCT showed peripheral 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 vivo studies show, CC-induced clot formation and enhanced fibrinogen release from platelet granules which promotes fibrin clot formation. DNase I can strongly inhibit ATP secretion, 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.

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PO0216
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-ttdTomato 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 50um 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

PO0217
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 MNPs 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-electron microscopy 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 24 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

PO0218
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 cilipathies. Here we tested if cilia acting via mitochondria are involved in AKI.

Methods: We previously showed that the exocyst trafficking complex is necessary for ciligenesis. 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 (SLC34a-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 spare 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 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 intracristae 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

PO0219
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.
Pericyte and Macrophage C5aR1 Mediate Renal Fibrosis


University of Virginia, Charlottesville, VA; National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD; Purdue University System, West Lafayette, IN.

Abstract: We reported that kidney injury (AKI) is widespread, identified in 30% of post-operative and 50% of ICU patients, and associated with increased rates of chronic kidney disease (CKD) and end stage renal failure. Peritubular capillary beds are significantly damaged, and it causes vascular rarefaction during many types of AKI. Vascular rarefaction is closely associated with post-AKI CKD progression. Vascular endothelial growth factor (VEGF) is a well defined angiogenic protein via its major receptor, VEGF receptor (VEGF-R2). However, prior work from other investigators demonstrated a role of VEGF-R2 as a negative regulator of pericyte function and vessel maturation. The functional implications of the VEGF-R2 signaling in renal stroma remains poorly understood.

Methods: We generated genetic mouse models for renal stromal cells (RSCs)-specific loss-of-function of VEGF-R2 with constitutively expressed Foxd1-Cre (C5aR1-/-) and tamoxifen inducible Foxd1-Cre (iC5aR1-/-). AKI/CKD models induced either by a renal ischemia/reperfusion injury (IRI) model or by low/dose repeated treatment of cisplatin were performed. Mice are monitored for the development of AKI and post-AKI CKD using serum chemistries and tissue analysis.

Results: cVEGF-R2-/- protects against ischemic AKI in male and female mice. Specifically, cVEGF-R2-/- reduces renal tubular injury and microvascular rarefaction. cVEGF-R2-/- also mitigates CKD progression post ischemic AKI. cVEGF-R2-/- reduces expression of kidney injury markers, HareV and Lcn2, in a cisplatin-AKI/CKD model. Interestingly, iVEGF-R2-/- demonstrates higher degree of protection against ischemic AKI as compared to cVEGF-R2-/- studies. We showed previously that iVEGF-R2-/- shows mild defects in kidney development. Our new data suggests that iVEGF-R2-/- decrease leakage of nephrin by the mutation during kidney development.

Conclusions: These data suggest that VEGF signaling in renal stroma cells exacerbates ischemic AKI and its post-AKI CKD progression as well as cisplatin AKI.

Funding: NIDDK Support, National Institute of Diabetes and Digestive and Kidney Diseases.
**PO0224**

A Novel Renoprotective Strategy: Upregulation of PD-L1 Expression Mitigates Cisplatin-Induced AKI

**Jun Zhang, Shenwen V. Gu, Susu-Wei Hsu, Ching-Hsien Chen. University of California, Davis, Davis, CA.**

**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 regarding 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 showed 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 in vivo inhibition appeared to be dose-dependent. Interestingly, 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.

**Funding:** Other U.S. Government Support, Commercial Support - Dialysis Clinic, Inc. (C-3917)

**PO0225**

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 excretion of the distal 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 initiate 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 (calbindin) marker to phenotype acute kidney injury secondary to cisplatin administration.

**Funding:** Other NIH Support - Funded by NIH GM123330, ES005022, ES007148, CA072720, and CA046934.

**PO0226**

Neutral Ceramidase and Autophagy Play Diverse Roles in Cisplatin-Induced AKI and Fibrosis

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**Background:** Cisplatin (CDDP) is 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 analyze CDDP-induced AKI. To characterize renal outcomes in CDDP-induced AKI, we developed a) a high-dose model and b) a repeated low dose model.

**Results:** 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.

**Funding:** This project is supported by grants from NIH CA072720, and CA046934.

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Underline represents presenting author.
**PO0227**

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 phospho-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 binds to nuclear factor-kappa-B-activating protein (NKAP). Following cisplatin-induced phosphorylation at ser159 and ser163, the interaction of MARCKS with NKAP was inhibited, contributing to 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)

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**PO0229**

Decreased IFT88 Causes Cilia Shortening and Mitochondrial Dysfunction in Cisplatin-Induced Tubular Injury

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**Background:** Renal primary cilia are associated with the pathogenesis of various diseases, including acute kidney injury (AKI). The length of the primary cilia dynamically change during the progression of diseases: tubular primary cilia shortened in cisplatin-induced AKI mouse model. However, its relevance in kidney disease and the underlying mechanism are largely unknown. Tubular damage in AKI closely links to mitochondrial dysfunction. Thus, we investigated the interaction between primary cilia and mitochondria in cisplatin-induced tubular injury.

**Methods:** C57BL/6 mice with cisplatin-induced AKI were euthanized at 72 h after disease induction to collect blood and kidney samples. In vivo experiments, we used RPTEC/TERT1 cells, which are human proximal tubular epithelial cells that maintain the cilia length at high cell densities, and knocked down IFT88 (IFT88-KD), a cilia maintenance protein, by siRNA. Cisplatin-treated or IFT88-KD cells were assessed for the cellular phenotypic changes or mitochondrial metabolic function using the Flux Analyzer. We conclude loss of NHERF1 results in increased levels of GSSG, a modifier of thioredoxin and inhibitor of GSH synthesis in oxidizing conditions, and lower 72h post treatment in KO compared to WT.

**Results:** We found that the expression of protein IFT88 was decreased in damaged tubules of cisplatin-induced AKI mice. These data were consistent with that IFT88 expression decreased in the cisplatin of cisplatin-treated RPTEC/TERT1 at mRNA and protein levels in association with shortening of the primary cilia, suggesting the pathogenic link between tubular damage and IFT88-mediated cilia alteration. Interestingly, IFT88-KD cells significantly exhibited shorter cilia as compared to control siRNA-transfected cells and showed downregulation of mitochondrial oxidative phosphorylation capacity and decreased ATP production, indicating the contribution of IFT88 to mitochondrial homeostasis. Of note, such mitochondrial alteration linked to tubular inflammation. Our findings suggest that tubular mitochondrial dysfunction in cisplatin-induced AKI is mediated by a decreased IFT88 with shortening cilia, at least in part.

**Conclusions:** Tubular mitochondrial damage followed by tubular injury in AKI may occur by the alteration of IFT88 expression, and subsequent cilia shortening in the tubular epithelial cells.

**Funding:** NIDDK Support
Figure a-d: scRNAseq UMAP highlights S3 and S3T2. Feature plot of Aqp1 and smFISH of Agt (green) localizes to S3T2.

Figure a-d: a scRNAseq UMAP highlights S3 and S3T2 to SpT highlighting S3 and S3T2. c-d Feature plot of Aqp1 and smFISH of Agt (green) localizes to S3T2.

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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 diuretic 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 3.8% on the 5th day of 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.

PO0236
Carfilzomib-Induced Thrombotic Microangiopathy Effectively Treated with Eculizumab
Jorge M. Chancay rodriguez, Fadi Salem, Mohamed Rizwan Al Rasheed, Priya Deshpande. Mount Sinai Health System, New York, NY.

Introduction: Proteasome inhibitor (PI), Carfilzomib, have been associated with drug-induced microangiopathy (DITMA) in rare cases1. We present a patient with acute kidney injury (AKI) from Carfilzomib-induced DITMA who was successfully managed with Eculizumab, which is a monoclonal antibody that inhibits the alternate pathway of the complement cascade.

Case Description: A 56-year-old woman with refractory IgG Lambda Multiple Myeloma (MM) was admitted with fatigue and decreased oral intake one week after restarting Carfilzomib. She had been on Carfilzomib in the past and tolerated it well. On admission, she had no oliguric AKI with a serum creatinine (Scr) of 12mg/dL (one week prior to restarting Carfilzomib, her Scr = 0.8mg/dL). Peripheral smear revealed numerous with schistocytes and thrombocytopenia. Carfilzomib was immediately discontinued. Serologic work up, including ADAMS13, was within normal limits. Her free kappa/lambda ratio 0.41. She was dialyzed twice for clearance and underwent a renal biopsy. The renal biopsy showed diffuse thrombotic microangiopathy (TMA) with minimal tubulointerstitial fibrosis. Eculizumab 900mg weekly was started, and Scr declined to 1.6mg/dL over 3 weeks. She did not require further hemodialysis treatments. Currently, her Scr is 1.1mg/dL, and she is on Eculizumab 1200mg every two weeks.

Discussion: Our case is the fourth report using Eculizumab in Carfilzomib induced DITMA. The timing of our patient’s Carfilzomib exposure supports that DITMA caused her AKI (as opposed to MM-induced TMA). The first line of treatment requires immediate cessation of the drug. Interestingly, Bluitani et al, demonstrated the activation of the alternate complement pathway in a patient with Carfilzomib-induced TMA, indicated by elevated levels of fragment Bb and membrane attack complex (MAC)7. Portuguese et al, proposed that Carfilzomib may lower the gene expression of Complement factor level 3.6, which is a key regulator of TMA. Eculizumab 900mg weekly was started, and Scr declined to 1.6mg/dL over 3 weeks. She did not require further hemodialysis treatments. Currently, her Scr is 1.1mg/dL, and she is on Eculizumab 1200mg every two weeks.

PO0237
Tubulointerstitial Lupus Nephritis with Coexisting Renal Limited IgG4 Disease

Introduction: The classic pattern of Lupus Nephritis (LN) is an autoimmune condition limited to increased renal limited glomerulonephritis. Rare cases have been described with predominantly tubulointerstitial nephritis (TIN) with tubulointerstitial immune deposits in the absence of significant glomerular lesions. We describe a patient with such pattern of disease along with co-existing renal limited IgG4 related disease (IgG4 RD).

Case Description: 72 year old woman with a past medical history presented with fever, malaise and cough for 3 days. It was associated with occasional epistaxis and dyspnea. On examination, she had bilateral lower extremity edema. Vital signs included blood pressure 107/74 mmHg, without fever or respiratory distress. Laboratory workup showed creatinine (Scr) of 2.3 mg/dl (baseline 1.5 mg/dl), sodium 137 mg/dl, serum creatinine kinase (CK) levels of 170 U/L (38-174 U/L), thyroid secreting hormone levels (TSH) of 97.77 uIU/L. Her liver biochemistry was normal. She underwent a renal biopsy that showed immune complex mediated chronic active tubulointerstitial injury and interstitial fibrosis. Eculizumab 900mg weekly was started, and Scr declined to 1.6mg/dL over 3 weeks. She did not require further hemodialysis treatments. Currently, her Scr is 1.1mg/dL, and she is on Eculizumab 1200mg every two weeks.

Discussion: Our case is the fourth report using Eculizumab in Carfilzomib induced DITMA. The timing of our patient’s Carfilzomib exposure supports that DITMA caused her AKI (as opposed to MM-induced TMA). The first line of treatment requires immediate cessation of the drug. Interestingly, Bluitani et al, demonstrated the activation of the alternate complement pathway in a patient with Carfilzomib-induced TMA, indicated by elevated levels of fragment Bb and membrane attack complex (MAC)7. Portuguese et al, proposed that Carfilzomib may lower the gene expression of Complement factor level 3.6, which is a key regulator of TMA. Eculizumab 900mg weekly was started, and Scr declined to 1.6mg/dL over 3 weeks. She did not require further hemodialysis treatments. Currently, her Scr is 1.1mg/dL, and she is on Eculizumab 1200mg every two weeks.

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with non-specific systemic illness. 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. 1:1024 (normal <1:128). Bartonella PCR was negative. Both TTE and TEE were negative. Broader infectious workup was negative for ASO titers, Borrelia antibody, Quantiferon/A, HIV and Respiratory panel were negative. Renal cultures, assays for hepatitis B/C, HIV and Respiratory panel were negative. Renal biopsy showed an MPGN-pattern proliferative glomerulonephritis with necrotizing crescents. IF displayed global 3+ granular staining for both IgG and C3 as well as trace granular C1q. EM confirmed mixed mesangial (dominant), subendothelial, and a crescents. IF displayed global 3+ granular staining for both IgG and C3 as well as trace granular C1q. EM confirmed mixed mesangial (dominant), subendothelial, and a few distinct subepithelial hump-like deposits by EM, suggestive of an infection related hypoxia and blood-tinged sputum concerning for pulmonary/renal syndrome and was admitted for gastrointestinal bleed and AKI. He was given blood, intravenous fluids and right percutaneous nephrostomy. It is not identified, and instead a combination of dietary and pharmacologic factors are to be 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, A, dDNA, C3, C4, and C1q. EM confirmed mixed mesangial (dominant), subendothelial, and a few distinct subepithelial hump-like deposits by EM, suggestive of an infection related glomerulonephritis. With a biopsy suggesting an infectious process and BAL without evidence of alveolar hemorrhage, immunosuppression and PLEX were discontinued. Broader infectious workup was negative for ASO titers, Borrelia antibody, Quantiferon/AFB cultures, and BAL for fungal organisms. However, Bartonella IgG was positive at 1:1024 (normal <1:128). Bartonella PCR was negative. Both TEE and TEG were negative for valvular lesions. Additional patient history elucidated recent acquisition of a pet cat and multiple scratches. Treatment focus shifted from immunosuppression to antibiotics.

**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.

**Case Description:** An 84-year-old female presented with creatinine of 7.85mg/dl (baseline 0.81mg/dl) during a workup for painless 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. Renal biopsy showed an MPGN-pattern proliferative glomerulonephritis with necrotizing crescents. IF displayed global 3+ granular staining for both IgG and C3 as well as trace granular C1q. EM confirmed mixed mesangial (dominant), subendothelial, and a few distinct subepithelial hump-like deposits by EM, suggestive of an infection related glomerulonephritis. With a biopsy suggesting an infectious process and BAL without evidence of alveolar hemorrhage, immunosuppression and PLEX were discontinued. Broader infectious workup was negative for ASO titers, Borrelia antibody, Quantiferon/AFB cultures, and BAL for fungal organisms. However, Bartonella IgG was positive at 1:1024 (normal <1:128). Bartonella PCR was negative. Both TEE and TEG were negative for valvular lesions. Additional patient history elucidated recent acquisition of a pet cat and multiple scratches. Treatment focus shifted from immunosuppression to antibiotics.

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most arteriolar walls and tubular basement membranes. There was no immune complex deposition and no immune deposits. This was indicative of severe, acute, subacute and chronic TMA involving all small arterial vessels with acute tubular necrosis. The patient required hemodialysis without renal recovery.

Discussion: TMA is reported in metastatic adenocarcinoma. Cancer treatment can also cause TMA. This was unlikely to be the TMA as it had not been present a few months since the last dose. There are no cases reported of radiation causing renal limited TMA which we thought could also be a potential cause. Hypertension and severe anemia with schistocytes were the only clues to a TMA process. The elevated laktoglobin and normal platelet count was unusual. The TMA is thought to be likely secondary to paraneoplastic syndrome or possibly from the radiation treatments.

 wednesday - thursday - saturday - sunday - other

PO0243
Myeloid-Specific PKM2 Deletion Reduces Kidney Damage in Oxa-
lithiasis-Induced AKI
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Background: Reprogramming of immune cell metabolism has been associated with the development of kidney injury. The M2 isoform of pyruvate kinase (PKM2) catalyzes a critical stage of glycolysis, which was shown to be a crucial metabolic pathway for proinflammatory macrophage activation. We investigated 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 (PKM2 fl/fl Cre+) vs. wild-type (PKM2 fl/fl Cre−) mice. Mice were fed a diet containing either CaOx-nephrotoxic littersmates (PKM2+/-) by a single i.p. injection of calcium oxalate (NaOx, 100mg/kg) and 3% NaOx in drinking water for 24hr before sacrifice. Healthy controls received only vehicle. Serum creatinine and urine were evaluated as markers of renal function. CaOx crystal deposition (Pizzolato staining), IL-6, NGAL, and KIM-1 mRNA expression (quantitative PCR), Macrophage number/phenotype (FACS), and lactate levels were assessed in kidney tissue.

Results: In PKM2−/−, intrarenal CaOx deposition increased the serum levels of creatinine and urea, as well as the expression of IL-6, NGAL and KIM-1 in kidney tissue compared to healthy controls (p<0.01). Despite a similar deposition of crystals, loss of renal function and markers of renal inflammation/injury were reduced in PKM2−/− vs. PKM2+/- (p<0.05). FACS analysis indicated that the number of F4/80+ CD11b+ cells in kidneys were similarly elevated by CaOx in both PKM2−/− and PKM2+/-; Ly6M−/− mice. The macrophages with the pro-inflammatory phenotype Ly6C+CD206− were significantly reduced in PKM2−/− vs. PKM2+/- mice (p<0.01). 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 (2019/02893-9 and 2017/05264-7), CNPq and CAPES.

Funding: Government Support - Non-U.S.

PO0244
High-Content Imaging of Kidney Cell Function to Elucidate Mechanisms of Antiviral Drug Toxicity
Adam Pearson,1 Dominik Haenni,2 Andrew Hall.1,2 Universitat Zurich, Zurich, Switzerland; 1University Hospital Zurich, UniversitatsSpital Zurich, Zurich, Switzerland.

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. Tenofivir 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 due to 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 Tenofivir diprophosphate (TFVpp), a structural analogue of ATP. Using an in vitro assay of complex V activity, we observed a dose dependent inhibition with TFVpp. 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 depletion and mitochondrial dysfunction, which might ultimately explain toxic effects in patients. As the PT solute transport is heavily dependent on aerobic respiration, ATP depletion might trigger compensatory mitochondrial biogenesis, leading to hypertrophy.

Funding: Government Support - Non-U.S.

PO0245
Immunological Changes Following Cholinoic Anti-Inflammatory Pathway Stimulation
William Nash, Shini Tanaka, Mark D. Okusa. University of Virginia School of Medicine, Charlottesville, VA.

Background: The cholinergic anti-inflammatory pathway (CAP) protect mice from ischemia reperfusion injury (IRI). The interactions and mechanisms that regulate this protective response 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 vascular glumatic transporter 2 promoter. Cells were collected from the spleen 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, all optogenetic VNS led to a reduced number of CD45+ cells from the spleen. Within the CD45+ 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 guanine nucleotide exchange factors (Arhgef5) that could regulate function.

Conclusions: Cholinergic stimulation triggers reorganization of immune cell populations in response to in vivo exposure. The downstream alterations in gene expression 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

PO0246
Reduced Levels of Cyclic-GMP and Inhibition of cGMP-Dependent Protein Kinase Activate p21(127) and p27(127) and Lead to Renal Fibrosis and Dysfunction
Shobhit Das, Kandasamy Neelamgarm, Kailash N. Pandey. Tulane University Health Sciences Center School of Medicine, New Orleans, LA.

Background: Targeted-deletion of Npr1 (coding for guanylyl cyclase/natriuretic peptide A, GC-A/ANP) in extons VNS-treatment inhibits hyperplastic 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 p21(127) and p27(127), cell-cycle regulatory proteins that inhibit cyclin and cyclin-dependent kinase (cyclin-CDK) complex.

Methods: We examined the activation of CDK blocker (p21(127)/p27(127)) in Npr1 gene-knockout (0-copy); Npr1+/- mice and the GC inhibitor, AT7195-treated and CGMP-dependent protein kinase c(GIK) inhibitor, Rp-8-Br-cGMPs (Rp)-treated wild-type Npr1+/- and gene-duplicated 4-copy (Npr1+/-) gene using Western blot and quantitative real-time PCR. Systolic blood pressure (BP) was determined by non-invasive tail-cuff method.

Results: Renal cGMP levels and cGK activity were significantly decreased in 0-copy (p<0.01) compared with untreated control animals. Increased phosphorylation of p-Erk1/2 (3-fold), p-p38MAPK (4-fold), p21(127) (6-fold), p27(127) (5-fold) occurred in 0-copy, A7195-treated 2-copy mice, but only a small increase in 4-copy mice compared with untreated control animals. Increased phosphorylation of p-Erk1/2 (3-fold), p-p38MAPK (4-fold), p21(127) (6-fold), p27(127) (5-fold) occurred in 0-copy, A7195-treated 2-copy mice, but only a small increase in 4-copy mice compared with untreated control animals. Increased phosphorylation of p-Erk1/2 (3-fold), p-p38MAPK (4-fold), p21(127) (6-fold), p27(127) (5-fold) occurred in 0-copy, A7195-treated 2-copy mice, but only a small increase in 4-copy mice compared with untreated control animals.

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 cGMP/cGK axis by repressing the CDK inhibitors, p21(127) and p27(127).

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.
Incubation of Acetyl-CoA Carboxylase in Acutely Injured Tubular Cells Exacerbates DNA Damage and Mitochondria Fission in Diabetic Nephropathy
Xiaohuan Liu,1,2 Jiuhua Li,1 Shun-Yang Cheng,1 Guixia Li,1,3 Joseph V. Bonventre,1 Brigham and Women’s Hospital, Boston, MA; The Second Hospital, Checllos College of Medicine, Shandong University, Jinan, China; 3Shenzhen Third People’s Hospital, Shenzhen, China.

Background: Both diabetes and acute tubular injury (ATI) alter lipid metabolism of proximal tubules. Inhibiting lipogenesis causes G2/M 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 α-SMA. ATI was induced by a single deribeterin toxin (DT) injection in Akita mice in which the DT receptor (DTR) was introduced genetically into the kidney tubule (AkitaSIX2-DTR). Mice were fed a high-fat diet (HFD). The expression ratio of p-ACC/ACC was determined at 3 days after DT and markers for tubular injury and DNA damage (p-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 α-SMA in human DN specimens. At day 3 after DT, ATI increased the p-ACC/ACC ratio in the Akita 3H2O mice on HFD and resulted in enhanced expression of p-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 (MFF) without a further increase of p-H2AX. Etomoxir, which blocked acylcarnitine entry into mitochondria, reduced MFF and p-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 as a measure of cell proliferation. An unpaired T-test was used to compare ANG-3777 or HGF versus vehicle (dimethyl sulfoxide) treatment.

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).

Conclusions: 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.

A Combination of Contrast Media and Radiation Increases DNA Damage and Delays DNA Damage Repair in Mouse Kidneys
Shu Fujino, Shigehiro Doi, Toshiki Doi, Ayumu Nakashima, Takao Masaki. Department of Nephrology, Hiroshima University Hospital, Hiroshima, Japan.

Background: Contrast-induced nephropathy (CIN), resulting from contrast media (CM) administration, is a major complication of angiographic procedures. CIN may also be induced by exposure to radiation. However, the molecular mechanism of CIN has only been investigated using a CM-injected rodent model. Here, we examined the dual effect of CM and irradiation (IR) on DNA damage and repair in in vitro and in vivo.

Methods: Human renal tubular epithelium (HK)-2 cells were stimulated by medium containing 100 μg iodine/ml of iohexol (Ihx-HK2), 1 Gy of X-ray irradiation (IR-HK2), or both (Ihx+IR-HK2). Mannitol-treated cells were used as an experimental control (Man-HK2 or Man+IR-HK2). For the in vivo study, ischemic reperfusion injury (IRI)

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was induced in mice after right kidney removal, then IRI mice were treated with 200 μL saline and/or 320 mg/kg/day γ-irradiation 24 h after injury. CN was performed without performing immunohistochemistry, immunofluorescence staining, and western blotting for DNA damage markers (γH2AX, PATM, 53BP1, and RAD51), an oxidative stress marker (8-OHdG), a macrophage marker (F4/80), and klotho.

Results: Immunofluorescence staining revealed increased expression of γH2AX, 53BP1, and RAD51 in Ihx+IR-HK2 compared with Ihx- or IR-HK2. These proteins remained highly expressed at 24 h in Ihx-IR-HK2, but not in Ihx- or IR-HK2. Cells positive for γH2AX, pATM, 53BP1, and RAD51 were significantly increased in IRI/CIN+IR mouse kidneys. As a result of DNA damage and delay DNA damage repair, which are accompanied by increased levels of oxidative stress and inflammation and downregulation of klotho expression.

Conclusions: Both CM administration and exposure to radiation induce DNA damage and delay DNA damage repair, which are accompanied by increased levels of oxidative stress and inflammation and downregulation of klotho expression.

PO0251
Whole-Transcriptome Sequencing of Proximal Tubule Cells Exposed to Free Light Chains
Rohit Unadkat,1 Vecchi Batuman,1,2 Tulane University School of Medicine, New Orleans, LA; 2SLFCHS, Southeast Louisiana Veterans Health Care System, New Orleans, LA.

Background: Despite medical advancements, molecular markers for early detection of kidney injury (KI) are limited. Serum creatinine, the only functional marker for KI, has poor predictive accuracy, particularly in the early stages of AKI due to free light chains in multiple myeloma (MM) patients. Identification of new markers would be highly useful in a select group of MM patients who do not present initially with a detectable rise in creatinine.

Methods: Human kidney proximal tubule cells (PTCs; RPTEC cell line) were exposed to κ or λ FLCs. Control/ treated cells were harvested, and total RNA (mRNA) was isolated following standard procedures for whole transcriptome analysis. Whole transcriptome sequencing by RNA sequencing for whole transcriptome was performed by using Illumina NextSeq 500 to generate ~60M paired-end 75bp reads per sample. After initial data quality checking by FastQC and RseqC, bioinformatics analysis was performed using TopHat, Samtools, and Picard. For further classification, annotation, and visualization 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, BS2) and ERK signaling (KCTD12, IF6, MAP3K, ERK1/2, JNK, p38), and inflammation (CXCL6, TNFA, IL6, CXCL8, IL8, IRAK1, IRAK4, TAFK6, NFKB, IKBA, IKK) as well as miRNAs (hsa-146a-5p, hsa-miR-574-3p, hsa-miR-331-3p, hsa-miR-125a-5p) in FLC induced tubular injury in MM patients. We also found a K1 mechanism involving cross-talk among innate immunity, ERK signaling, and the inflammatory pathway by different FLCS types.

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

PO0252
Single-Cell Profiling of AKI in Mice Highlights Differential Immune Cellular Response Programs in Regeneration and Fibrosis
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Background: After acute injury the kidney has the ability to regenerate and repair to a certain extent. On the other hand, maladaptive injury response leads to kidney fibrosis and chronic kidney disease. We are only beginning to understand the complex interactions of epithelial, stromal and immune cells involved in these adaptive processes.

Methods: Here we profiled gene expression changes at single cell resolution over time in acute injuries of mice subjected to mild and severe bilateral ischemia-reperfusion injury (IRI). Immune function, structure, bulk and single cell gene expression analysis was performed on day 1, 3 and 14. We used gene regulatory network and trajectory analyses to define key drivers of successful and failed regeneration.

Results: Gene expression resulted in similar kidney function decline as analyzied by serum BUN; however long ischemia led to severe kidney fibrosis, while mild ischemia prompted minimal structural changes. In total, we obtained scRNAseq data for >160,000 cells. IRI lead to very significant cell proportion changes including a decrease in renal tubule cells, progenitor cell clusters, and increased numbers of immune cells involved in innate and adaptive immune functions. Whole transcriptome sequencing for whole transcriptome was performed by using Illumina NextSeq 500 to generate ~60M paired-end 75bp reads per sample. After initial data quality checking by FastQC and RseqC, bioinformatics analysis was performed using TopHat, Samtools, and Picard. For further classification, annotation, and visualization 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, BS2) and ERK signaling (KCTD12, IF6, MAP3K, ERK1/2, JNK, p38), and inflammation (CXCL6, TNFA, IL6, CXCL8, IL8, IRAK1, IRAK4, TAFK6, NFKB, IKBA, IKK) as well as miRNAs (hsa-146a-5p, hsa-miR-574-3p, hsa-miR-331-3p, hsa-miR-125a-5p) in FLC induced tubular injury in MM patients. We also found a K1 mechanism involving cross-talk among innate immunity, ERK signaling, and the inflammatory pathway by different FLCS types.

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,2 Paul W. Crawford,3 Moustafa A. Moustafa,2 Wenli Luo,4 Alex Goldfarb,5 Renal Associates PA, San Antonio, TX; 1California Center of Renal & Vascular Research, Clincs, El-Fayoum, CA; 2South Carolina Nephrology & Hypertension Center, Inc, Orangeburg, SC; 3Akebia 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 ferric 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 (1 g/day) or 2 tablets BID (4 g/day). At Wk 12, if Hb ≤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 changes in transferrin saturation (TSAT), ferritin, and phosphate to Wk 48.

Results: This analysis included 183 of 206 randomized patients. Groups were well matched, with mean age 69.5±10.3 y and 54% with CKD due to diabetes. Mean BL sCr was 3.3±1.6 mg/dL (110±60 µmol/L). Hb was 9.6±1.5 g/dL and 80% of patients were Hb responders (>1.2 g/dL increase) at BL. At Wk 48, the percentage of responders was 73% in BID and 72% in TID groups. No significant differences were observed between groups in adverse events. The percentage of patients with a >10% increase in Hb from BL to Wk 24 was 50% in BID and 47% in TID. Incidence of serious AEs was 13.9% in BID and 17.3% in TID groups. Fewer 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 - Akebia Therapeutics, Inc.

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**PO0255**

**Triferic (Ferric Pyrophosphate Citrate, FPC) Maintains Hemoglobin and Reduces IV Iron: Results from a Single-Site 2-Year Observational Analysis**

Marc L. Hoffman,1 Richard Delvalle,2 Raymond D. Pratt,1 Rockwell Medical Inc, Wixom, MI; Center for Renal Replacement, LLC, Lincolnwood, IL

**Background:** Triferic (ferric pyrophosphate citrate, FPC) is approved as an iron (Fe) replacement product for anemia in hemoglobin (Hgb) in adult patients (pts) receiving chronic hemodialysis (HD). Trial data have demonstrated that FPC maintains Fe stores and Hgb while reducing IV Fe usage with a well-tolerated safety profile. We now report one clinic’s experience using FPC for all HD patients (pts) during a 2-year period.

**Methods:** FPC was added to centrally delivered liquid bicarbonate to provide 110 μg Fe/dialyze. All patients received FPC at each HD. Anonymized retrospective data from the electronic health record were collected between Sep 2016–Dec 2018. A recommended FPC Fe protocol was provided, but the clinic was allowed to adjust anemia management at their discretion. Supplemental Fe gluconate (IV Fe) was administered according to a protocol based on serum ferritin and TSAT values. All pts receiving IV Fe received single doses of 125 mg elemental Fe up to a max of 500 mg Fe/month when criteria for supplementation were met. During the first 4 months of FPC, the center converted pts from epoetin alfa (EPO) to darboepoetin alfa (INN), therefore INN equivalents were calculated using the published conversion guide (EPO dose/300). IV iron and ESA use were standardized and changes from pre-FPC were reported for Hgb, IV Fe and ESA usage. KDQoL data were available for the years 2016–2018.

**Results:** Within 3 months of initiation of FPC, Hgb increased by 0.3 g/dL and was maintained during the observation period. Total IV Fe dose was significantly reduced by 78.4%. Darboepoetin equivalent doses were reduced from pre-FPC by 31.5% by the end of the observation period. Compared to the first year of assessments (2016), post FPC assessments of QoL showed improvements in the Burden of Kidney Disease (KD), Symptoms and Problems of KD and Effects of KD on daily life scales. No adverse events related to FPC were reported.

**Conclusions:** This observational study demonstrates that FPC is a well-tolerated replacement for IV Fe when administered to all patients in a HD unit. The findings of this real-world observational study align with those of clinical trials in terms of reduction of IV Fe use and maintenance of Hgb. ESA was gradually reduced and the KDQoL showed improvements in the burden and symptoms of kidney disease.

**Funding:** Commercial Support - Rockwell Medical Inc.

**PO0256**

**Roxadustat Lowers Risk of Red Blood Cell Transfusion in Patients with Anemia of CKD**

Steven Fishbane,1 Robert Provenzano,2 Anjay Rastogi,2 Daniel W. Coyne,1 Robetorio Pecoits-Filho,3 Chaim Charytan,1 Maksym Pola,2 Lona Poole,1 Gopal Sahni,2 Willis Chou,1 Tyson T. Lee,1 Kien-Hung F. Yu,1 Northwell Health, Great Neck, NY; 2Wayne State University, Detroit, MI; 3University of California Los Angeles, Los Angeles, CA; 4Washington University in Saint Louis School of Medicine, Saint Louis, MO; 5Arbor Research Collaborative for Health, Ann Arbor, MI; 6Nephrology Associates, PC, New Rochelle, NY; 7AstraZeneca, Warrikon, Poland; 8 FibroGen Inc., San Francisco, CA; 9Renal Associates PA, San Antonio, TX.

**Background:** RBC transfusions may cause reactions, lead to allo-sensitization, or increase the risk of blood-borne infections. Reducing the need for RBC transfusions is desirable. This analysis assessed whether roxadustat, an oral hypoxia-inducible factor prolyl hydroxylase inhibitor, treats anemia by enhancing erythropoietin synthesis and reducing transferrin synthesis and increasing iron availability via reducing hepcidin and increasing iron transport. We assessed the effect of roxadustat on iron parameters in patients with NDD-CKD.

**Methods:** Patients were randomized to double-blind roxadustat or placebo in 3 pivotal NDD-CKD trials. Oral iron was administered without restriction per discretion of the treating physician, and intravenous (IV) iron use was limited to rescue therapy. Mean changes from baseline (BL) in Hb, hepcidin, and iron parameters were evaluated. Pooled results are reported.

**Results:** Overall, 4277 patients were evaluated (roxadustat N=2391; placebo N=1886). Mean eGFR was 20 ml/min/1.73 m² in both groups. Roxadustat was superior to placebo in increasing mean Hb from BL (9.1 g/dL for both groups) averaged over Weeks 24–52: 1.9 vs 0.2 g/dL (P=0.0001). IV iron use was required in 2.1% of roxadustat vs 4.8% of placebo patients during the first 52 weeks after randomization. Roxadustat reduced hepcidin and increased both transferrin and serum iron (Figure). Reductions in ferritin and transferrin saturation occurred predominantly in patients with the highest BL values of hepatocyte nuclear factor-4α expression. Mean (±SD) baseline values were 785 (±382) ng/mL and 44 (±35)% for hepcidin and transferrin respectively. Roxadustat reduced mean % change from baseline at Week 24 in hepcidin vs placebo by 21% (−54.9% vs −33.6%, P<0.001) and in transferrin by 23% (−27.4% vs −4.9%, P=0.002). Reductions in transferrin and transferrin saturation were associated with a mean increase in serum iron of 7.4 μg/dL (P<0.001). In the 20% of patients with baseline serum ferritin >600 ng/mL, reductions in hepcidin and transferrin were even more pronounced.

**Conclusions:** Roxadustat increased both serum iron and iron-carrying capacity (transferrin) while simultaneously inducing erythropoietin and correcting anemia in patients with NDD-CKD, without the need for regular IV iron supplementation.

**Funding:** Commercial Support - AstraZeneca

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**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>RBC transfusion risk reduction vs placebo</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NORDIC (N=1079)</td>
<td>0.92 (0.73, 1.18)</td>
<td>&lt;0.001</td>
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</tr>
<tr>
<td>HARMONY (N=706)</td>
<td>0.92 (0.72, 1.18)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>FREEDOM (N=292)</td>
<td>0.89 (0.69, 1.16)</td>
<td>0.31</td>
<td></td>
</tr>
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PO0258

Health-Related Quality of Life in Roxadustat-Treated Patients with Anemia and Non-Dialysis-Dependent CKD

Daniel W. Coyne,1 Roberto Manlio-Karim,2 Pablo E. Pergola,3 Carol A. Pollock,4 Roberto Pescitello-Filho,5,6 Tyson T. Lee,7 Elise Hardy,2 Kim-Hung P. Yu8 Washington University in Saint Louis School of Medicine, Saint Louis, MO; 9South Texas Kidney Specialists, P.A., McAllen, TX; 1Renal Associates PA, San Antonio, TX; 2The University of Sydney, Sydney, NSW, Australia; 3Arbor Research Collaborative for Health, Ann Arbor, MI; Pontificia Universidade Catolica do Parana Departamento de Medicina, Curitiba, Brazil; 4Fibrogen Inc, San Francisco, CA; 5AstraZeneca, 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 (HRQOL) by reducing physical capacity and energy levels. Studies have demonstrated a direct relationship between HRQOL scores and hemoglobin (Hb) levels in non-dialysis-dependent (NDD) and dialysis-dependent patients with CKD. We assessed the impact of roxadustat on HRQOL 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 post-treatment HRQOL measurement were included. Mean changes from baseline to Week 12 in HRQOL scores were compared between the treatment groups.

Results: Least-squares mean treatment differences favored the roxadustat group at Week 12 in the majority of measures analyzed (Table). Between-group differences were larger in subgroups with lower (ie, worse) baseline scores. 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 HRQOL measures vs. placebo in patients with NDD-CKD.

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

Table: Mean CFB in HB averaged w/eeks 28–52 Regardless of Rescue Therapy (ID, DDI)*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>LSM Difference (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>0.12 (0.35, 0.68)</td>
<td>0.0050</td>
</tr>
<tr>
<td>Anemia A</td>
<td>0.21 (0.06, 0.36)</td>
<td>0.0059</td>
</tr>
<tr>
<td>Anemia B</td>
<td>0.12 (0.04, 0.21)</td>
<td>0.0450</td>
</tr>
<tr>
<td>Anemia C</td>
<td>0.14 (0.07, 0.22)</td>
<td>0.0017</td>
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PO0259

Subgroup Analyses of Efficacy of Roxadustat for Treatment of Anemia in Patients with Incident Dialysis-Dependent CKD

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Background: Roxadustat is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor that stimulates erythropoiesis and improves iron metabolism.

Methods: 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: ROX (n=2390) 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]), corresponding to a least-squares mean (LSM) difference of 1.72 (95% CI: 1.65, 1.79) (p<0.0001). The results of all subgroup analyses were consistent with those for both the primary US efficacy endpoint and the percentage of patients requiring rescue therapy in the overall NDD population (Table). Significantly fewer patients required rescue therapy during roxadustat treatment vs. placebo (8.9% vs. 31.1%), corresponding to a hazard ratio of 0.19 (95% CI: 0.16, 0.23) (p=0.0001). The effect was consistent in all subgroups and especially pronounced in patients with baseline Hb <8.0 g/dL (18.1% vs. 59.3%) and those with baseline eGFR <100 mL/min/1.73m2 (14.8% vs. 48.3%).

Conclusions: The efficacy of roxadustat vs. placebo for a larger mean CFB in Hb and fewer patients that received rescue therapy was consistent across a wide range of prespecified subgroups in the NDD-CKD population.

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

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Background: Roxadustat is a novel, orally bioavailable, heterocyclic small molecule that reversibly inhibits inhibitory- inducible factor (IFHI) prolyl hydroxylase enzymes and activates HIF and transcription of HIF-responsive genes, including erythropoietin.

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: -2.02 g/dL (p<0.0001), respectively. The rate of transfusion was approximately 4 times higher in patients with Hb between 8.0 and <10.0 g/dL vs. those with Hb ≥10 g/dL. 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/dL 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 2.4% at Weeks 28-52. Mean MCV 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.

PO0263
Roxadustat Increases Hemoglobin in Non-Dialysis-Dependent (NDD) 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 that stimulates erythropoiesis by increasing endogenous erythropoietin and improving iron metabolism.

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 period dose evaluation/titratin. 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 and it was maintained at Weeks 28-52. Mean MCV 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.
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 quintile. Roxadustat dose requirements at Week 24 were based on mean weekly dose in mg per kg of mean BL weight.

Results: Overall, 1538 roxadustat-treated DD-CKD patients were assessed and had a mean BL Hb of 10.5 g/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 1.2 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 a 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 Table, 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 98.61 to 75.80 pg/mL (P < 0.001).

Funding: Commercial Support - AstraZeneca

PO0267

Roxadustat Treatment Corrects Anemia to Hemoglobin (Hb) Values ≥10 g/dL in the Majority of Patients with Non-Dialysis-Dependent Chronic Kidney Disease (NDD-CKD)
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Background: The KDIGO clinical practice guidelines recommend the treatment of anemia in NDD-CKD patients with Hb <10 g/dL to reduce associated symptoms and prevent the need for red blood cell transfusions. Roxadustat is a hypoxia-inducible factor prolyl hydroxylase inhibitor studied for the treatment of anemia in patients with CKD through increasing erythropoietin synthesis and enhancing iron utilization. We studied the percentage of patients with NDD-CKD treated with roxadustat achieving Hb ≥10 g/dL.

Methods: Patients with Hb <10 g/dL and eGFR <60 mL/min/1.73 m2 were randomized to roxadustat or placebo in 3 pivotal double-blind NDD-CKD trials (OLYMPUS, ANDES and ALPS). The cumulative percentage of patients with Hb ≥10 g/dL for at least 2 consecutive visits was analyzed monthly over 12 months of roxadustat treatment, using the number of patients remaining on roxadustat treatment at each time point as the denominator. Hb values were censored for 6 weeks following rescue therapy.

Results: In total, 2391 patients received roxadustat. Mean Hb at baseline was 9.1 g/dL and mean eGFR was 19.7 mL/min/1.73 m2. Among patients still on roxadustat treatment, the cumulative percentage of patients with Hb ≥10 g/dL for at least 2 consecutive visits was 38.3%, 75.5%, and 87.0% at months 1, 2, and 3, respectively, and 96.4% at month 6. Among patients still receiving roxadustat treatment at 12 months, the cumulative percentage with confirmed Hb ≥10 g/dL was 99.0%.

Conclusions: Roxadustat effectively raised Hb levels in NDD-CKD patients, with over 95% of patients achieving Hb ≥10 g/dL after 5 months of treatment.

Funding: Commercial Support - AstraZeneca

PO0263

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
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 (HIF) stabilization was capable of promote 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 darbepoetin alfa (DA; once weekly [DD]; once every two weeks [NDD]). Pts were titrated to maintain target hemoglobin. Ophthalmological assessments (funduscopic photograph, optical coherence tomography) were performed by centralized grading; vision acuity measurements were performed at baseline, week 18, and week 24. Results were compared between study groups using the Wilcoxon rank-sum test. Rates of emergent adverse events (AEs) were assessed.

Results: A total of 302 DD pts (150, roxadustat; 152, DA) and 262 NDD pts (131, roxadustat; 131, DA) were randomized and received ≥1 dose of study drug. Results from the ophthalmological funduscopic photograph assessments are reported in Table 1. No meaningful changes were observed 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.

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 darbepoetin 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. Treatment-emergent adverse events (TEAEs) were assessed.

Results: A total of 262 pts were randomized to CGs and received ≥1 dose of roxadustat (n=131) or DA (n=131); 70 pts were allocated to RG and received ≥1 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 efficacy 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; noninferiority of roxadustat efficacy against DA was evaluated.

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.

PO0270

HIF Prolyl Hydroxylase Inhibitor Improves Exercise Endurance and Hardly Affects Instantaneous Force in Mice

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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 not been fully understood. 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 Diabetic Patients with CKD

Methods: The Canadian Organ Replacement Register was used to identify 35,945 adults 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: Era 1 (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 102.9 g/L in 2007 to 93.9 g/L in 2015 corresponding with a doubling in the prevalence of hemoglobin <80 g/L (8% to 17%) and a reduction in ESA use (49% to 44%). A total of 11,810 events were observed during 66,844 person years of follow-up. After multi-variable adjustment, Era 3 was associated with an 8% relative risk reduction in the primary outcome compared to Era 1 (hazard ratio (HR) 0.92, 95% confidence interval (CI) 0.88-0.96), driven by a decrease in all-cause mortality (HR 0.90, 95% CI 0.85-0.94) without a reduction in AMI or stroke. In a model without era, neither hemoglobin nor ESA use was an independent predictor of mortality.

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 <90 g/L, which represents a substantial shift in practice and merits further investigation in terms of patient-centered outcomes.

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PO0274
Cost and Healthcare Resource Use in Patients with Anemia in CKD
Using Linked Us Claims and Electronic Health Records

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 ≥2 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 confirmatory eGFR (baseline period). Total site- specific costs and selected healthcare resource utilization were analyzed and stratified by presence of baseline Hb range, CKD stage, sex, and insurance type.

Results: Of 22,720 patients (n = 228) had baseline anemia, 77% (17,437) did not; females accounted for 60% and 56% of the patients, mean ages ≥70 (SD) were 70 (14) and 70 (12) years, and median follow-up times were 2.9 and 3.8 years, respectively. Baseline anemia prevalence by CKD stage was 18% (stage 3a), 25% (3b), 41% (4), and 60% (5). Median per patient total costs were $49,012 and $31,667, total hospitalization costs were $334,797 and $226,925, and total ER costs were $2,232 and $1,891, respectively. Median annual number of transfusions doubled (2 vs 1) and annual transfusion cost was 50% greater in patients with vs without baseline anemia, respectively. Slightly increased

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
costs were associated with male sex and were markedly increased by advancing CKD stage (≥3a), baseline HB <10, and supplemental Medicare and non-capitated insurance coverage.

**Conclusions:** Anemia is associated with substantially added direct cost and healthcare resource utilization experienced by patients with non-dialysis CKD, in both early and advanced stages and with lower HB. Effective management of anemia in CKD offers an opportunity to address this ongoing burden.

**Funding:** Commercial Support - AstraZeneca

**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 years (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 12.36 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 patients with an undetected Hb level 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) from Inovalon’s Medical Outcomes Research for Effectiveness and Economics (MORE®) Registry® linked to eGFR and hemoglobin (Hgb) values from Prognosis laboratory data. Patients with ≥2 consecutive eGFR tests with eGFR 15-59 mL/min/1.73m2 (≥90 days apart) and severe anemia (Hgb <9 g/dL; January 1, 2018) were retained for analysis; patients on maintenance dialysis were excluded. Severe anemia was defined as Hgb<10 g/dL, measured within 90 days of index eGFR. Red blood cell transfusion (RBCT) during a 12-month follow up was identified using procedure codes. A logistic regression model identified baseline factors associated with receiving RBCT.

**Results:** A total of 1,305,334 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 13.5% in MORE® cohort, with prevalence among Medicare Advantage patients 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 both FFS and MORE® cohorts primarily in Medicare Advantage. Marginal clinical factors influence the odds of severely anemic NDD CKD patients receiving RBCT.

**Funding:** Commercial Support - AstraZeneca

Table reports percentages. Marginally-adjusted prevalence derived using logistic regression models (age, sex, education, marital status, income, health insurance, employment, smoking, alcohol use, vascular disease, chronic 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.**

**PO0277**

**Association of Anemia with Activities of Daily Living in CKD: The National Health and Nutrition Examination Survey (NHANES), 1999-2016**

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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=33,300; 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 using WHO criteria. ADL impairment was defined as "some difficulty" in performing ADL activity.

**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%C.I: 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, education, marital status, income, health insurance, employment, smoking, alcohol use, vascular disease, chronic heart failure, coronary heart disease, angina pectoris, heart attack, stroke, arthritis, chronic obstructive pulmonary disease, body mass index, hypertension, diabetes, and hyperlipidemia).

**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 Linked Claims and Electronic Health Record data (IBM Health, Armonk, NY). Pts were aged ≥18 with ≥2 eGFR measures ≥60 mL/min/1.73 m2 ≥90 days apart. Anemia was defined as the presence of any observed HB <10 g/dL within a 6 months period of confirmatory eGFR (anemia BL period). In addition, the BL period for disease history was defined as the start of pt data +6 months, and for lab measures and medications was defined as date of the second confirmatory eGFR +6 months. Pts with active bleeding, chronic dialysis, and tenofovir derivatives therapy were excluded. 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: Of the total study cohort (N=22,720), 23% (n=5283) 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-y were 0.8 and 0.7 for ACS, 1.6 and 0.8 for HFh, respectively, and 0.7 in both groups for S. The incidence of HFh in patients with TSAT <25% or 25-45% was 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories (G4 and G5) were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 20.3% and 36.1%, respectively. Lower eGFR categories were 2.0%, 4.2%, 9.2%, 2.0280
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 the 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.
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PO0281
Lower Transferrin Saturation (TSAT) Is Associated with Worse Health-Related Quality of Life (HRQOL) in Non-Dialysis 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 NDD-CKD stage 3 to 5 patients to test the association between TSAT and ferritin with HRQOL.
Methods: Patients from Brazil (N=205), France (N=2015), and the US (N=293) in the Chronic Kidney Disease Outcomes and Practice Patterns Study (CKDopps, 2013 to 2019) with TSAT, ferritin, and HRQOL data 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: 2513 patients were included. In the primary analyses, TSAT ≤15% and both ferritin <50 ng/mL and 200-399 ng/mL were associated with worse PCS scores, while MCV 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.

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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). We report the results 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) after 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. 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 levels 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 anemia-stimulating agents were excluded. Response to iron therapy was defined as improvement in both hemoglobin and hematocrit after iron therapy. Changes of serum iron were used as a surrogate measure of adherence to iron therapy. Data are presented as median (interquartile range).

Results: We identified 44 children (48% boys) who met the inclusion criteria. Median age was 11 (5-15) years, glomerular filtration rate (GFR) 46 (31-60) mL/min/1.73m². Ferrous sulfate was used in 86.4% of children. The interval between visits was 61 (31-120) days. Iron therapy resulted in a significant increase in transferrin saturation (14 (0-21%), p<0.01) and serum iron (45 to 65 μg/dL, p<0.01). While there was an overall improvement of hemoglobin (from 10.6 to 11.2 g/dL, p<0.02), 45% of children did not respond to iron therapy. Non-responders had a significantly smaller change in serum iron after iron therapy compared to responders (3 vs. 35 μg/dL, p=0.03), likely indicating low adherence to iron therapy by non-responders. Baseline age, GFR, hemoglobin, transferrin saturation, serum iron, and serum ferritin were not different between responders and non-responders. Baseline body weight and height Z scores were significantly lower in non-responders than in responders (-0.67 vs. 0.12, p=0.04 and -1.66 vs. -0.25, p=0.02, respectively), possibly representing differences in nutritional status.

Conclusions: This is the first study that systematically assesses response to oral iron therapy in children with pre-dialysis CKD after 2012 Kidney Disease Improving Global Outcomes (KDIGO) guidelines. Response to iron therapy may be related to medication adherence and baseline nutritional characteristics of study participants.
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 <.05) assessed educational effect. Cramer’s V was used to calculate the effect size (0.00-0.15 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=.001, V=.156; Activity 2: N=93, P=.001, V=.162 Individual question-level improvement was also demonstrated: 21% of nephrologists (N=75, P=.05; V=.169) improved at correctly identifying the mechanism of action of HIF-PHIs 20% of nephrologists (N=75, P=.05; V=.197) improved at recognizing clinical trial data for HIF-PHIs 33% of nephrologists (N=92, P=.05; V=.315) improved at recognizing clinical trial data for HIF-PHIs 21% of nephrologists (N=93, P=.05; V=.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

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

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 chi-square test (5% significance level, P <.05) assessed educational effect. Cramer’s V was used to calculate the effect size (0.00-0.15 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<.05; V=.216) improved at correctly identifying the mechanism of action of HIF-PHIS 11% of nephrologists (P=.72; V=.032) demonstrated improvement at selecting the recommended use of erythropoiesis stimulating agents (ESAs) in the treatment of anemia 21% of nephrologists (P<.05; V=.181) improved at recognizing clinical trial data of HIF-PHIS 47% reported increased confidence in understanding HIF-PHI clinical trial data Continued educational gaps: 52% of nephrologists did not recognize the mechanism of action of emerging HIF-PHIS 47% of nephrologists did not recognize the role of ESAs in the treatment of anemia 31% 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

Treatment Pathways of Non-Dialysis-Dependent CKD Patients with Anemia: A Report from the DISCOVER CKD Retrospective Cohort

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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.

Funding: Commercial Support - independent educational grant from AstraZeneca and Fibrogen

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 demographic characteristics, 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%
PO0289
Patient Preferences Study for Treatments of Anemia in CKD Patients Not on Dialysis (NDD)
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Background: Erythropoietin analogues (EAs) are a mainstay of treatment of anemia in adult patients with CKD but they are associated with increased risk of cardiovascular (CV) events. Furthermore, their mode of administration (intravenous or subcutaneous [SC]) may represent a barrier to some patients. As such, the aim of this study was to understand patients’ valuation of attributes associated with CKD anemia treatments.

Methods: Adult (≥18 years) patients from UK, Spain, Germany, and France, who had NDD CKD anemia and were being treated with EAs, participated in this online discrete choice experiment (DCE). Patients were presented with choice tasks, each with two anemia treatment options described in terms of five attributes (mode of administration, need for iron supplementation, risk of gastrointestinal [GI] side effects, risk of major CV events, and impact on energy levels). A multinomial logit model with an error component was used to analyze participants’ choices and estimate their treatment preferences. Estimated preferences were used to determine maximum level of CV and GI risk that patients were willing to tolerate to improve other treatment features.

Results: Between November 2019 and March 2020, 209 eligible patients (53% male) completed the DCE survey. The mean (SD) age was 53.78 (12.73) years; patients had been diagnosed with CKD 6.02 (7.49) years prior, and with CKD anemia 3.45 (4.44) years prior. Patients were found, on average, to value each of the five attributes associated with the treatments of CKD anemia. Patients were willing to tolerate a 5.12% (95% CI: 1.99; 8.25) increase in the risk of a major CV event and an 11.73% (95% CI: 4.96; 18.50) increase in the risk of GI side effects to switch from an at-home SC injection administered once every 2 weeks to an at-home oral pill administered three times a week. Patients would be willing to tolerate a 20.31% increase in the risk of GI side effects and an 8.36% increase in the risk of a major CV event to move from sometimes having a lot of energy to always having a lot of energy.

Conclusions: Patients would be willing to tolerate increased risks of CV and GI events to obtain an oral treatment for NDD CKD anemia and to always have a lot of energy.

Funding: Commercial Support - Astellas Pharma, Inc.

PO0290

Background: We studied the effect of online education designed to improve the clinical performance of clinicians in the OB/Gyn and primary care setting related to iron deficiency anemia (IDA) management in women.

Methods: The continuing medical education (CME) activity was a 45-minute online text- and video-based activity focusing of different aspects of anemia management in the women’s health setting. The impact of the education on performance outcomes was measured with a follow-up Planned Change Assessment® (PCA) survey immediately post-education to assess planned changes in clinician practice. Survey participants were contacted 8 weeks later to assess reported actual changes in practice.

Results: In total, 1,239 clinicians completed the initial PCA questionnaire 275 OB/Gyn physicians, 142 OB/Gyn NPs and PAs, 446 PCPs, and 376 NP/PA in the primary care setting Of those, 1,171 (95%) indicated they planned to make changes 3,610 changes were planned, an average of 3.1 per complete PC of immediate PCA completers, 92 completed the follow-up PCA 89 completers (97%) made 331 changes in practice, an average of 3.1 per completer Of immediate PCA completers, 92 completed planned, an average of 3.1 per completer. As such, the aim of this study was to understand patients’ valuation of attributes associated with CKD anemia treatments.

Results: Between November 2019 and March 2020, 209 eligible patients (53% male) completed the DCE survey. The mean (SD) age was 53.78 (12.73) years; patients had been diagnosed with CKD 6.02 (7.49) years prior, and with CKD anemia 3.45 (4.44) years prior. Patients were found, on average, to value each of the five attributes associated with the treatments of CKD anemia. Patients were willing to tolerate a 5.12% (95% CI: 1.99; 8.25) increase in the risk of a major CV event and an 11.73% (95% CI: 4.96; 18.50) increase in the risk of GI side effects to switch from an at-home SC injection administered once every 2 weeks to an at-home oral pill administered three times a week. Patients would be willing to tolerate a 20.31% increase in the risk of GI side effects and an 8.36% increase in the risk of a major CV event to move from sometimes having a lot of energy to always having a lot of energy.

Conclusions: Patients would be willing to tolerate increased risks of CV and GI events to obtain an oral treatment for NDD CKD anemia and to always have a lot of energy.

Funding: Commercial Support - Astellas Pharma, Inc.

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 iron turnover, increase hepcidin levels, decrease iron status, and increase hemoglobin concentrations in anemic chronic kidney disease (CKD) patients. Increased EPO induces erythropoiesis secretion of erythropoiferone (ERF), which acts on the liver to suppress serum hepcidin production. To determine whether vadadustat mechanisms of action are dependent on ERF, we treated wild type (WT) and ERF knockout (EKO) mice, with and without 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 ERF mRNA, minimal marrow ERF mRNA, and no increase in ERF 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 ERF-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 HIF1α and EPO on FGF23 production and metabolism in adult patients with CKD but they are associated with increased risk of cardiovascular (CV) events. Furthermore, their mode of administration (intravenous or subcutaneous [SC]) may represent a barrier to some patients. As such, the aim of this study was to understand patients’ valuation of attributes associated with CKD anemia treatments.

Conclusions: Vadadustat ameliorates CKD-associated anemia independently of ERF, 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 - Aketbia Therapeutics, Inc.
Figure 1. Reactive oxygen species (ROS) and Heme Oxygenase-1 levels in red blood cells (RBC) from healthy controls (CON-RBC) and patients pre (PreHD-RBC) and post (Post/HD-RBC) hemodialysis. Data are shown as median and interquartile range of the Mean Fluorescence Intensity (MFI). ***p<0.001 and **p<0.01 represent the difference compared to CON-RBC. AP<0.001 represents the difference between pre- and post/HD-RBC.

PO0293
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, concomitant use 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 PHI11303 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 loc), 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 [s]PD 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 (CFIB) at Week 24 was noted between treatment groups. The final median dose for subjects on treatment changes was the same for those receiving and those not receiving PB (6 mg), with no meaningful difference in the Hgb at Week 24 (mean [s]PD: 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

PO0295
Hemoglobin Requirements of Clinical Trials Involving Anemia in CKD and Implications on Future Work: A Systematic Literature Review

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. Forty-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 medians (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 (9.1-11.1), 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 - Akebia Therapeutics, Inc.

PO0296
Excessive Decrease of Hematocrit After Discontinuation of Dapagliflozin Yoshiharu Wada,1 Yoshiyuki Hamamoto,3 Yoshishira Nakatani,3 Sachiko Honjo,1 Yamato Keida1, Yohei Seno,1 Kanako Iwasaki,1 Yorihiro Iwasaki,1 Jun Fujikawa,4 Hiroko Kakuta,1 Akihiro Hamaski,4 Tizuka 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 long 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.

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

Underline represents presenting author.
Methods: A total of 8 patients (male: n=4; age: 54.4±1.9 [mean±SD] years, BMI: 27.1±3.4 kg/m²; HbA1c: 9.2±1.2 %) with type 2 diabetes who were newly admitted 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 between 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 and hematocrit (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±2.14 %; 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 to continue to decrease 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 original level 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 open-heart surgery prevents AKI and prolongs organ function (cardiac transplant). 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 (20x10^6) were loaded into a hollow fiber Cell Expansion System (Quantum®, TERUMOBCR; pre-conditioned for cell adhesion with Fibronectin) and expanded using xMEM with 5% human Platelet Lysate (iPFL). 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 500x10^6 MSCs. The number of exosomes/nanoparticles derived from the 5% iPFL, per se was 4.1±10^11/mL. Post seeding of MSCs in the bioreactor, exosome numbers in the perfusate decreased and stabilized at 1.1±10^11/mL. The size of collected exosomes was between 60 and 100 nm.

Conclusions: The data from this pilot study demonstrate that iPFL-derived exosomes or nanoparticle 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 speciating 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 a point-of-care true GFR measurement for an individual, and possibly obviate the use of estimated GFR from ensemble equations. The plasma pharmacokinetics of the novel fluorescent compound MB-102, constructed to have the properties of a GFR tracer agent, is compared to that of iohexol, an established GFR tracer agent.

Methods: Intravenous administration of MB-102 followed immediately by iohexol (Omnipaque 300) was given to 120 subjects enrolled with estimated GFR in the range from normal to stage 4 CKD. Fifteen blood draws post-administration over 12 hours were used to investigate the plasma decay. Plasma was analyzed for both agent concentrations at each time point. Analysis of MB-102 in plasma used methodology developed internally, and analysis of iohexol used the standard multi-step method employing an internal standard, drying, and reconstitution.

Results: Plasma pharmacokinetic parameters, which includes GFR, were determined from the concentration vs. time data for each agent separately using standard pharmacokinetic software. For every subject, each agent exhibited a two-compartment model, the initial compartment being the vascular to tissue equilibrium, and the terminal compartment containing the slow metabolites. The terminal-compartment yield 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 (rsquared = 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.

Figure 1: Circles are data, line is a linear regression.

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 equilibrated with OAT1 (cPTEC-OAT1) exposed to 10-240min of dialysate and uremic plasma were evaluated for metabolic activity, membrane integrity (LDH release), inflammatory response (IL-6 and IL-8), oxidative stress (ROS) and OAT1 function (fluorescein uptake). Further, cPTECs grown on biofunctionalized hollow fiber membranes were extraluminally exposed to dialysate fluid, intraluminally perfused with human uremic 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 (IA3-AA)), 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 LDH 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±0.9 fold increase in ROS production was noticed. Still, exposure of cPTEC-OAT1-containing hollow fiber membranes were extraluminally exposed to dialysate fluid, intraluminally perfused with human uremic plasma (30min) and assessed for PBUTs clearance (indoxyl sulfate (IS = 2980±1438; KA = 223±120; L-Kyn = 324±100; HA = 6547±1278 and I3-AA = 884±130 mmol/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 GBM. 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. Phenotypal 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. Proliferation 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 cytoskeleton regulation, ECM-cell interaction, proliferation and transcription factors, suggesting that long-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 pathological conditions.

Funding: NIDDK Support, Private Foundation Support

PO0301

Chronic AMPK Activation Reprograms 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, differentially programmed 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 AMPK and TGFβ signaling enhances increased respiration induced by activation of AMPK.

Methods: Primary HREC were seeded on polystyrene tissue culture plates (100,000 cells/cm²). 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: Concomitant 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 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

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

Underline represents presenting author.

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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 (PixeeMo™ 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 PixeeMo™ 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 PixeeMo™ 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 10 cells/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.

**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 40,000 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.

**Results:** The network predictions matched the references in total kidney volume for a single patient at 5 treatments over a 3-week period. Model time constant and steady-state gain were obtained for a single patient at 5 treatments over a 3-week period.

**Conclusions:** 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.

**PO0305**

**A Simplified Fluid Dynamics Model of Ultrafiltration**

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**Background:** We recently presented a novel approach for the design of personalized ultrafiltration rate (UFR) profiles during hemodialysis (HD) treatments. The success of this approach depends on an accurate parameter estimation of a simplified fluid volume dynamics during ultrafiltration.

**Methods:** We used a simplified model derived from a validated fluid volume model during HD comprising intravascular and interstitial pools, microvascular refilling/filtration, and lymphatic flow. Input data used for parameter estimation are UFR profile and hematocrit (HCT) from CLIC obtained during actual HD treatments. Estimation was based on initial 30-min segment of the data and the model was validated based on the subsequent 30-min response. Model time constant and steady-state gain were obtained for a single patient at 5 treatments over a 3-week period.

**Results:** Estimation/validation results (Figure 1) demonstrate reasonable accuracy of the simplified fluid dynamics model. Underlying model parameters of a single patient exhibit significant variability between similar days of treatment and between treatment days (Figure 2). Both HCT response to same UFR profile (steady-state gain) and response time (time constant) vary by as much as 100%.

**Conclusions:** Successful estimation of fluid volume model parameters during HD is feasible which supports the concept of online design of personalized UFR profiles. A non-negligible variability of a patient’s model parameters may complicate the design of personalized UFR profiles.
PO0306

Human Amniotic Membrane as a Novel Scaffold for Induced Pluripotent Stem Cell-Derived Kidney Organoids

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Background: Human inducible pluripotent stem cells (hiPSCs) can be differentiated into kidney organoids that can be used to tissue-engineer functional renal tissue. However, there are several challenges to therapeutic implementation. Among these is how to elicit organoids in a manner that allows for both vascularization and filtrate outflow. Previous research has demonstrated in animal models, that kidney organoids can be perfused when implanted in the kidney subcapsular space. One limitation though is that there is no obvious filtrate outflow tract. Furthermore, in ESRD patients there would likely be significant fibrosis or even cystic disease that would prevent successful perfusion and filtrate outflow of kidney organoids implanted in a similar manner. Alternative heterotopic organoid implantation strategies should be considered. Examples include, but are not limited to, peritoneal implantation (with peritoneal dialysis catheter drainage) or tissue engineered tubular constructs for ureteral anastomoses. Here we describe a biomaterial, decellularized human amniotic membrane (dHAM), that could be used for differentiation of iPSC derived kidney organoids. Because kidney organoids will be exposed to mechanical forces in heterotopic implant locations, we examine the effects of mechanical stretch on the structure of kidney organoid tubules.

Methods: We decellularized dHAM with mild detergents, and differentiated kidney organoids in a manner previously described by the Little research group. We constructed a titanium stretch device that allowed for kidney organoid differentiation and uniaxial stretch of the dHAM acutely or over 10 days. We performed multiphoton microscopy to image the kidney organoids and then used 3D reconstructions to measure tubular volumes. Results: We have observed that dHAM can be differentiated on dHAM, and that uniaxial stretch of the dHAM elongates and increases tubular volumes within the kidney organoids, without tubular disruption or increased cell death.

Conclusions: dHAM is a promising scaffold for studying effects of mechanical forces on human kidney organoids in vitro. dHAMS could be used to facilitate the implantation of kidney organoids into the peritoneum or other heterotopic locations. The constructs have the flexibility to be used as a patch, modified into tubes after rolling, or form sac-like structures.

Funding: Other NIH Support - NIN NHIBB

PO0307

Renal Cell-Derived Extracellular Vesicles Improve Functional Phenotype of Kidney Tubuloids

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Background: Kidney tubuloids (KT) are adult stem cell-derived organoid that hold great potential in translational bioartificial kidneys (BAK). However, reproducing complete cell maturation and function remains a challenge. Extracellular vesicles (EVs) are cell-derived structures that regulate several cellular processes. In the kidney, EVs mediate interorgan communication through the transfer of bioactive molecules. This study aimed to investigate the use of renal EVs as modulator of KT phenotype by increasing the levels of organic anion transport 1 (OAT1), involved in renal waste handling, and explore their use for BAK engineering.

Methods: EVs from conditionally immortalized proximal tubule epithelial cells overexpressing OAT1 (cPTEC-OAT1) were isolated with 100 K filters, quantified by nanoparticle tracking analysis and incubated with KT. The 24 h conditioned media (CM) of cPTEC-OAT1, depleted or not of EVs, were used as controls. Gene expression was determined by QPCR and Western blotting. For renal tubule engineering, KT were seeded on hollow fibers and were exposed to EVs or CM. Molecule integrity and cell polarity were analyzed by immunofluorescence and confocal microscopy.

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 cPTEC-OAT1. In addition, renal EVs can support KT to form tight monolayersons on hollow fiber membranes. Further research is aimed at a full functional characterization of these bioengineered proximal tubules for application in BAK.

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 being 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 significant 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.

PO0309

Feature-Rich Covalent Stains for Interrogation of Kidney Tissue

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Background: Fluorescence microscopy is a workhorse tool in biomedical imaging but often poses significant challenge to practitioners in achieving bright or uniform labeling. In addition, while antibodies are effective specific labels, they often suffer penetration in thick tissues, loose binding in heavily fixed or processed specimens (e.g., FFPE tissue), high cost, and inconsistent reproducibility or commercial availability. Thus, it would be highly useful to develop a simple yet robust labeling alternative that could rapidly produce even staining for thick tissues and be compatible with a wide range of simple processing or clearing methods.

Methods: We use conventional fluorescent dyes to covalently label abundant chemical functional groups on kidney tissues. These include the use of amine-reactive...

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

Underline represents presenting author.
dyes for proteins and aldehyde-reactive dyes for carbohydrates. We term this approach Fluorescent Labeling of Abundant Reactive Entities (FLARE).

Results: We first showed FLARE’s utilities in freshly fixed mouse kidneys (≈100 μm) using super-resolution fluorescent microscopy. Within glomeruli, the carbohydrate stain specifically labeled the basement membranes of the capillary loops and the mesangial matrix, while the amine stain revealed mitochondria and brush border microvilli (Fig. A). 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 transplanta bilegenged engineered 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 of HUVECs and human glomerular cells. The recellularized grafts 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 thromboresistance 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%. Finally, 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 Regulations
Renal Tubular Epithelial Cell Function
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Background: Damage to renal proximal tubular 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 Tenvorwell inserts. Conditionally immortalized mouse RTPEC were grown TBM substrates. To induce stiffening, TBM was treated with the chemical crosslinker genipin. Decellularized TBM was characterized by western blot and immunofluorescence staining. Viability of the matrix and morphology of RTPEC were confirmed by LIVE/DEAD Viability/Cytotoxicity Kit. Real-time PCR was performed on RTPEC to evaluate the effect of stiffness on multiple genes related to kidney fibrosis and RTPEC differentiation.

Results: Western blot analysis of decellularized TBM showed the presence of lamin and collagen I 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 ANKRD1) 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 culture 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 RTPEC 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 phosphaturic 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’; Moldemutast) 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 reduced renal Egr-1 expression (p<0.01). Renal 1,25D anabolic Cyp27b1 and catabolic Cyp24a1 mRNAs were up and downregulated, respectively, in BAY-treated CKD mice. This extended treatment resulted in decreased BUN (p<0.01) and reduced expression of renal fibrosis markers (p<0.01). The bone marrow EpoR, Transferrin receptor, and Erfe mRNAs were all upregulated (p<0.05-0.01), and liver hepcidin expression was downregulated in both control and CKD groups treated with BAY (p<0.05-0.01). 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 stone 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-aminomethylnucleoside 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 normal 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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**PO0314**

**Cell Cycle Acceleration in Parathyroid Glands Is Caused by the Suppression of LncRNA Gas5 Expression in the Presence of a High-Phosphorus Diet in an Adenine-Induced CKD Rat Model**

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**Background:** Chronic kidney disease (CKD), especially secondary hyperparathyroidism (SHPT), is strongly associated with systemic calcification, including that in blood vessels. Therefore, it is important to elucidate its underlying pathological mechanism. SHPT is characterized by an unusually increased proliferation of parathyroid cells. We analyzed the expression of multiple cyclins, cyclin-dependent kinases (CDks) and CDk inhibitors and demonstrated that the accelerated cell cycle in SHPT is caused by a reduction in CDK1B1 expression (ASN 2019). To investigate the mechanism underlying SHPT development, we analyzed factors regulating cell cycle in parathyroid glands using two-photon imaging.

**Methods:** CKD was induced by a diet containing 0.75% adenine. For 5 days, few rats in the CKD and control groups were fed a diet containing 0.9% phosphorus, and the remaining rats were fed a diet containing 1.3% phosphorus. We investigated the expression levels of approximately 20 miRNAs, such as mir-221, known to regulate cell cycle. We analyzed the expression of multiple cyclins, cyclin-dependent kinases (CDks) and CDk inhibitors and demonstrated that the accelerated cell cycle in SHPT is caused by a reduction in CDK1B1 expression (ASN 2019). To investigate the mechanism underlying SHPT development, we analyzed factors regulating cell cycle in parathyroid glands using two-photon imaging.

**Results:** There were no significant differences in miRNA expression levels among the four groups (Figure 1). Gas5, known to be downregulated in prostate cancer cell line, directly upregulates CDK1B1 expression and further interacts with E2F1, which binds and activates CDK1B1. This strengthens the binding between E2F1 and CDK1B1 stronger. It was observed that the expression of Gas5 was significantly decreased when the high-phosphorus diet was added to the CKD environment, and E2F1 expression did not change significantly (Figure 2).

**Conclusions:** These results suggest that parathyroid cell proliferation might be due to the suppression of Gas5 expression in response to the addition of the high-phosphorus diet to the CKD environment, with a subsequent reduction in CDK1B1 expression.

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**PO0315**

**Treatment with β,γ-Methylenedadenosine 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 PZK receptor agonist β,γ-ATP promotes vascular smooth muscle cell (VSMC) calcification. Here, we aimed to evaluate whether β,γ-ATP 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-ATP (n=10) from start of the study until sacrifice at wk7. 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 TNP and SOST were analyzed by qPCR. AMC was evaluated by analysis of total Ca content in the arteries and quantification of the area % calcification on 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-ATP 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-ATP significantly reduced the Ca content in the aorta (mean ± SEM; vehicle 1.49 ± 1.51 mg Ca/g wet tissue vs β,γ-ATP 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-ATP did not significantly affect PWV scores. Treatment with β,γ-ATP also did not alter the mRNA expression of bone-like marker genes.

**Conclusions:** β,γ-ATP 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-ATP mediates its inhibitory effects on AMC probably by interfering with the formation of Ca-P crystals via its breakdown product methylene bisphosphonate. Further research will be conducted to evidence this hypothesis.

**Funding:** Government Support - Non-U.S. Underline represents presenting author.

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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 progressive rat model of CKD-MBD, the Cd 1/2 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 3 weeks of age (~60% NL kidney function) and ended at 28 weeks (~25% NL kidney function). Serum biochemistries, aorta and heart 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
PO0317
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-MBD

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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 CKD (CKD+); 2) CKD+ treated with ferric citrate (CKD+ + CIT); 3) CKD+ treated with IV iron sucrose (CKD+ + IV iron); and 4) CKD+ treated with IV iron sucrose and ferric citrate (CKD+ + IV iron + CIT). The rats were treated for 10 weeks. At sacrifice, the renal cortical tissue was collected for analysis.

Results: Ferric citrate changed markers of oxidative stress and bone metabolism compared to untreated CKD rats. Ferric citrate decreased oxidative stress markers and increased FGF23 levels in CKD rats.

Conclusions: Ferric citrate treatment improved oxidative stress and bone metabolism compared to untreated CKD rats.

PO0318
Upacicalcet, a Novel Non-Peptide Calcimimetic for the Treatment of Secondary Hyperparathyroidism, Has a Low Risk of Hypocalcemia

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Background: Calcimimetics are widely used for the treatment of secondary hyperparathyroidism (SHPT) in chronic renal failure patients. However, there are some problems with calcimimetics treatment. One of the biggest problems is hypocalcemia that leads to treatment interruption. Upacicalcet is expected to be a novel non-peptide calcimimetic that does not cause excessive hypocalcemia from the results of clinical studies. In the present study, we investigated the pharmacological characteristics of upacicalcet and effect on hypocalcemia in preclinical studies.

Methods: In vitro study was conducted using human CaSR-expressing (hCaSR) HEK-293T cells. In vivo study, upacicalcet was intravenously administered in a single dose to Double-Nephrectomized (Double-Nx) rats, an animal model of SHPT, and serum intact parathyroid hormone (iPTH) and Ca concentrations were measured.

Results: Upacicalcet increased the intracellular Ca2+ concentration in hCaSR-HEK-293T cells dose-dependently. Additionally, upacicalcet shifted the EC50 value for extracellular Ca2+ to lower concentrations in a dose dependent manner. In Double-Nx rats, 0.3, 3, and 30 mg/kg of upacicalcet dose-dependently reduced the serum iPTH level at 24h and 48h after administration, and the reductions were significantly greater than that in Control (P<0.01). Upacicalcet 0.3 mg/kg: 397±40 pg/mL vs. Control: 1306±80 pg/mL; P<0.001, 48h; upacicalcet 0.3 mg/kg: 795±91 pg/mL vs. Control: 1889±77 pg/mL; P<0.001.

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.
Methods: Aortic valve leaflets from commercial pig hearts were dissected and randomly assigned to experimental groups. Whole leaflets were cultured in individual wells. Two growth media were used for cultivation: standard growth medium and an antimony/oligoblastic growth medium. The latter was employed to inhibit contraction of the leaflet into a ball-like structure. Calcification was induced in the growth media by supplementing with 10 nM 1α,25-(OH)2D3 (but not CDP) or 10 nM 1α,25-(OH)2D3 and 0.1 μM b-glycerophosphate. 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: Osteodifferentiation with calcium accumulation was in principle absent when standard medium was used. However, when the antimony/oligoblastic 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 - Sanfilhi Therapeutics, Government Support - Non-U.S.

PO0321
Amelioration of Uremic Vascular Calcification After Experimental Aorta Transplantation
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Background: CKD causes a shift in phenotype of the vascular smooth muscle cell (VSMC) to a secretory cell and promotes vascular calcification (VC). Our aim was to study whether VC is reversed by transplantation of an 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 alfalfa/fenugreek treatment. The abdominal aorta of the uremic rat was transplanted into a normal rat (uremic ATx, n=16). Control groups were: 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 stable 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 1.9±0.18 vs. uremic 3.74±0.18 vs. uremic ATx 1.67±0.61), Sfrp1 (control 1.0±0.2 vs. uremic 13.69±4.47 vs. uremic ATx 2.62±0.84), ANKH (control 1.6±0.5 vs. uremic 10.43±6.90 vs. uremic ATx 4.94±1.72), Posnt (control 1.0±0.34 vs. uremic 3.19±0.77 vs. uremic ATx 1.74±0.85), Fnt1 (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 upregulated Wnt inhibitor sclerostin showed a trend towards downregulation by ATx. Activins 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 vascular calcification after experimental aorta transplantation.

Funding: Government Support - Non-U.S.

PO0322
Impaired Arterial Vitamin D Signaling Is Pathogenic in Vascular Calcification
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Background: Conflicting data exists as to whether vitamin D receptor agonists (VDRa) are protective of arterial calcification. This is confounded by inherent physiological differences between human and animal experimental models and conflicting published data. Herein, the study aims to address these problems by leveraging frontiers in human arterial organ culture models.

Methods: Human arteries were collected from 24 patients (healthy controls, n=12; end-stage CKD, n=12). Cross-sectional and interventional studies were performed using arterial segments with normal and calcified (containing 5mmol/L CaCl2 and 5mmol/L b-glycerophosphate) medium, ex vivo. To assess the role of VDRa therapy, arteries were treated with either calcitriol or paricalcitol.

Results: Human arteries express a functionally active vitamin D system, including VDR, 1α,25-hydroxylase and 24-hydroxylase (24-OHase) components and these were dysregulated in CKD arteries. Arteries from CKD patients exhibited reduced capacity to synthesize 1,25(OH)2D, increased basal expression and excessive induction of the vitamin D catabolic pathway in response to VDRa. VDRa therapy increased VDR expression in physiological conditions but reduced the 1α,25-OHase enzyme expression in patients with CKD.

Conclusions: Maladaptation of arterial vitamin D signaling components occurs in CKD. VDRA exposure can exert vasculo-protective effects and seems critical for the regulation of arterial health in CKD.

Funding: NIDDK Support

PO0323
Analysis of Human Jackstone Protrusions Show a Protein-Rich Core, Suggesting That Proteins Drive Their Rapid and Linear Growth
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Background: Jackstones are urinary stones that have arm-like extensions from the body of the stone. This morphology of stone has been long recognized but poorly studied.

Methods: Micro CT was used to analyze 96 jackstones from 47 different patient specimens. Additional analyses included infrared spectroscopy (IR), fluorescence microscopy, and immunohistochemistry for Tamm-Horsfall protein (THP)

Results: Jackstone cores consisted of an X-ray lucent core (high in protein by IR) and a tightly layered calcium oxalate monohydrate (COM) shell that matched the COM on the stone body. The layering in the shell region showed that the arms had grown at a more rapid pace way from the center of the stone than had the stone body. Microscopy studies showed brilliant autofluorescence in the core region but less in the COM shell. Immunno-staining showed that THP content was richer in the core region than in the shell.

Conclusions: We hypothesize that the protein-rich core of a jackstone arm preferentially binds more protein from the urine and resists deposition of COM, such that the arm tip grows rapidly, with the sides (shell) of the arm being covered with COM layers just like the body of the stone. This hypothesis suggests enrichment of growth-accelerating proteins in the core of the jack arm, which bind preferentially to the protein-rich tip but which bind less avidly to the COM surface of the stone. Identification of such proteins could provide clues as to how proteins modulate the deposition of mineral layers in kidney stone growth.

Funding: NIDDK Support

PO0324
Hyperphosphatemia Contributes to Inflammation, Iron Dysregulation, and Skeletal Muscle Wasting
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Background: Fibroblast growth factor (FGF) 23 is a phosphaturic hormone that promotes phosphate (Pi) excretion. In patients with chronic kidney disease (CKD), serum levels of Pi & FGF23 gradually rise as renal function declines & associates with various pathologies such as systemic inflammation, anemia, vascular calcification & muscle wasting. Our previous studies have shown FGF23 induces inflammatory cytokine expression by targeting hepatocytes via FGF receptor 4 (FGFR4). Other studies have shown Pi accelerates vascular calcification and other, whether Pi contributes to inflammation, anemia or skeletal muscle wasting remains unclear. Here we compare the
effects of Pi versus FGFR23 to determine their contributions towards these CKD-associated pathologies in different stone types. In an ANOVA of the mean LEU by patient adjusted for the number of stone removal procedures, LEU in Br SF was higher than in CaOx SF (p=0.01).

Conclusions: Dipstick LEU is informative in SF aside from predicting infection. Dipstick LEU was significantly higher in Br SF than in CaOx SF but NIT, indicating that Pi 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 reflect the papillary histopathology.

Funding: NIDDK Support

Table. Dipstick LEU by Sex and Stone Type

PO0327

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 phosphate (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 dietary calcium reabsorption, which are accompanied by urinary events such as calcium and/or phosphate wasting. Outcomes are not alleviated in FGFR4 knockout mice. Furthermore, we study primary hepatocytes treated with FGF23 or Pi to examine movement of the expression levels of this gene is linked to extended lifespan in mice. The present comparative study aimed to establish the movement of this gene in extended lifespan in mice. The presence of this gene is linked to extended lifespan in mice.

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 VN. 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 (Cp: 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 the RN. 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 expression is significantly increased in the liver of NMR, while the gene is absent in the liver of RN. The higher levels of α-klotho were similar in kidneys of NMR and RN. Further experimental work is required to clarify whether the hepatic expression of α-klotho might contribute to the longevity of the NMR.

Funding: Government Support - Non-U.S.

PO0328

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 KD/QO guideline, patients use cationic binders to bind phosphate (Pi) in the gastrointestinal and prevent its uptake. FDA-approved phosphate binders include lanthanum salts, sevelamer, and calcium carbonate. 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.

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 following ways. (1) Treatment lowered serum phosphorus into the K/DOQI target range in all patients. (2) Although treatment increased serum magnesium concentrations, [Mg2+] was in the high normal range and comparable to the intracellular magnesium concentration. (3) Short-term treatment raised the Tp value. Since lower values are associated with accelerated conversion of soluble calcioprotein particles composed of

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amorphous calcium phosphate to secondary (insoluble) calciprotein particles containing negative 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 citrates and propionates can be effectively and safely administered to 4-5 CKD patients of all ages. Additional preclinical studies are underway to confirm that calcium magnesium citrates and propriates can be effectively and safely administered to hyperphosphatemic 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 affect 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 adipogenesis at the expense of osteogenesis. Recent studies have implicated MSCs as mediators of osteoporosis due to the disrupted endochondral bone development and aging individuals, similar to 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 influences later lineage commitment choices. Vitamin D supplementation is a common therapeutic intervention for osteoporosis in postmenopausal women. In key for patients with CKD-associated osteoporosis, 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 (FeC) 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 anemia on FGF23 pathways are unclear.

**Methods:** Iron and Pi utilization was tested in a mouse model of CKD receiving FeC, with and without osteocyte deletion of FGF23 (floxed-Fgf23/Dmp1-Cre). Male mice (n=4–7) with the genotype flox-Fgf23/Dmp1-Cre and -Cre were placed on a customized 0.2% adenine (AD)-containing diet for 6 weeks to induce FeC in the presence of or absence of 10 mg/kg of AD.

**Results:** After the diet regimen, iFGF23 increased significantly in all CKD mice (p=0.05-0.01), iFGF23 was lower in Cre+ mice fed FeC (p=0.01), with Cre+ AD-only mice following a similar trend, demonstrating that the Dmp1-Cre was effective in reducing FGF23. Bone DMP1 mRNA was reduced by 50% prior to the onset of proteinuria at 4 weeks of age and remained low at all time points throughout CKD progression; each p<0.05 vs. age-matched WT.

**Conclusions:** These data show that reduction in FGF23 expression occurs prior to major reductions in kidney function and precedes alterations in osteocyte metabolism, cortical bone loss, and FGF23 elevation in CKD. Although further studies are needed to identify the factors that suppress FGF23 expression in CKD, FGF23 administration might represent an effective therapeutic strategy to prevent alterations in bone and mineral metabolism in early CKD.

**Funding:** NIDDK Support

**PO0332**

**A Role of FHL2 in the Pathogenesis of VOT and Calcification Induced by High Phosphate**

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**Background:** Hyperphosphatemia is germane to the development and progression of arterial medial calcification (AMC) in patients with chronic kidney disease. Vascular smooth muscle cells (VSMCs) to osteoblast-like cells differentiation (VOT) induced by high phosphate is a crucial step in AMC. Either β-catenin or HIF-1α signal activated by high phosphate promotes VOT and calcification in VSMCs. As an adaptor protein, four-and-a-half LIM domains protein 2 (FHL2) has been demonstrated involving in β-catenin and HIF-1α signaling, respectively. However, the potential role and mechanism for FHL2 in high-phosphate-induced VOT and AMC remains to be clarified.

**Methods:** The regulation and function of FHL2 in high-phosphate-induced VOT and calcification were examined in cultured VSMCs. The expression of FHL2 in AMC induced by high phosphate was examined in cultured arterial rings. The regulation of FHL2 on β-catenin and HIF-1α signaling during VOT was also examined in VSMCs, respectively.

**Results:** The expression of FHL2 was induced in VSMCs and arterial rings cultured in a high phosphate environment. Knockdown of FHL2 suppressed high-phosphate-induced Rux2 and osteocalcin expression and calcium deposition, whereas ectopic expression of FHL2 was sufficient to induce the expression of Rux2 and osteocalcin in VSMCs. Downregulation of FHL2 partially inhibited the high-phosphate-induced upregulation of active β-catenin and β-catenin-mediated gene transcription, whereas ectopic expression of FHL2 was able to induce active β-catenin and β-catenin-mediated gene transcription. Similarly, downregulation of FHL2 partially inhibited the expression of HIF-1α induced by high phosphate, while ectopic expression of FHL2 enhanced HIF-1α-mediated gene transcription, although it didn’t significantly increase the expression of HIF-1α. Moreover, high phosphate induced physical interactions between FHL2 and β-catenin, FHL2 and HIF-1α, respectively, especially in the nucleus. Meanwhile, high phosphate also induced a combination of β-catenin and HIF-1α, suggesting that the high-phosphate-induced upregulation of FHL2 facilitates the formation of a FHL2/β-catenin/ HIF-1α ternary complex.

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Underline represents presenting author.
Conclusions: Our results suggest that FHL2, through activating β-catenin and HIP-1α signaling, plays a notable role in regulating high-phosphate-induced VOT and could be a potential therapeutic target for AMC in patients with chronic kidney disease.

Funding: Government Support - Non-U.S.

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 cardiac receptor, activin A, is responsible for systemic activation of activin receptor (ActRII) 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 Rosα26 cre ERT+/inhbafl/fl mice. Inhibition of Activin A in CKD was accomplished by either knockdown in Rosα26 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 Rosα26 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 conditional knockout with an osteoblast-specific deletion of OGR1 (OB-cKO).

Methods: OB-cKO mice were generated from a col1a-cre mouse and an OGR1flox/flox mouse. We examined bones from 3 month old female mice using micro-computed tomography (μCT) and immunohistochemistry. Bone marrow mesenchymal stem cells (BMSC) from femurs of OB-cKO and wild type (WT) mice were differentiated to OB. Mineralization was detected with alizarin red and gene expression was analyzed by QPCR. All indicated changes are significant (p<0.05).

Results: Immunofluorescent staining of OGR1 in differentiated OB from BMSC confirmed the absence of OGR1 in OB-cKO cells compared to WT. μCT demonstrated an increase in tibia cortical bone area (0.76±0.01 vs 0.71±0.01 mm²), but no change in femoral cortical bone in OB-cKO compared to WT. Femoral trabecular bone was decreased (8.64±1.03 vs 11.81±0.70 %BV/TV), but there was no change in tibia trabecular bone. Alizarin red staining of differentiated BMSC showed greater mineralization of OB from OB-cKO mice compared to WT (5.14±0.02 vs 4.39±0.03 relative intensity). Relative gene expression of col1a1 (1.53±0.15 vs 0.88±0.10), osteocalcin (1.79±0.05 vs 1.13±0.18) and Rankl (2.89±0.48 vs 1.11±0.21) was higher in differentiated BMSC from OB-cKO mice compared to WT cells.

Conclusions: Our results demonstrate that specific loss of OB OGR1 alters the response of bone to endogenous acid on bone content, in vitro mineralization and gene expression compared to WT, indicating that the response of OGR1 in the OB is independent of the response in OC. Characterization of the direct role of OGR1 in acid-induced bone resorption may assist in understanding bone loss associated with the metabolic acidosis in patients with chronic kidney disease.

Funding: NIDDK Support, Private Foundation Support

PO0335

Testing Patterns for CKD-MBD Abnormalities Before and After Treatment

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Background: We examined patterns of testing, treatment, and retesting after treatment initiation in CKD-MBD to determine if they were concordant with KDIGO guidelines.

Methods: We utilized 2010-19 data from IBM Explorys, an electronic health database. We created cohorts of incident CKD stage 3, 4, and 5 patients using a diagnosis code for CKD stage and a confirmatory eGFR lab value. Patterns of lab test ordering for PTH, phosphorus, 25D, calcium, and ALP and drug prescribing for activated vitamin D compounds, nutritional vitamin D, and phosphate binders were assessed during follow-up. We estimated the cumulative incidence of lab retesting following treatment (with death as a competing risk). We used multivariable Cox regression to examine whether pre-treatment test result values predicted retesting.

Results: We identified 215,553 stage 3, 43,576 stage 4, and 11,407 stage 5 CKD patients; mean follow-up was 2.3, 1.7, and 0.6 years, respectively. Only 46% of stage 4 and 41% of stage 5 patients underwent a PTH test; only 74% and 73%, respectively, a test for phosphorus, and only 38% and 25%, respectively, a test for 25D. By one year after treatment with activated vitamin D compounds, only 50% (stage 3), 53% (stage 4), and 60% (stage 5) of patients had received retesting for PTH [Figure]. By one year after treatment with 25D, retesting of 25D occurred in 46% (stage 3), 49% (stage 4), and 55% (stage 5) of patients by one year. Pretreatment levels of PTH and 25D were not associated in a graded fashion with retesting after treatment commenced.

Conclusions: Frequency of initial testing and retesting following treatment initiation are suboptimal. Unexpectedly, patients with the highest and lowest pre-treatment levels of PTH and 25D, respectively, did not have the highest rate of retesting, suggesting room for improvement.

Funding: Commercial Support - OPKO
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 test 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 benefitting synergies of Systems Biology and AI in modeling complex processes.

Funding: Veterans Affairs Support

Change in Ca flux distributions over time in the simulated patient cohort.

PO0337

Mineral Metabolism Changes in Renal Transplantation

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Background: Successful renal transplant restores many physiologic abnormalities. The aim of this study was to analyse the evolution of CKD-MBD patients (alpha-klotho, fibroblast growth factor (FGF) 23, sclerostin, parathyroid hormone (PHT), bone alkaline phosphatase (BAP), calcitonin, vitamin D (vitD), phosphorus (Pi), Calcium (Ca) and Magnesium (Mg)) pre and post transplantation.

Methods: Prospective cohort study of de novo renal transplanted patients (pts). A inclusion and after 12 months (time 0 and 1) pts performed laboratory evaluation. The differences between values (time1 - time 0) is the delta value. Associations between variables were performed Wilcoxon matched-pairs test and Spearman correlation test. STATA software was used and p < 0.05 was considered statistically significant.

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. Drug doses 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 a 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 completely compromises the 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 (d-25(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, n=43), non-dialysis chronic kidney disease (CKD; eGFR < 60 ml/min/1.73m², n=24), and kidney failure treated with hemodialysis (n=20). We measured d-25(OH)D, and deuterated 24,25-dihydroxyvitamin D (25(OH)D), concentrations 5 minutes, 1, 2, 3, and 4, 7, 14, 21, 28, and 56 hours post-administration. We calculated 25(OH)D clearance using non-compartmental analysis of d-25(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 50.2±12.4 years, 48 men, 53 caucasian (78.8%), median BMI 24.5 (21.4 – 27.8), median dialysis vintage 55 (42 – 84). We observe a significant reduction on Pi, Mg, PTH, calcitoni, sclerostin, bAP and FGF23. Both Ca and alpha-klotho levels increased, with no significant changes in vitD levels. With restoring renal health (time 1) and comparing with time 0, PTH maintaining the negative correlation with sclerostin (ρ=-0.02) and the positive correlation with FGF23 (p=0.002); modify the correlation with Pi, becoming a negative correlation instead of positive (ρ=-0.001) and gain new correlations with Ca (ρ=-0.001) and vitD levels (ρ=0.03). Also, PTH correlated with the delta FGF23 (ρ=-0.4, p<0.003) and sclerostin correlated with delta PTH (ρ=0.01). FGF23 didn’t have statistical association with Pi or Ca levels after transplant, contrasting with positive associations in pre transplant (ρ=0.002, p<0.0001). On the contrary, sclerostin developed a new correlation with Pi (ρ=0.0004) and a negative correlation with Ca (ρ=0.01). We didn’t find correlations between these molecules and alpha-klotho.

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 Pi seemed to be directly influenced by the level of PTH in post transplant, and those minerals seemed to be key factors for sclerostin secretion.
Results: The mean age of the study cohort was 64 ± 11 years; 41% were female and
30% were black. Mean eGFR was 90 ± 23 ml/min/1.73m², 31% of participants
had CKD and 23% had CKD. In fully adjusted models, a doubling of VMR and
fracture risk did not reach statistical significance. A higher VMR was associated with a lower risk of fracture [HR 0.71 (95% CI 0.51, 0.97) per doubling of VMR],
but in those with CKD or kidney failure [p-for-interaction = 0.052], 25(OH)D
clearance did not differ compared with before vitamin D supplementation,
although lower 25(OH)D clearance was correlated with a larger increase in serum 25(OH)D
clearance following supplementation (r = -0.53).

Conclusions: Through pharmacokinetic 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
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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 catalytic product
24,25-dihydroxyvitamin D [24,25(OH)2D3] and a higher ratio of 24,25(OH)2D3 to 25(OH)D,
(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)2D3, 25(OH)D3, 25(OH)2D3, and VDBP in
Seattle, WA; 1University of California San Francisco, San Francisco, CA; 2Tufts Medical Center, Boston, MA; 3Wake Forest University School of Medicine, Winston-Salem, NC.

Results: Study participants had mean age 75 ± 3 years, 49% were female, 42% were
black, and 23% had CKD. Lower VDBP concentrations were not associated with any of the BMD measurements. There were 194
fractures in follow-up. A higher VMR was associated with a lower risk of fracture [HR 0.71 (95% CI 0.51, 0.97) per doubling of VMR],
but in those with CKD or kidney failure [p-for-interaction = 0.052], 25(OH)D
clearance did not differ compared with before vitamin D supplementation,
although lower 25(OH)D clearance was correlated with a larger increase in serum 25(OH)D
clearance following supplementation (r = -0.53).

Conclusions: Through pharmacokinetic 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, Private Foundation Support

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 marker of vitamin D status due to variability in vitamin D binding protein (VDBP) between individuals and
groups. The vitamin D metabolite ratio [VMR, the ratio of 24,25(OH)2D3 to 25(OH)D3] is a marker of vitamin D status that has been hypothesized to be independent of variability in
VDBP. This hypothesis has not been directly evaluated.

Methods: We measured 25(OH)D3, 24,25(OH)2D3, 1,25(OH)2D3, and VDBP in
377 community dwelling older adults that participated in the Health Aging and Body
Composition Study. 24,25(OH)2D3 and 25(OH)D3 were used to calculate the VMR.
We used linear regression to assess the relationship between VDBP with the VMR,
24,25(OH)2D3, 25(OH)D3, and 1,25(OH)2D3.

Results: Study participants had mean age 75+3/ years, 52% were female, 40% were
black, and 24% had CKD. Lower VDBP concentrations were associated with male sex,
lower serum albumin and Gc2/Gc2 VDBP phenotype in multivariable models. In
fully adjusted models, each 1% higher VDBP was associated with a 0.92%, 0.76% and
0.57% higher 24,25(OH)2D3, 25(OH)D3, and the 1,25(OH)2D3 (Table 1). The VMR was
independent of VDBP concentration, [0.16% (95% CI -0.11, 0.44)] higher VMR per
1 ml/min/1.73m² increase in VDBP, p = 0.247.

Conclusions: In diverse cohort of community dwelling older adults, the VMR was
independent of VDBP concentration 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-Analyses of the Impacts of Supplementation with Nutritional Vitamin D on Mineral and Bone Markers in Non-Dialysis CKD

Noel Gunnarsson,1 Giuseppe Cianciolo,2 Rosa Lauppe,1 Philipp Csmor,3 Fei Zhao,2 Marcus Kaisser,3 Becco Soro,2 Jordi Bover1
1Quantum AB, Stockholm, Sweden; 2Vifor Pharma Ltd, Glattbrugg, Switzerland; 3Fundacio Puigvert, Barcelona, Spain; 4Universita di Bologna, Bologna, Italy.

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 0.30 mg/dl, 95 % CI 0.24 to 0.36 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 efficiently 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 NVD patients with SHPT is limited.

Funding: Commercial Support - Vifor Pharma

PO0343
Fibroblast Growth Factor 23 (FGF23)-Calcification Propensity, and Heart Failure with Preserved Ejection Fraction (HFpEF) in Patients with CKD: The CRIC (Chronic Renal Insufficiency Cohort) Study
Alexander S. Leidner,1 Xuan Cai,1 Leila R. Zelnick,2 Nina Bansal,2 Andreas Pasch,1 Mayank Kansal,1 Jing Chen,1 Amanda H. Anderson,1 James H. Sondheimer,2 James P. Lash,2 Raymond R. Townsend,2 Alan S. Go,31 Raymond A. Isakson,1 Myles Wolf,1 Tamara Izakova,1 1Northwestern University Feinberg School of Medicine, Chicago, IL; 2University of Washington, Seattle, WA; 3University of California San Francisco, San Francisco, CA; 4Tufts Medical Center, Boston, MA; 5Wake Forest University School of Medicine, Winston-Salem, NC.

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. FGF23 is an osteocyte-derived hormone involved in phosphorus homeostasis and
is implicated in HF development. Calcification propensity (T50) is an in vitro
assessment of the time for secondary calciprotein particle formation.

Methods: Using multivariable adjusted Cox proportional hazards models, we investigated the associations of FGF23 and T50 with incident HFpEF. FGF23 and T50 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.

Funding: NIDDK Support, Other NIH Support - R01s and K awards

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PO0345
Renal Clearance of Intact and C-Terminal FGF-23 in Man
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Andrew N. Hoofnagle,1 Charles Ginsberg,1 Ronit Katz,4 Alexander Bullen,1
Shilpa Sharma,1,3 University of California San Diego, La Jolla, CA; 1VMER/VA San Diego Healthcare System, San Diego, CA; 1Maasticht Universitair Medisch Centrum+, Maastricht, Netherlands; 1University of Washington, Seattle, WA; 1University of California Los Angeles, Los Angeles, CA.

Background: The ratio of C-terminal (cFGF23) to Intact FGF23 (iFGF23) 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 bilateral renal veins (RV), and renal blood flow (RBf) was measured using 133 Xenon washout. Single pass % reductions of each measure ([Ao – RV]/Ao*100) was 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/iFGF23 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 ifGF23 was 37% higher (C/I ratio 0.73±0.10). The clearance of cFGF23 and iFGF23 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 iFGF23 and c-terminal fragments) is similar to Cr, whereas iFGF23 clearance is higher, suggesting that renal clearance of c-terminal fragment clearance is low. While renal cFGF and iFGF23 clearance were both reduced in persons with lower eGFR, the relative efficiency of clearance of cFGF23 vs. iFGF23 appeared similar across the range of eGFR.

Funding: NIDDK Support

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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
Joseph B. Pike,1 Elvis A. Akwo, Loren Lipworth, Adriana Hung, Talat Alp Ikizler, Cassianne Robinson-Cohen. Vanderbilt University Medical Center, Nashville, TN.

Background: Observational studies suggest that elevated levels of circulating fibroblast growth factor-23 (FGF-23) contribute to the burden of cardiovascular disease, in the setting of chronic kidney disease and in the general population. These studies can suffer from confounding and reverse causation, limiting their ability to identify causal associations. Mendelian randomization (MR) has emerged as a powerful study design to provide evidence supporting or refuting causality by utilizing the genetic determinants of a risk factor. We used MR to evaluate whether genetically predicted higher FGF-23 levels are associated with the risk of coronary artery disease (CAD).

Methods: We performed two-sample MR of the relationship between FGF-23 and CAD with the use of summary statistics from the CARDioGRAMplusC4D consortium’s genome-wide association meta-analysis of 48 studies with a total of 60,801 CAD cases and 123,504 non-cases. We selected 5 single nucleotide polymorphisms (SNPs) robustly associated with FGF-23 at genome-wide significance among 16,624 individuals as instrumental variables.

Results: A genetic predisposition to higher FGF-23 levels was associated with CAD. In conventional MR analysis, the odds ratio of CAD was 1.44 (95% confidence interval 1.14 to 1.80) per 10-fold increase in genetically predicted FGF-23 levels. Results were consistent in sensitivity analyses using the weighted median and heterogeneity- penalized model averaging methods.

Conclusions: This study provides evidence that FGF-23 levels are causally associated with risk of CAD. Whether interventions to lower FGF-23 result in decreased risk of CAD remains to be determined but warrants investigation.

Funding: NIDDK 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.
Factors Associated with Change in Fibroblast Growth Factor 23 Levels from Midlife to Late-Life: The ARIC Study
Junichi Ishigami,1 Yasuyuki Honda,1 Amy B. Karger,2 Elizabeth Selvin,1 Josef Coresh,3 Pamela L. Lutssey,2 Kunihiro Matsushita,1 Johns Hopkins University, Baltimore, MD;1 University of Minnesota, Minneapolis, MN.

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 of age (above vs. below median), sex, race, ever smoke, high BMI (as vs. <30 kg/m²), hypertension, diabetes, history of CVD, and reduced eGFR (a vs. <60 ml/min/1.73m²) using multivariable linear regression models.

Results: The mean FGF23 level 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 (AFCGF23, 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 eGFR, 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 of kidney function deserves future investigations.

Table: Factors associated with changes in FGF23 levels from midlife to late-life. Multivariable linear regression analysis unadjusted for chosen covariates.

<table>
<thead>
<tr>
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<th>Adjusted difference in FGF23 change (pg/mL)</th>
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<td>66.17</td>
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<td>28.3 (19.7 to 37.1)</td>
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<tr>
<td>No</td>
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<tr>
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<td>E/e wave</td>
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Effects of Adjustment for Iron Parameters, Inflammation, and Kidney Function on the Associations of C-terminal and intact FGF23 with Mortality

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 correlated 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 to 0.99 (0.76, 1.28) with eGFR 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 impacts 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

PO0348
Factors Associated with Change in Fibroblast Growth Factor 23 Levels from Midlife to Late-Life: The ARIC Study

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
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, limited results of studies regarding the role of individual biomarkers are available. 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 in relation to death and KRT.

Methods: Events of death and KRT in 454 participants of the Progredir 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 (DiaSort® assays) and factors derived from factorial analysis was evaluated through Cox and Competitive Risk models (R package “compnr”).

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 was associated with death and KRT (Table). The addition of BAP and PTH (with interaction) to a reference model significantly improved the model fit for death (p=0.01). The addition of FGF-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 bone turnover but also vascular calcification. FGF-23 is associated with the risk of death, and FGF-23 remained associated with KRT (Table). The addition of BAP and PTH (with interaction) to a reference model significantly improved the model fit for death (p=0.01). The addition of FGF-23 with interaction with P significantly 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 Group

Background: The prospective Dialysis Outcomes and Practice Patterns Study (DOPPS) has collected data since 2002 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 bias of events were reported. Mortality analyses were nested within these data. Hazard ratios (HRs) and 95% confidence intervals (CIs) were reported for PTH levels compared with normal, no adjustment or adjusted PTH levels compared with normal.

Results: Mean patient age was 65 (median age 65, IQR: 59-71) years, 59% male, and 56% diabetic. In univariable analysis, PTH levels were significantly associated with events but did not improve prediction. Mortality rates were highest in the highest PTH tertile, similar to previous analyses. The HRs were 1.39, 1.30, and 1.34 for tertiles 2, 3, and 4, respectively, compared with the lowest tertile. After adjustment for confounders, the highest tertile remained associated with death, and PTH remained associated with both death and KRT. After adjustment for confounders, PTH remained associated with death and KRT. After adjustment for confounders, PTH remained associated with death and KRT.

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.

Funding: Commercial Support - This abstract was sponsored specifically by Amgen Middle East FZ-LLC. Global support for the ongoing DOPPS Programs is provided without restriction on publications by a variety of funders. For details see https://www.dopps.org/AboutUs/Support.aspx.

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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, i65-i6). 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 osteoblastic and osteoclastic 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
Kittrawee Kritmetapak,1 Louis A. Losbanos,2 Jolanne M. Hines,3 Katherine O’Grady,3 Candice Z. Ulmer,1 Hubert W. Vesper,3 Felicity T. Enders,1 Ravindra Sinha1,2 Rajiv K. Benner,2 Khon Kaen University, Khon Kaen, Thailand; ‘Centers for Disease Control and Prevention, Atlanta, GA; 3 Mayo Clinic, Rochester, MN.

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 carboxy-terminal region-specific antibodies and elution from matrix, full-length PTH and PTH fragments were identified and quantitated using LC-HRMS. PTH 1-84 was simultaneously measured using an intact PTH (iPTH) immunoassay.

Results: Full-length PTH 1-84 and eight PTH fragments (PTH 28-84, 34-77, 34-84, 37-77, 37-84, 38-77, 84-45, and 84-45) 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 carboxy-terminal immunocapture 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 decreases to less than 17-23 mL/min/1.73 m2. PTH values measured by LC-HRMS are lower than those obtained from an iPTH immunoassay in severe CRF.

Funding: Other NIH Support - R01DK107870

PO0354
Management of Secondary Hyperparathyroidism Among Patients Who Transition from Daily At-Home To Three-Times-Weekly Oral Cinacalcet Given In-Center
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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 (SHP) in hemodialysis (HD) patients. Moreover, a larger prospective chart review of 195 in-center HD patients describes the safety and potential utility of 3X weekly in-center administration of cinacalcet to control secondary hyperparathyroidism (SHP) 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 a ≥8 years of age, receiving standard in-center HD, Medicare beneficiaries, and having a history of transition 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 modeled means 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 patients transitioning 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.

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

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.

Methods: We retrospectively reviewed PTH levels of ESKD patients 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.

Results: 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.

Conclusions: ETC treatment was effective and well tolerated with no serious adverse events, although hypocalcemia was common. ETC was effective and well tolerated with no serious adverse events, although hypocalcemia was common. ETC was effective and well tolerated with no serious adverse events, although hypocalcemia was common. ETC was effective and well tolerated with no serious adverse events, although hypocalcemia was common. ETC was effective and well tolerated with no serious adverse events, although hypocalcemia was common. ETC was effective and well tolerated with no serious adverse events, although hypocalcemia was common. ETC was effective and well tolerated with no serious adverse events, although hypocalcemia was common. ETC was effective and well tolerated with no serious adverse events, although hypocalcemia was common. ETC was effective and well tolerated with no serious adverse events, although hypocalcemia was common. 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PO357

A Real-World Observational Study of Calcimimetic Use in Hemodialysis (HD) Patients with Secondary Hyperparathyroidism (SHPT) in Europe

Marco Joel

Indirect Comparison of Treatments for Secondary Hyperparathyroidism

Background: Calcium, oral cinacalcet (CIN) and intravenous etelcalcetide (ETEL), are approved for treating SHPT in adult patients on maintenance HD. Data on real-world use of calcimimetics are needed to provide guidance in clinical practice.

Methods: In this observational study, Chronic HD patients treated with calcimimetics for at least 3 months, and with serum calcium values within ±0.8 days following a calcimimetic initiation, were included. Data on demographics, clinical history, laboratory values and calcimimetic use were abstracted from medical charts.

Results: Interim data for 503 HD (96 CIN and 407 ETEL) patients from 57 sites across 6 countries were analyzed. Calcium levels had decreased by ≥5% and CIN use for 5 mg and 2.5 mg was recorded in ≥35% and ≥45% of CIN patients respectively. Table 1 summarizes median PTH and mean total calcium (Ca) and phosphate (P) levels. Among 341 ETEL and 79 CIN patients who had normal Ca at baseline, the cumulative incidence of hypocalcemia (<2.1 mmol/L) at 3 and 6 months was greater for CIN (47% and 58%) than ETEL (35% and 52%). As recorded in medical charts, nausea and vomiting rates at 12 months were similar for CIN (3.7% and 1.8%) and ETEL (3.6% and 1.9%). ETEL persistence (89.6%) was greater than CIN (71.8%) at 12 months. During follow-up, 13.5% switched from CIN to ETEL and 2.5% from ETEL to CIN. The proportion of patients achieving ≥30% reduction in PTH from baseline was greater for CIN than ETEL at 6 months (64% vs 54%) but similar at 12 months (73% vs 74%).

Conclusions: This is the largest real-world study on calcimimetics 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.

Funding: Commercial Support - AMGEN

PO358

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, the only 2 treatments indicated for the treatment of SHPT in non-dialysis CKD (ND CKD) are cinacalcet (CIN) and beta-calcimimetics (BCTs) to be included in a Network Meta-Analysis (NMA). In all the comparator groups, were considered being placebo. A quality assessment was done with the GRADE method. The treatment effects of ERC and PCT were compared using random effects in a frequentist setting, and a sensitivity analysis with a Bayesian approach performed using random effects model. Comparisons were made between the overall treatment effects of the drugs.

Results: Nine RCTs comprising a total of 1426 patients were included in the analyses. Compared to placebo, treatment with both ERC and PCT lowered levels of PTH in a statistically significant manner. No statistically significant differences in PTH reduction were found between ERC and PCT. Treatment with PCT significantly increased calcium levels compared to placebo (effect size: 0.30 mg/dl, 95% CI: 0.21 to 0.40 mg/dl), whereas a statistically significant effect for CIN (effect size: 0.10 mg/dl) was not significant (95% CI: 0.03 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: These analyses using a well tolerated treatment option for the early management of SHPT in patients with ND CKD.

Funding: Commercial Support - Vifor Pharma

PO359

Parathyroideectomy 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 has been hypothesized that treating hyperparathyroidism (HT) can ameliorate these disturbances. However, the effects of parathyroideectomy (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, performance, body fat and resting energy expenditure (REE) in patients with severe SHPT due to ossified parathyroid glands and parathyroid of dual x-ray absorptiometry, and REE was examined by indirect calorimetry. Participants completed the SARC-F questionnaire.

Results: At the 6 months after PTX, 20 patients who already completed the protocol, showed a significant drop in PTH [1510(1368-1885) vs. 91(38-260) pg/mL; p<0.01] and improvements of strength tests: HGS(27.4±14 vs 31.4±16 kg p=0.01); SP(26.5±15 vs 31.6±16 kg p=0.01) and LPC(24±2 vs 30±4 kg p<0.01). In addition, there was an improvement of SARC-F [10±1 vs 6±1 p=0.01] and BMI [30±7 vs 28±2 kg/m² p<0.01]. A significant increase in bone mineral content [1.81±0.22 vs 2.22±0.26 kg p=0.001], fat mass [21.8±4 vs 24.5±9 kg p<0.01] and visceral adipose tissue [530±287 vs 975±432 g] was seen. No change was noted in skeletal muscle index and in REE [1643±1573 kcal/d p=0.7). We noticed an increase in KIF-1B [199±201 u/ml p=0.04] and HOMA index [1.6±1.72 p=0.02], but no variation was found in serum albumin.

Conclusions: In hemodialysis patients with SHPT undergoing PTX, there were improvements of muscular function and bone mass, but not of muscle mass, at 6 months after PTX. Our findings suggest that PTH-associated sarcopenia is mediated not only by a decrease in muscle mass but also by muscle dysfunction.

Funding: Commercial Support - Orion Pharma

PO360

Indications and Justification for Parathyroideectomy in Secondary Hyperparathyroidism

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Introduction: Hyperparathyroidism (HT) is a common complication of CKD, which is treated by diet, medications and surgery. Parathyroideectomy (PTEctomy) is reserved for patients with refractory HT. There are no guidelines for the timing or type of surgery. We describe five patients with HT, who were treated with different modalities with unsatisfactory outcomes.

Case Description: We present 5 patients in a table format. Patient 1 had total PTEctomy, which resulted in decalcification needing hospitalization. After 3 years, they remain hypocalcemic requiring high doses of Vit D and calcium. Selecting a suitable phosphate binder in this patient was difficult due to hypocalcemia. Patient 2 underwent total PTEctomy with autotransplantation which resulted in low calcium levels that resolved over time, but PTH levels remained very low. Patients 3 and 4 refused surgery and their PTH levels fluctuated significantly, failing to levels much below the acceptable level of 600 pg/ml. Patient 5 underwent partial PTEctomy and 2 enlarged PT glands were removed. This resulted in lower calcium and higher PTH levels than prior to surgery.

Discussion: The medical management for PHT in all patients failed. We opted for surgery when the PTH levels were in a range of 1300 to 4000 pg/mL. The surgeon decided the type of surgery. In patient 1, intraoperative PTH was measured that resulted in removal of only three glands. But within a very short time, the PTH bounced back to 2500 pg/L which was much higher than our surgical limit. Therefore, the parathyroideectomy was performed. We cannot recommend specific surgical modality based on this experience. Therefore, we strongly feel that there is a need for larger controlled studies to elucidate specific guidelines for treating refractory HT.
Palatal Brown Tumor in a Dialysis Patient

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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.

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.

Etelcalcetide 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.

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 infancy.2,3 We present a patient who developed hypercalcemia 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 lab 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.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.5-7 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 (Calcitromin, Pamidronate and Denusomab) along with improved mobility has successfully lowered serum calcium in these patients. One patient had hypocalcemia after Denusomab administration, hence needed careful monitoring.

Hypercalcemia cases post liver transplant.

Figure 1: Calcium trends and treatments.
Methods: Patient level data was collected via an online, HIPAA-compliant form in June 2019 as part of an independent chart audit. A total of 1,015 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 been on dialysis 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 1.77 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. Ethnicity 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 Calcitriol, and Normal FGF7 Concentrations Characterizes Chronic Renal Failure in Humans

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Background: Fibroblast growth factor 23 (FGF23), a phosphatonin produced by osteocytes, regulates phosphate (Pi) homeostasis and is increased in CKD. A recent study showed that low serum (s) concentrations of FGF7 may contribute to hyperphosphatemia in patients with hyperphosphatasia, 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 varying estimated glomerular filtration rate (eGFR). Relationships between these parameters and eGFR were explored.

Results: For sFGF of 60 or more (n=29), 45-59 (n=14), 30-44 (n=9), 15-29 (n=13), and under 15 mL/min/1.73 m2 (n=10), the median (IQ25-75) iFGF23 concentrations were 46.1 (40.8-56.1), 43.1 (39.2-49.2), 45.4 (39.5-53.8), 47.7 (38.5-54.6), and 46.1 (40.8-54.6) pg/mL, respectively (P<0.01). At comparable eGFRs, median (IQ25-75) iFGF7 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=0.81). Negative correlations between Pi and s FGFR (r=-0.46; P<0.01), iPTH and s FGFR (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, 36.57-81.43). iFGF7 concentrations did not significantly correlate with 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.

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PO0369

Effects of a Reduced Phosphorus Diet on the Circulating Metabolome in Healthy Adults

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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 has focused on changes in specific endocrine factors in the blood. Less is known about the effects of nutritional phosphorus changes in specific analytes of note within each of these pathways are depicted in the Figure. 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

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

Underline represents presenting author.

Change in select metabolites in response to phosphorus-reduced diet

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 oxhydroxide (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 Pharmaceutical Binders Used in Dialysis Patients Included in ESRD Seamless Care Organizations
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Background: A prior observational study using real world data and estimates of hospitalization costs based on national data, found patients continuing sucralfate oxyhydroxide (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 Medicare dialysis patients in the U.S. By providing quality care, ESCOs may control costs by avoiding unnecessary hospitalizations. The aim of this analysis was to assess hospitalizations 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 <$000 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), CaAC ($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
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Background: Phosphate binders (PBs) are the primary therapeutic treatment for hyperphosphatemia in ESRD patients receiving dialysis. Medicare 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 1995 and May 2020. Studies included in the review 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 found to be 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 oxyhydroxide (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. Our one 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
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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).

Results: 205 participants underwent randomization. The mean (± SD) baseline age was 59±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 antihypertensives 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 carbonate 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 BP. 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
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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 (RW) examining the efficacy of TEN as monotherapy to treat hyperphosphatemia (HP) in patients with CKD on dialysis (NCT0342725) 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 (≥5.4 mg/dl) in patients with CKD on dialysis (NCT 03824587).

Results: In the monotherapy study, 219 patients were randomized to the RT, 164 patients (75%) completed the RT, and of these, 152 (93%) completed the RW. 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 RW 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<5.4 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 nausea which was less than 2% of patients treated with TEN.
**PO0375**

**Efficacy and Safety of Add-on Tenapanor to Phosphate Binders for Refractory Hyperphosphatemia in Japanese Patients on Hemodialysis:**

### Background:
Among hemodialysis (HD) patients, some patients have poorly controlled serum phosphorus levels, even when 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 thus 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, Phase 2 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+PB or PLA+PB group in a 1:1 ratio. Starting dose of tenapanor was 30 mg BID, which could be reduced in a stepwise 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:
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 (≤6.0 mg/dL) at the end of treatment was 87.0% in the tenapanor group and 74.2% in the PLA group. Diarrhea was the most frequent adverse event (tenapanor=65.2%; PLA=16.7%), all 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 combination of tenapanor with PB could be the utmost needs to better control serum phosphorus in HD patients with refractory hyperphosphatemia.

**Funding:** Commercial Support - Kyowa Kirin Co., Ltd.

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**PO0377**

**Changes in Serum Phosphorus Among Patients Who Switch from Sevelamer Carbonate to Sucroferric Oxyhydroxide or Other Phosphate Binders After Persistent Hyperphosphatemia**

**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 oxyhydroxide (SO) monotherapy, or (2) Non-SO binders [Calcium Acetate, Lanthanum 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/selection 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. All PSMs/CEMs and IPTWs 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

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**PO0378**

**The Effect of Phosphate Lowering Using Sucroferric Oxyhydroxide on Endogenous Calciprotein Particle Formation in Dialysis Patients:**

**Background:** We have recently demonstrated in a randomized, controlled, cross-over study in 39 chronic hemodialysis patients with hyperphosphatemia that high-dose phosphate binder therapy with 2000 mg/d of sucroferric oxyhydroxide (SO) over two weeks significantly reduces calcification propensity as determined by the T<sub>c</sub>-test compared with a two-week wash-out phase (Cejka, Kidney Week 2019, FR-PO149). Based on these results, we hypothesized that SO would influence endogenous calciprotein particle (CPP) formation and crystallization, i.e. conversion from primary to secondary CPP.

**Methods:** To test this hypothesis, we conducted post-hoc analyses of our RCT (74% men, mean age 65±27 years, median dialysis vintage 24, IQR 16–36 months). We compared native serum CPP levels (measured by a fluorescent probe-based flow cytometry assay) by Wilcoxon matched-pairs test and hydrodynamic radii (R<sub>c</sub>) of secondary CPP formed after enrichment with exogenous calcium and phosphate (measured by three-dimensional cross-correlation dynamic light scattering) by paired t-test between the phosphate binder washout and high-dose treatment phase.

**Results:** Upon SO therapy serum phosphate levels decreased from 2.28±0.5 mmol/L to 1.63±0.43 mmol/L (p<0.0001), coincident with a reduction (median, IQR) in primary

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

*Underlines represent presenting author.*

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PO0379

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 start and in ≥5 months during SO therapy. The current retrospective study assessed changes in sP and phosphate binder (PB) pill burden in pts prescribed SO in managing sP among dialysis pts. Previous real-world analyses included HD pts prescribed SO within the first 2 years following SO availability in the US (2014 Cohort, Kalantar 2018). With greater physician experience with SO and increased availability, prescription patterns may have changed over time. The current retrospective study assessed changes in sP and phosphate binder (PB) pill burden in pts prescribed SO in managing sP among dialysis pts.

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 (33 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≤5.5 mg/dL increased from 21.9% at -1M to 40.4-44.4% at 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≤5.5mg/dL.

PO0380

Assessment of Serum Phosphorus Levels in Patients Following Administration of Ferric Pyrophosphate Citrate: A Retrospective Study

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Background: Iron deficiency is common among hemodialysis patients contributing to chronic anemia. Ferric pyrophosphate citrate (FPC) is FDA-approved to replace iron and maintain hemoglobin in adult hemodialysis patients by delivering iron directly and rapidly to transferrin. FPC is a mixed-ligand iron complex in which iron is bound to phosphates, vitamin C, and citrate. Phosphorus regulation in ESRD patients can be challenging thus administering products containing phosphates risks increasing serum phosphorus in addition to exacerbating underlying endocrine abnormalities. The objective of this study is to assess any changes in phosphorus levels in hemodialysis patients receiving FPC.

Methods: Retrospective data from patients at a single center hemodialysis clinic was realanalyzed looking at serum phosphorus level of hemodialysis patients receiving FPC over a one-year span of time. The data analyzed included serum phosphorus levels prior to initiating therapy compared to serum phosphorus levels after being administered FPC.

Results: Forty-nine patients were included in the study. Median serum phosphorus values were at pre-therapy (median 4.8), 1-month of FPC (median 4.7, p=0.56), 6-months of FPC (median 4.8, p=0.49), and 12-months of FPC (median 5.1, p=0.36) as represented in Figure 1.

Conclusions: After analysis of serum phosphorus levels in hemodialysis patients receiving ferric pyrophosphate citrate, the findings show that there was no difference in average sP among phosphorus levels before and after therapy. Clinicians who are prescribing this medication should be aware that there is no increase in serum phosphorus in patients while receiving this therapy considering how difficult it can be to regulate phosphorus along with managing the potential consequences of phosphorus abnormalities.

Figure 1

PO0381

Real-World Effectiveness of Sucroferric Oxyhydroxide (SO) in Lowering Serum Phosphorus (sP) Among a Contemporary Hemodialysis (HD) Cohort: A 6-Month Follow-Up

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Background: Clinical trial and real-world data demonstrated the effectiveness of SO in managing sP among dialysis pts. Previous real-world analyses included HD pts prescribed SO within the first 2 years following SO availability in the US (2014 Cohort, Coyne 2017). With greater physician experience with SO and increased availability, prescription patterns may have changed over time. The current retrospective study assessed changes in sP and phosphate binder (PB) pill burden in pts prescribed SO in 2018-2019 (2018 Cohort) and compare these results to the 2014 Cohort findings.

Methods: We included adult Fresenius Kidney Care HD pts first prescribed SO monotherapy during 5/2018- 5/2019, on other PB monotherapy during a 3-month baseline (BL), and had sP measured the month before SO start and in ≥5 months during SO. We compared BL to quarterly (Q1, Q2) means, calculated using mixed-effects linear regression, for PB pill burden and lab measurements.
Results: Compared to the 2014 Cohort, the 2018 cohort (n=208) was larger (vs 424), older (56 vs 51 years with shorter dialysis vintage 11 vs 16 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% pts 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 at 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 sP ≤ 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

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 levels 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 ≥0.1 mg/dL to 6.1–9.9 mg/dL after 1st WO. Thereafter patients were randomized to one of 5 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 (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 group). The mean change in serum phosphorus at the end of treatment from baseline was 6.0 mg/dL in the PLA group, -0.64 mg/dL in the 5 mg 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<0.001).

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 (VitD) deficient. VitD is subsequently prescribed and has documented health benefits, including nephro-, cardio-, and immune- protection. This paired study sought to evaluate and compare VitD metabolism in CKD patients and healthy controls (HC) under both 25(OH)D3 daily for 12 weeks. At week 12 (Phase 2), participants received their final dose of D, after 25(OH)D was confirmed to be replete (≥30 ng/mL). Blood was collected at serial time points for up to 336 h at each phase for determination of D3, 25(OH)D3, 1,25(OH)2D3, and 24,25(OH)2D3. Metabolism ratios (MR) were defined by the area under the plasma concentration-time curve (AUC) of pre-cursor to a subsequent metabolite. Analyses for differences were assessed by ANOVA with a Tukey-Kramer post-hoc test.

Results: Metabolism was differentially altered by VitD status and CKD. Significant differences in assessment of MR were determined in both an immediate precursor to the next metabolite in the sequence and by the parent compound (D3) to the final metabolite in the metabolism sequence. The metabolism of D3 to 25(OH)D3 and of 25(OH)D3 to 1,25(OH)2D3 were significantly decreased by CKD severity, with differences more pronounced after VitD repletion.

Conclusions: CKD severity decreased metabolism by the cytochrome 2R1 and 2B13 pathways resulting in reductions in the D3 to 25(OH)D3 and 25(OH)D3 to 1,25(OH)2D3 respectively. Daily dosing leading to repletion appears to decrease the overall conversion of cholecalciferol to its metabolites in HC and CKD patients, possibly due to saturation of metabolism pathways. Future research will evaluate the influence of daily vs. intermittent dosing on metabolism efficiency.

Funding: Other NIH Support - NIGMS

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 (NHE3) and is dosed as one small pill (<12x7 mm) twice daily. Two previously conducted pivotal trials of TEN met their primary efficacy endpoint. 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 ≤10.0 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=807) 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. Conclusion: 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.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
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 (8h NAE) 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 UHCO3−)] 2 hours after oral NaHCO3 and bovine (0.5 mmol/kg bw), assuming 50% body wt HCO3−, normal space of distribution] in 224 patients with CKD stages 1-3 due to macroalbuminuric, non-diabetic, hypertension-associated nephropathy.

Results: Because Pcit, UcitV, UcitV/Pcit, and PTCO2, each directly associated with eGFR [p<0.01] and because H^+ retention inversely associated with eGFR [p<0.01], we adjusted reported associations for eGFR. PRAL associated directly with 8h NAE [p<0.01, R²=0.05] and inversely with UcitV/Pcit [p=0.03, R²=0.13] but not with PTCO2 [p=0.15], H^+ retention [p=0.85, UcitV/p=0.21] or Pcit [p=0.49]. PTCO2 inversely associated with H^+ retention [p=0.02, R²=0.06] but not with 8h NAE [p=0.14], UcitV [p=0.59], Pcit [p=0.11] or with UcitV/Pcit [p=0.79]. By contrast, H^+ retention associated inversely with UcitV [p=0.01, R²=0.52] and UcitV/Pcit [p=0.01, R²=0.20] not with 8h NAE [p=0.12].

Conclusions: Ongoing dietary acid intake assessed by PRAL inversely associated with UcitV/Pcit, although quantitatively less than did H^+ retention [R²=0.13 vs. 0.20], but did not contribute with the remaining measures of acid-base status. By contrast, steady-state acid-base status associated with 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.
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; laboratory 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 ± 3.4. 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 at 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 1-year 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=0.0004), iPTH (r=0.6; p<0.001) and total cholesterol levels (r=0.3, p=0.01) were correlated with the score. Coronary calcium percentile was correlated with Adragão score in the two time points (p=0.0001; p=0.002), with presence of valvular calcifications in time 1 evaluation (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.

Clinical Outcomes in Patients with Calcifications 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 findings persisted even after adjusting for baseline eGFR, bmi, 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 0.38-0.89; 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.

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 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-oclusive finger skin capillary recruitment. Secondary outcomes included capillary recruitment during venous congestion, heat-induced skin hyperemic response, and flicker-light-induced retinal arteriolar and venular dilation.

Results: The mean age of the cohort was 60 years, 48% were women, 7% had an eGFR < 60 ml/min/1.73 m², and the mean serum phosphate concentration was 3.2mg/dl. The mean UPE was 874 ± 315 mg/dl. 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 predominately with normal kidney function. Relationships between urine phosphate, serum phosphate and microvascular function require further exploration.

Funding: NIDDK Support, Private Foundation Support

References:
1. Relations calculations for age, sex, body mass index, smoking status, body fat distribution, use of antihypertensive medications, use of non-steroidal anti-inflammatory drugs, eGFR, and serum calcium.

<table>
<thead>
<tr>
<th>Table 1: Association of 24-Hour Urine Phosphate Excretion and Serum Phosphate Concentration with Microvascular Outcomes</th>
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<tr>
<td>UPE (mg/dl)</td>
</tr>
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<td>675</td>
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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 been suggested.

Case Description: A 62-year-old female with a LDLT (2008) complicated with CKD III, lupus nephritis, hypothyroidism, presented with painful, bilateral, medial calf ischemic ulcerations, which on punch biopsy revealed calciphylaxis. Her baseline iPTH, calcium, phosphorus, and 25-hydroxyvitamin D, was 372 pg/mL, 9.4 mg/dL, 3.8 mg/dL, and 17.4 mg/dL, respectively. She was on calcitriol 0.75 mg/daily, ergocalciferol 50,000 units weekly and cinacalcet 30 mg 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.

Image 1 & 2: Calciphylaxis wound in the Lower Extremity Image 3: Resolution of wound after Calcifediol

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 VV/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 hours.

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.

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**PO0396**

**Penile Calciphylaxis: Challenges in Its Diagnosis and Management**

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**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.
PO0397
High Turnover Bone Disease After Successful Parathyroidectomy in a Dialysis Patient
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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, complicated by calciphylaxis 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 demonstrable 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 is often presumed, but not established. In this patient, osteoporosis was related to high bone turnover, despite near-total PTX in 2014 for secondary hyperparathyroidism and bx proven severe HPT bone disease, complicated by calciphylaxis 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 demonstrable decrease in bone turnover and volume.

Figure 1: Anterior iliac crest bone biopsy: 1A – Trichrome stain 10x showing osteoclastic activity with tunnelling in trabecular bone and increased osteoid volume and surface 1B – Fluorescent microscopy for tetracycline labelling 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, Kazuhiro 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 I 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.

Discussion: 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 reabsorption, 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.

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1171
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 > 130 pg/mL) 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 and 5.4% of G4/G5 had PTH > 130 pg/mL (OR 95%CI 7.331 to infinity). Multivariable linear regression analysis showed the independent predictors of cortBMD Z-scores were PTH (β=0.21, p=0.005), which positively correlated with 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 cortBMD Z-score below -2 SD (OR 95%CI 7.331 to infinity). Multivariable linear regression analysis showed the independent predictors of cortBMD Z-scores were PTH (β=0.35, p<0.001) and 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 prediction.

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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PO0404

Low Bone Turnover and Increasing Calcification with Lower Trabecular Bone Score in Early CKD Patients

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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 absorptiometry 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±17 mL/min/1.73 m². On bone histology low turnover was found at the higher eGFR levels in 78% and normal or high turnover at lower eGFR levels. Mineralization was normal in all. Bone volume was normal in 75% and slightly low in the others. Correlation between bone parameters and cEGR are shown in Table 1. Coronary artery calcium (CAC) score was above 400 in 31%, between 100 and 400 in 24%, and less than 100 in 45% of patients. TBS correlated negatively with CAC-scores (R=0.43, p=0.02), and hip fractures (R=0.49, P=0.0001). The mean area of AGEs deposits in the cortical bone was 5.4±12.1%; cortical thickness were negatively correlated with serum pentosidine levels (R=-0.27; P=0.02) and age (R=-0.235; P=0.04); cortical porosity was positively correlated with serum pentosidine levels and correlated with their risk for osteoporotic fractures. Serum pentosidine levels were associated with low thickness of cortical bone. Cortical porosity was associated with serum glycosylated 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.

PO0405

Bone-Derived Hormones, Mineral Metabolism, Cardiovascular Disease, and Patient Survival in ESRD

Ana Carolina 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,1 Bruna F. Corrêa,1 M. Guadalupe Cabral,2 Fernando E. Nolasco,1,2 Ana Carolina Ferreira,1,2,3 Diary Carri Cabral, Lisbon, Portugal; 1Nova Medical School, Lisbon, Portugal.

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 grow factor (FGF) 23, sclerostin, parathyroid hormone (PTH), bone alkaline phosphatase (bAP), vitamin D (vitD), phosphorus (Pi), Calcium (Ca) and Magnesium (Mg)], and echocardiographic findings [left ventricular mass index (LVMi) measured by Devereux formula (sclerotic calcifications), vascular calcifications and patient (pts) outcomes].

Methods: We performed a prospective cohort study of a sample of ESRD pts listed for renal transplant. All pts were submitted to renal transplant and were followed for 12 months. Patient and graft survival were recorded. At inclusion, demographic and clinical data were collected, laboratory evaluation, bone biopsy and X-ray of the pelvis and hands (Ardaglo 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 included 85 pts. Mean age 50±12.7 years, 59 men (69.4%), 66 caucasian (77.6%). The mean LVMi was 108.5 (92 – 129) g/m², with 32 patients presenting LVH and 19 valvular calcifications. Median Adraglo score was 1 (0 – 2). At the end of 12 months, 4 pts died and 5 had graft failure (non-primary function). Alpha-klotho correlated with Pi (R=0.0061) and negatively with PTH and absence of valvular calcifications (p=0.05). FGF23 correlated with Pi (p=0.001), Ca (p=0.004), PTH (p=0.003), Mg (p=0.002), and inversely with bAP (p=0.003), and presented a marginal association with Adraglo score (p=0.06). We didn’t find correlations between FGF23 and alpha-klotho or dialysis vintage or echocardiographic characteristics. Sclerostin correlated negatively (p<0.007) and PTH (p=0.04). The 3rd sclerostin tertile was associated with high scores of vascular calcifications (p=0.02). Lower levels of sclerostin were associated with pt survival at the end of 12 months (p=0.02).

Conclusions: Sclerostin. A bone formation inhibitor, seems to act as a risk factor for vascular calcifications and worse outcomes.

PO0406

Bone Mineral Density Is Not Associated with Coronary Artery Calcification in Children and Young Adults with CKD

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Background: Coronary artery calcification(CAC) has been linked with bone demineralization in older adults with CKD, but there are no studies examining this relationship in children and young adults. We studied bone mineral density(BMD) by tibial peripheral quantitative CT(pQCT) and measures of vascular health to examine the association between bone demineralization and vascular calcification in a young CKD population.

Methods: Patients with CKD4-5 and on dialysis aged 5-30 years underwent tibial pQCT [for cortical(cortBMD) and trabecular BMD(trabBMD)], cardiac CT for CAC, ultrasound for carotid intima-media thickness(IMT), carotid-femoral pulse wave velocity(cPWV) and measurement of routine serum biomarkers. All measures were expressed as Z-scores and adjusted for age, and height. CAC was expressed as Agatston score (AS).

Results: One hundred participants [median 13.82 years(IQR 10.7 to 16.5), 20% above median (44% female 57%), BMI 61.2±3.1 kg/m², height 1.55±0.11 m, 59 (56%) were male, 41 (48%) Caucasian and 16 (19%) diabetics; dialysis vintage was 21 (10-44) months. Dialysis frequency was <2.0 AU, serum pentosidine 71 (44–121) pmol/mL and glycated hemoglobin 5.4 (5-6); cortical bone volume, thickness and porosity were 22.3±9.8 μm³, 619±213 μm and 1.55 (0.9-2.7); respectively, AGEs in skin were correlated with age (R=0.53; P=0.0001), risk for major osteoporotic fracture (R=0.56; P=0.0001) and hip fractures (R=0.49; P=0.0001). The mean area of AGEs deposits in the cortical bone was 5.4±12.1%; cortical thickness were negatively correlated with serum pentosidine levels (R=-0.27; P=0.02) and age (R=-0.235; P=0.04); cortical porosity was positively correlated with serum pentosidine levels and correlated with their risk for osteoporotic fractures. Serum pentosidine levels were associated with low thickness of cortical bone. Cortical porosity was associated with serum glycosylated 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.
Nephrolithiasis at Baseline Did Not Increase the Risk of Nephrocalciosis Progression After Long-Term Bursosumab 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 (NCT025526160, NCT02015705), bursosumab significantly improved serum phosphorus concentrations in adults and children with XLH. We examined subject characteristics and long-term safety of bursosumab by the absence or presence of nephrocalcinosis (NC) at baseline (BL) from these trials.

Methods: Adults were randomized (1:1) to bursosumab 1.0 mg/kg every 4 weeks or placebo for 24 weeks; after 24 weeks, adults received bursosumab through 96 weeks. Children were randomized (1:1) to bursosumab 0.8 mg/kg every 2 weeks or oral phosphate and active vitamin D (Pi/D) for 64 weeks. NC was defined at BL and during study by ultrasonography 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 without NC at BL, those with NC had longer duration of treatment with Pi/D during childhood (mean [SD] 13.2 [3.2] vs 11.3 [4.9] 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 573 adults with NC at BL and 5/6 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 <4.0 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 and NC at BL was associated with longer duration of Pi during childhood. In children with XLH, NC at BL was associated with longer duration of Pi and D pre-enrollment and with BL hypercalciuria. With long-term bursosumab, the presence of NC at BL did not increase the risk of NC progression.

Funding: Commercial Support - Ultragenyx Pharmaceutical Inc.

PO0409

Proton-Pump Inhibitors Are Associated with Decreased Urinary Citrate Excretion

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Background: Proton-pump inhibitors (PPIs) may increase the risk of kidney stone formation, but the mechanism(s) has not been elucidated. PPI-associated hypomagnesemia 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 pKa values 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 nephrocalcinosis 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<0.012, ΔF=4.24, df=9,34). 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 hyperparathyroidism such as genetic polymorphisms of the renal-sodium-citrate co-transporter, chronic metabolic acidosis, or the use of carbonic anhydrase inhibitors, high animal protein diet intake, and incomplete distal RTA.

Funding: Commercial Support - Ultragenyx Pharmaceutical Inc.

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 vs 4.6, p=0.002), CaP SS (5.9 vs 1.0, p=0.05), and lower urine oxalate (1.7 vs 2.7, p=0.001) compared with men. There were no differences by sex in CaOx SS or urine oxalate 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. Citrate was also associated with change in -0.01 (-0.01 to -0.002) mg/l citrate. Calcium and oxalate were not significantly associated. For CaP SS, high urinary phosphorus and pH (1.3 vs 0.8 to 1.7) were associated with higher CaP SS (Calcium 0.01mg, 0.008 to 0.12mg; pH 1.3 vs 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 - Novo Nordisk.

PO0407

A Randomized, Double-Blind, Placebo-Controlled Trial Assessing Efficacy of Standard and Low-Dose Hydrochlorothiazide Treatment for Prevention of Recurrent Caleorous Nephrolithiasis (NOSTONE Trial)

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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 10th 2017. A total of 416 patients 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 results of this study will affect many patients currently treated with hydrochlorothiazide for the prevention of recurrent nephrolithiasis.

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.
Dietary Intake and Risk of Incident and Recurrent Kidney Stones

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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 the 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 to a 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 BMI, fluid and energy intake. Dietary calcium 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

Table of results

| Table 1: Table of results for the cross-sectional study of metabolic profiles and the association with kidney stone disease in the Nurses’ Health Studies I and II |
|---------------------------------|----------------|----------------|----------------|
| Nutrient                         | Adjusted odds ratio for incident KS formers (controls) | 95% confidence interval | P-value |
| Calcium                         | 0.53 (0.28, 0.99) | 2.09 (1.18, 3.69) | 0.01 |
| Phosphorus                      | 0.72 (0.48, 1.09) | 1.80 (1.30, 2.49) | 0.01 |
| Magnesium                       | 1.49 (0.99, 2.25) | 2.70 (1.54, 4.77) | 0.01 |

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 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, CI- 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. Pycnolithotomy 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 urine 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.
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 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.

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 acidogenic 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 markers 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, Chicago, Il) from patients seen in Urology and Nephrology divisions, UVMMC 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 (hypertension, obesity, dyslipidemia, diabetes) were evaluated. Trends across groups were tested using linear contrasts in analysis of variance.

Results: 1250 unique patients, 49% F, 703 with stone composition met 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 high protein intake. P=0.05 for sulfates (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
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 (P_Ox) 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 P_Ox results. Subsequently, a standardized analytical protocol was established, and P_Ox concentrations were measured in a large cohort of patients with CKD.

Methods: We tested the effects on P_Ox results of storage time at room temperature (RT), storage on dry ice and maintenance of samples at -80°C. P_Ox results of storage time at room temperature (RT), storage on dry ice and maintenance of samples at -80°C.

Results: P_Ox concentrations increased rapidly when samples were maintained at RT. This was most relevant for P_Ox < 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 P_Ox measurement was 44.0 (17.9) ml/min/1.73 m². More than half of the patients had a P_Ox concentration below 2.0 μM. P_Ox correlated positively with urinary albumin to creatinine ratio and inversely with eGFR (P < 0.001). In the lowest eGFR quartile, median eGFR was 25.1 ml/min/1.73 m² (IQR 20.3 - 28.1) with a median P_Ox 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 P_Ox assessment in large patient cohorts. Our study presents a critical and useful modification of the complex preanalytical procedure. Moreover, we demonstrate that P_Ox concentrations in patients with CKD are substantially lower than previously reported. The present study may serve as a reference for sample handling to assess P_Ox in clinical trials and to determine its role in CKD progression.

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

Underline represents presenting author.
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-dialysis 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-10b-5p, miR-195, miR-125b-2-3p, and miR-378a-3p) were shown to decrease throughout all models tested, while 1 mRNA (SULF1) was noted to exhibit the opposite trend comparatively. 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 SULF1 levels increased. Adding serum miR-125b-2-3p, miR-378a-3p, and SULF1 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.

PO0421
Clinical Characteristics and eGFR and Urine Albumin-to-Creatinine Ratio Distribution According to the 2012 KDIGO CKD Classification
From a Report of the DISCOVER CKD International Retrospective Cohort
Juan Jose Garcia Sanchez,1 Juan I. Carrero,2 Supriya R. Kumar,2 Roberto Pecoisits-Filho,3,4 Glen James,5 Hildo J. Heerspink,6 Stephen Nolan,1 Lam S. Carolyn,7,8 Hungta (Tony) Chen,1 Eiichiro Kanda,4 Alyshah Abdul Sultana,9 Naoki Kashihara,9 Mikhail Kosiborod,10 Carol A. Pollack,11 David C. Wheeler,12 AstraZeneca, Cambridge, United Kingdom; Karolinska Institutet, Stockholm, Sweden; AstraZeneca, Gaithersburg, MD; Arbor Research Collaborative for Health, Ann Arbor, MI; Pontificia Universidade Catolica do Parana Escola de Medicina Campus Londrina, Londrina, Brazil; Rijksuniversiteit Groningen, Groningen, Netherlands; National Heart Centre Singapore, Singapore, Singapore; Duke-NUS Medical School, Singapore, Singapore; Kasawaki Ika Daigaku, Karashiki, Japan; Saint Luke’s Mid America Heart Institute, Kansas City, MO; Royal North Shore Hospital, St Leonards, NSW, Australia; University College London, London, United Kingdom.

Background: Contemporary studies describing the prevalence and characteristics of patients with CKD categorised according KDIGO 2012 are scarce. We describe patient characteristics and the prevalence of CKD according to the 2012 KDIGO categories in patients with CKD.

Methods: The DISCOVER-CKD retrospective cohort of patients was extracted using real-world data from the integrated Limited Claims and Electronic Health Record (LCLCRD) data in TriNetX. Patients were aged ≥18 years, with at least 1 UACR measure and ≥1 eGFR measure, and without first diagnostic coding of CKD (Stages 3A to ESRD) or two estimated glomerular filtration rate (eGFR) closest to index was used to categorise patients. Descriptive analyses were used to summarise prevalence and patient characteristics.

Results: Preliminarily, among 22229 included patients, 63.6% (n=10979, TriNetX) and 78.6% (n=3813, LCEC) had normal to mildly increased albuminuria, 26.6% (n=4581, TriNetX) and 17.9% (n=6889, LCEC) had moderately increased albuminuria and 9.8% (n=1694, TriNetX) and 5.5% (n=273, LCEC) had severely increased albuminuria (Figure 1). Hypertension and type 2 diabetes were the most common comorbidities (prevalence >60%) and their prevalence increased with albuminuria.

Conclusions: This study, utilising real-world data, fills an important knowledge gap regarding the characteristics of patients with CKD in different eGFR and UACR strata according to the KDIGO 2012 definitions.

Funding: Commercial Support - AstraZeneca

PO0422
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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 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=38,736). 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 pre or 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%, MI 11.3%, Stroke 8.9%; ESKD 16.8%; 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 and independent 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. 15-year CV, renal and mortality outcomes across the 3 UACR categories analyzed.

<table>
<thead>
<tr>
<th>UACR Category</th>
<th>0-30mg/g (n=1175)</th>
<th>30-199mg/g (n=1891)</th>
<th>200-5000mg/g (n=3491)</th>
<th>Total (n=6557)</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Event Rate</td>
<td>26.6%</td>
<td>31.3%</td>
<td>39.1%</td>
<td>31.9%</td>
<td>&lt;0.001</td>
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<td>Renal outcome</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>ESKD (progression to ESRD)</td>
<td>17.0%</td>
<td>20.7%</td>
<td>25.9%</td>
<td>21.2%</td>
<td>0.067</td>
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<tr>
<td>Dialysis</td>
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<td></td>
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<td>15.7%</td>
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<tr>
<td>Mortality</td>
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<td></td>
<td></td>
<td>18.5%</td>
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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 to creatinine ratio (ACR), KIM-1, and IL-18 were measured in 2,999 participants; urine a1m, NGAL, PiNP, 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% were 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 >50 mg/mg and 11% (95% CI: 4%-18%) lower mean urine IL-18 concentration at baseline. 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 as measured 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
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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 be 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: 1° 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 1° 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 mls/min in 39.6% and <60 mls/min in 5% 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%.

Conclusions: The combined 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 19% [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.
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 ng/mL vs 3.07 ng/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 ng/mL, p<0.0001). Fifty percent (10.4%) had 2 APOL1 risk alleles (35 for women vs 15 for men); among those, 3 (6%) developed CKD (p<0.007). 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 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 8 biomarkers of kidney tubule dysfunction and injury among 2,282 SPRINT participants with eGFR < 60 and evaluated their associations with frailty (Figure). Higher urine concentrations of MCP-1 & uromodulin [Umod], kidney injury molecule-1 [KIM-1], interleukin-18 [IL-18], uromodulin [Umod], and neutrophil gelatinase-associated lipocalin [NGAL]) among a random sample of 502 participants, and serum bicarbonate [sHCO3] 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 marker biomarkers were associated with 3MSE, whereas higher urine NGAL was associated with lower DSST scores. Lower concentrations of sHCO3 were associated with lower scores of 3MSE but not DSST (table). These associations were independent of demographics, eGFR, and albuminuria.

Conclusions: Among urine markers of tubule injury and dysfunction, only higher NGAL was associated with lower cognitive function testing by DSST. Similarly sHCO3 was associated with worse cognitive function by 3MSE 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-AI-6-2101; N01-AI-6-2103; N01-AI-6-2106; NIA grant R01-A0288050; NINR grant R01-RR012459, Veterans Affairs Support

Cross-sectional association between biomarker of kidney tubule 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 lipocalin [NGAL]) among a random sample of 502 participants, and serum bicarbonate [sHCO3] 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 marker biomarkers were associated with 3MSE, whereas higher urine NGAL was associated with lower DSST scores. Lower concentrations of sHCO3 were associated with lower scores of 3MSE but not DSST (table). These associations were independent of demographics, eGFR, and albuminuria.

Conclusions: Among urine markers of tubule injury and dysfunction, only higher NGAL was associated with lower cognitive function testing by DSST. Similarly sHCO3 was associated with worse cognitive function by 3MSE 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-AI-6-2101; N01-AI-6-2103; N01-AI-6-2106; NIA grant R01-A0288050; NINR grant R01-RR012459, Veterans Affairs Support

Cross-sectional association between biomarker of kidney tubule dysfunction with cognitive function.

Figure. Multinomial regression showing the baseline association between biomarkers of kidney tubule dysfunction and injury with frailty compared with fit older adults (less fit group omitted). Models were adjusted for age, sex, race, BMI, alcohol use, years of education, SBP and DBP, smoking status, urine creatinine, eGFR, and albuminuria.
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 function. NT-proBNP is significantly associated with the severity of GFR loss. However, the reference interval (RI) of NT-proBNP in non-dialysis 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, 589(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, 12.38-2519.90, 16.62-1411.05, 33.14-2945.05, 88.58-5533.73pg/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.
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 at 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, 226, and 162 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

Figure 1

PO0434
Association Between eGFR-Cystatin C/eGFR-Creatinine Ratio and Fat Weight
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Background: The ratio of eGFR-cystatinC/eGFR-creatinine less than 0.7 is a condition that demonstrates different filtration for small and large molecules and is associated with accumulation of othersecretes/protecting proteins, higher cardiovascular event and mortality risk. Though, we hypothesize that this ratio could also be an indirect reflection of certain body composition. For example creatinine/cystatin C ratio has been used as a marker for sarcopenia, whereas cystatin C is highly expressed in human adipose tissue and might be increased in obesity. So the aim was to explore whether eGFR-cystatinC/eGFR-creatinine ratio is valid independently on body composition measures.

Methods: Data were extracted from the population based Malmö Diet and Cancer (MDC) study (n= 28 449) cardiovascular cohort (MDC_CC) that enrolled a random sample of study subjects invited to participate in carotid artery disease epidemiological analysis (n = 6 103) during the year 1991-1994. Our study sample consisted of 5061 subjects who had body composition measurements and cystatin C available. Estimated glomerular filtration rate (eGFR) according to Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) 2012 creatinine-cystatin C equation was calculated. Bioimpedance analysis of body composition was estimated by following procedures provided by manufacturer (BIA-103 RJL Systems, Detroit, MI, single frequency (50kHz)).

Results: In our study sample 11% (n=564) of subjects, mainly women (n=562), were classified as with eGFR-cystatinC/eGFR-creatinine ratio lower than 0.7. Therefore, we applied logistic regression analysis explicit in women and compared 2430 women without SPS with the rest of the 562. We found that the ratio adjusted for age was associated with obesity (OR 3.49, p<0.001) and in multivariate analysis only with fat weight (OR 1.91, p<0.001). Lower lean weight showed also significant relationship with lower eGFR-cystatinC/eGFR-creatinine ratio, but not after adjustment to other cofounders.

Conclusions: The ratio of eGFR-cystatinC/eGFR-creatinine lower than 0.7 is dependent on fat weight in females from population based study.

PO0435
Discovery of Obesity and Adiposity-Related CKD Subgroups and Preliminary Metabolomics Findings: The CRIC Study
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Background: Obesity/adiposity perturbs the plasma metabolome, as does chronic kidney disease (CKD). Understanding the complex relationships across CKD patient subphenotypes, obesity, and the metabolome may shed light on finding novel risk factors and the mechanisms for CKD progression.

Methods: Among 1,529 participants in the Chronic Renal Insufficiency Cohort (CRIC) study (n = 634 known metabolites, after adjusting for demographics, health history, eGFR and UACR), we first generated consensus clustering with K-means on 20 baseline clinical adiposity-obesity-related attributes to identify patient subgroups. We individually examined the association of 634 known metabolites with the identified subgroups using separate multivariable linear models. Finally, Cox model was used to examine the prospective association of the adiposity-obesity subgroups (the biggest subgroup as reference) with CKD progression, ESRD, a composite cardiovascular disease outcome, and death.

Results: We identified four distinct adiposity-obesity-related CKD subgroups: Subgroup 1 (N=429) - favorable obesity/diabetes profiles and elevated lipid levels; Subgroup 2 (N=349) - favorable diabetes profiles, but slightly obese; Subgroup 3 (N=357) - less favorable diabetes profile, lower lipid levels and severe obesity; and Subgroup 4 (N=394) - less favorable diabetes profiles, but less obese. Among the 634 known metabolites, after adjusting for demographics, health history, eGFR and UACR, 260 were significantly associated with CKD subgroups at Bonferroni-adjusted p<7.9 x 10^-4. Survival analyses showed that compared to Subgroup 1 (ref), Subgroup 4 had the highest risk for CKD progression (HR 1.78, 95% CI 1.40, 2.26) and ESRD (HR 1.92, 95% CI 1.45, 2.52), and Subgroup 3 had the highest risk for the composite CVD outcome (HR 1.87, 95% CI 1.40, 2.50) and death (HR 1.51, 95% CI 1.09, 2.10).

Conclusions: With consensus clustering and metabolomics analysis, we discovered four distinct adiposity-obesity-related subgroups of CKD patients that were associated with numerous metabolites and different risks of clinical endpoints. Novel biomarkers that co-segregate with patient subgroups of high risk could reveal new insights into the obesity related biology of CKD progression and subsequent CVD events, and potentially suggest tailored therapeutic targets among CKD patients.

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 (historical EMR) were analysed. CKD patients (eGFR < 60 mL/min/1.73 m²) aged ≥18 years with a 1 record of urine albumin to creatinine ratio (UACR) were identified. T2D was ascertained any time before the index date (2 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 (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 an increased risk of adverse renal outcomes in 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 adverse renal outcomes in CKD patient with T2D compared to those without T2D. This is explained to 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.

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PO0438

Assocation 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, 0.75–1.01, 1.01–1.25, ≥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% Black, 5% Asian, 57% 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 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 (indicating lowest muscle mass) had the highest mortality risk for both eGFR strata, with the normal eGFR group having higher death risk than the low eGFR group (HR (95%CI): 1.86 (1.49,2.31) and 2.13 (1.75,2.59), respectively). In the highest CrCCR group (≥1.25) indicating more muscle mass, the normal eGFR group had the overall survival lower than those with low eGFR (HR (95%CI): 0.45 (0.27,0.73)).

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.

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

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Results: Among 3,930 patients, 1,374 were in PPI group, 119 were in H2 blocker group, and 2,347 had no medications. 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).

Conclusions: 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.

CKD Epidemiology, Biomarkers, Predictors
Poster

PO0440
Elderly Patients Are Likely to Have Faster CKD Progression if Plasma Brain Natriuretic Peptide (BNP) Is Elevated
Shiho Morimoto, Hiroshi Tanaka. Mihara Red Cross Hospital, Mihara, Japan.

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-dialysis CKD patients (median eGFR <60 mL/min/1.73m2) 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 (0.1641, 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. Among the 339 patients, 12% of 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.

Conclusions: Elevated plasma BNP might predict faster decline in eGFR in the elderly CKD patients.

PO0441
Pump-Proton 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 regarding renal outcomes in established CKD patients. 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 and H2B and CKD among patients with CKD stage 3 and 4 with at least 2 PCP 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.

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

Underline represents presenting author.
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), Sprectral-related modular 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 Lumixem-based assays and measured proteins in plasma and urine samples of two independent prospective cohort studies, the Boston Kidney Biopsy Cohort (BKBC, n=881), 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 hazard 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. snRNA 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. snRNA-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

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
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 reported 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 analyzed. 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 CKD 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, 0.87-0.88; meta-analyzed 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 or 2-year average eGFR 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.

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Comparison of Predicted Risk of Renal Replacement Therapy vs. eGFR for Arteriovenous Fistula Placement in CKD: A Retrospective Analysis
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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 nephrologist who had a nephropathy visit with an eGFR and a calculable 2-yr risk for 60 months before the start 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-yr 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-yr risk for patients, eGFR, laboratory values, and imaging.

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-yr RRT risk of 40% (73% and 49%) for eGFR threshold of 15 ml/min respectively compared to 83% and 54% respectively for 2-yr RRT risk of 80% (84% and 80%) compared to eGFR threshold of 15 ml/min/specificity and specificity was greater at 2-yr RRT risk of 80% (97% and 11%) for eGFR threshold of 15 ml/min respectively compared to 98% and 18% respectively for 2-yr RRT risk threshold of 80%). The AUC was greater between 2-yr 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-yr risk >40% compared to eGFR of 20 ml/min above a 1 year threshold of 25%.

Conclusions: In patients with CKD stage 4, 2-yr 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.
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 3592 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 3 years. The four measures included timed urinary albumin and protein excretion rates (AER, PER), albumin:creatinine ratios (ACR, PCR), albumin:protein:adjusted creatinine (accounting for creatinine production) (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

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 (CO2)
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 0.5mg/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 0.5mg/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 CKD patients. The incidence of hypophosphatemia in CHB patients was 1.7%. 50% of patients had hypophosphatemia during 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 70; 3Controls) evaluated for eGFR, creatinine, phosphorus, calcium, FGF-23, soluble 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): phosphorus 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±0.35 to 0.58±0.11 (CKD 1) and 0.71±0.074 to 0.64±0.095 (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 3.22±0.58 (CKD 1) and 4.32±0.42 to 3.35±0.85 mg/dL (p 0.001 CKD 2); FGF-23 from 55.01±1.65. to 51.27±11.17 (CKD 1); 65.42±4.80 to 56.60±11.23 (p 0.010 CKD 2); systolic BP from 127.95±3.14 to 121.05±4.40 (CKD 1); 134.22±3.54 to 118.38±9.08 (p 0.001 CKD 2) and diastolic BP from 85.14±3.80 to 83.29±8.03 (CKD 1); 89.11±4.74 to 80.33±6.02 (p 0.003 CKD 2) and a significant increase in eGFR ml/min from 95.17±5.50 to 97.75±20.26 (CKD 1); 109.82±8.56 to 74.04±11.07 (p 0.019 CKD 2) was observed. sKlotho increased from 700.79±27.82 to 879.39±18.87 (p 0.001 CKD 1); from 633.52±56.03 to 823.37±15.67 (p 0.001 CKD 2). Ca x P product declined from 36.10±8.41 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 and late stages of CKD. Dietary intervention can prevent decline 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.

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 specific period of the day alternating with a prolonged period of fasting. Preclinical 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 mg/dl/1.73 m2 to 38.8 mg/dl/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.
Future intervention trials should investigate whether a diet enriched in fibers would
with cardiovascular outcomes or kidney disease progression in individuals with
CKD. (≥45 ml/min/1.73 m²), and proteinuria.

dietary fiber intake and kidney and cardiovascular disease outcomes. Results were similar
compared to those in the highest fiber tertile (HR [95%CI], 1.18 [1.01, 1.38], p =0.04
adjustments, individuals in the middle and low fiber tertiles were at greater risk of death
4.5 years, there was an inverse association between
changes in dietary protein intake and outcomes among patients

Changes in Dietary Protein Intake and Outcomes Among Patients
with CKD
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Background: Protein energy wasting is common and associated with poor outcomes
in CKD while low protein diet is recommended to delay the development of ESRD.
However, the clinical relevance of the temporal change in dietary protein intake (DPI) in
real-world data remains unclear in this population.

Methods: We performed repeated collections of morning spot urine in a prospective
cohort of non-dialysis dependent veterans with CKD at a single institution. We assessed
urine urea nitrogen-to-creatinine ratio to estimate 24-hour urine urea excretion and then
estimated DPI using the Maroni formula. Among 345 patients who had data on DPI
between 6-12 months from the initial measurement, we estimated the slope of DPI in
mixed effects models and examined its association with subsequent ESRD and all-cause
mortality in cause-specific hazard models with adjustment for demographics, Charlson
Comorbidity Index, eGFR, urinary protein, smoking status, body mass index, and
baseline DPI.

Results: Patients were 68±10 years old, 97% were male, 36% were African American,
and their baseline eGFR was 34±12 ml/min/1.73 m². Baseline DPI was median 0.55 (IQR,
0.45–0.67) g/kg/day and its slope was 0.01±0.04 g/kg/day per year. During a median
follow-up of 4.2 years, 129 died (104/1000 PY) and 87 developed ESRD (83/1000 PY).
Decrease in DPI was associated 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.

Effect of Zinc Deficiency on CKD Progression and Effect Modification
by Hypoalbuminemia
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Background: Serum zinc (Zn) levels tend to be low in chronic kidney disease (CKD)
patients. However, it has not been shown whether zinc deficiency itself leads to poor renal
prognosis. The purpose of this study was to investigate the relationship between zinc
deficiency and CKD progression.

Methods: This is a retrospective cohort study using the CKD patient database of
electronic medical records (n=325). The study patients were classified into two groups: Zn
levels<60μg/dl (low-Zn group, n=165) and Zn levels≥60μg/dl (high-Zn group, n=162).
The primary outcome was defined as end-stage kidney disease (ESKD) or death, and the
observation period was one year. The relationship between low Zn levels and the outcome
was assessed using Cox proportional hazard model and by competitive risk analysis.
Furthermore, the propensity score-matched analysis for low Zn level was also conducted.

Results: Among the subjects, 51.7% were male; mean age, 69.3 years; mean Zn
level, 59.9μg/dl; and median eGFR, 20.4ml/min/1.73 m². The incidence of the primary
outcome was higher in the low-Zn group than in the high-Zn group (42.3% vs 19.1%,
mean±9.6). The average dietary fiber intake was 17.3±9.6

Conclusions: Dietary fiber intake may be associated with the risk of death, but not
with cardiovascular outcomes or kidney disease progression in individuals with CKD.
Future intervention trials should investigate whether a diet enriched in fibers would
influence mortality and other clinical outcomes.

Funding: Other NIH Support - NHLBI

Changes in Dietary Protein Intake and Outcomes Among Patients
with CKD
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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/1.73 m². 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
the 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 and kidney and cardiovascular disease outcomes. Results were similar
in sensitivity analyses by subgroups defined by age, gender, ethnicity, diabetes, eGFR
(< and ≥) 45 ml/min/1.73 m²), and proteinuria.

Conclusions: Dietary fiber intake may be associated with the risk of death, but not
with cardiovascular outcomes or kidney disease progression in individuals with CKD.
Future intervention trials should investigate whether a diet enriched in fibers would
influence mortality and other clinical outcomes.

Funding: Other NIH Support - NHLBI
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 modifying role of folate.

Methods: This was a prospective study, including a total of 935 hypertensive adults from a folate intervention trial (CSPPFT) 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/1.73m² 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, 0.90; 95% CI: 0.85, 0.95). Consistently, compared to the lowest tertile of baseline plasma Se (≤7.4 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 folate acid treatment (per 10-unit increment: OR, 0.97; 95% CI: 0.94, 1.00; P-interaction=0.036) or with a higher baseline folate concentration (≥90 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 folate acid supplementation or a higher folate level.

Funding: Government Support - Non-U.S.

Association between plasma Se and the outcome

*Adjusted for age, sex, eGFR, treatment group, BMI, MTHFR C677T polymorphisms, proteinuria, SBP, TC, glucose, smoking status at baseline, and averaged SBP during follow-up period.

PO0465

Relationship of Serum Triglycerides with Incident Albuminuria Among 114,817 US Veterans

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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 least 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 a3 MetS components.

Results: The meansSD 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/1.73m², 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 a3 MetS components. The association of TG with incident albuminuria was attenuated (Figure A). Moreover, stratification by number of MetS components showed similar linear associations between TG and incident albuminuria, especially in patients with ≥5 MetS components. In patients with ≥5 MetS components, the linear relationship of TG and incident albuminuria was attenuated (Figure B).

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 at-risk populations.

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

Underline represents presenting author.

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PO0466

Short-Term Associations of Triglycerides with Atherosclerotic and Non-Atherosclerotic Cardiovascular Disease Hospitalizations 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, with adjustment for demographics, and time-varying comorbidities and laboratory values.

Results: The cohort was 63±14 years old with a mean [IQR] TG 72[49,127] 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 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 stages 5 and stage 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.

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® EMR), 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 independently 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); P< 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 sociodemographic factors that affect health, further exploration of the potential reasons for the observed range of hazards across racial/ethnic groups is warranted.

Funding: Commercial Support - Tricida, Inc.

PO0469

Metabolic Acidosis Is Associated with CKD Progression: A Longitudinal Analysis of >100,000 US Community-Based Patients

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Background: To delay the progression of CKD, it is imperative to identify modifiable risk factors and then evaluate efficacy of interventions. Here we assess the role of metabolic acidosis as an independent risk factor for CKD progression in patients (pts) with non-dialysis-dependent CKD Stages 3-5.

Methods: De-identified electronic medical records (Optum® EMR), 2007–2019 were queried to identify pts with non-dialysis CKD Stages 3-5, (2 consecutive eGFR values ≥10 and <60 mL/min/1.73m2 90-365 days apart) followed by 2 consecutive serum bicarbonate values ≥28-365 days apart) followed by 2 consecutive serum bicarbonate values ≥90-365 days apart) followed by 2 consecutive serum bicarbonate values 28-365 days apart, a2 <22 mEq/L (metabolic acidosis) or 22 to <30 mEq/L (normal serum bicarbonate) and a2 yrs of post-index data or death within 2 yrs. Pts (N = 136,067) were followed for up to 11.5 yrs for evidence of CKD progression, measured as a ≥40% decline in eGFR from baseline and as progression of a ≥1 CKD stage from baseline using laboratory data. We describe outcomes at 2 yrs and used Cox proportional hazards models over the entire follow-up period to examine potential confounders: age, sex, race/ethnicity, eGFR, log albumin-to-creatinine ratio, diabetes, hypertension, heart failure, and weighted Charlson Comorbidity Index.

Results: 75,127 pts (55%) progressed 1 or more CKD stages within 2 yrs. The incidence of CKD progression within 2 years was significantly higher in pts with metabolic acidosis compared to pts with normal serum bicarbonate, irrespective of the endpoint (≥40% decline in eGFR: 38.3% vs. 20.4%, P< 0.0001; progression of a ≥1 CKD stage from baseline vs. 54.5%, P< 0.0001). During the up to 11.5 yrs of follow-up (median 4.2 yrs), serum bicarbonate was independently associated with CKD progression; hazard ratios per 1 mEq/L increase in serum bicarbonate were 0.969, CI: 0.965-0.973 for a ≥40% decline in eGFR and 0.975, CI: 0.972-0.977 for progression of a ≥1 CKD stage.

Conclusions: In pts with non-dialysis CKD, serum bicarbonate levels below 22 mEq/L were independently associated with increased risk of CKD progression. Large randomized trials targeting treatment of metabolic acidosis to slow CKD progression are needed. There was a 2.5–3.0% risk reduction for a ≥40% decrease in eGFR or progression by a ≥1 CKD stage for every 1 mEq/L increase in serum bicarbonate.

Funding: Commercial Support - Tricida, Inc.

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Underline represents presenting author.
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 urine citrate excretion (UcitV) might be a biomarker of covert acid (H+) retention in patients with CKD but with 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), 120 with CKD 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 macroalbuminuria, 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±1.2, 18.2±1.0, 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, 1.00±0.25, and 0.86±0.10 mmol/1.73 m², 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 mm/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: Hypercalcuria 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 2 (CONSORT). 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=0.417, 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 healthcare system in the 7-county metropolitan area in Minnesota and linked census tract data. Census tract measures (median value 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 a 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 women and 1.26 [1.17, 1.36] and 1.24 [1.15, 1.33] for men). Patients (<65 years) on Medicare vs. other 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 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.

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.

Results: Of the 3,330,893 MHS beneficiaries in this analysis, 105,504 (3.2%) were identified as having CKD. In confounder-adjusted models, CKD prevalence was statistically elevated in beneficiaries of black vs white race, lower vs higher income, and married vs single status (p <0.001). As expected, associations were partially or fully mitigated when further adjusting for suspected mediators, indicating the mediators may indeed be on the causal pathway between social risks and CKD.

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 VA data. More SDOH-ZCs were evident in the VA employment, environment, 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 (BP ≤130/80 mmHg, a1c ≤7%, sodium intake <2 g/day, regular physical activity, BMI 20-25 kg/m2, and smoking cessation) relative to those with no unmet needs.

Results: Among 1805 HANDLS participants, 899 (49.8%) reported at least one unmet health-related social need. Compared to those without unmet needs, those with unmet needs were younger (mean age 55.0 versus 57.8 years), more likely to be black (63.7% versus 38.5%), report income <125% of federal poverty level (46.8% versus 31.9%), and had higher eGFR (mean 90.0 versus 85.8 mL/min/1.73m2). The likelihood of achieving a higher number of protective measures was significantly lower for those with unmet needs compared to those without unmet needs (Table). Having unmet needs was significantly associated with lower likelihood of being a non-smoker and engaging in physical activity.

Conclusions: Individuals with unmet social needs may be less likely to achieve measures to prevent incident CKD and CKD progression.
**Association Between Air Pollution and Renal Outcomes: A Systematic Review and Meta-Analysis**

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**Background:** Although several risk factors of chronic kidney disease (CKD) have been well-established, mainly diabetes and hypertension, many remain less studied, such as chronic exposure to air pollution. Our purpose is to exhaustively summarize the current evidence on the association between air pollution and various renal outcomes.

**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, NO2, NOx, SO2, PM2.5, PM10, 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 has been assessed using the y2 test on Cochran’s Q statistic and quantified I2 calculation.

**Results:** Within 1214 eligible studies, 42 articles fulfilling the selection criteria were included in this work (11 cross-sectional, 15 prospective, and 16 retrospective cohort studies). The most significant associations are for PM10 exposure and higher risks of CKD, ESRD, and kidney cancer incidence; PM2.5 exposure and higher risks of CKD and ESRD incidence; PM2.5/PM10 exposure and higher CKD prevalence, as well as lower renal function (see details in Figure 1). These results should however be interpreted with caution, due to significant between-studies heterogeneity and risks of methodological bias.

**Conclusions:** Chronic exposure to particulate matter and nitrate dioxide seems to be associated with poorer renal outcomes. Further studies are warranted to confirm these results.

**PO0479**

**Prevalence and Severity of Hyperkalemia in Patients Referred to Nephrology Consultation: Epidemiologic Data from 1106 Mexican Patients at a National Reference Hospital**

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**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.

**Funding:** Commercial Support - AstraZeneca, Government Support - Non-U.S. S.
PO0480

Serum Potassium and Survival Among Advanced CKD Patients

Transplanting to Dialysis

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Background: Most laboratories designate a wide reference range for “normal” serum potassium levels (3.5–5.5 mEq/L), yet the precise concentrations associated with favorable outcomes in chronic kidney disease (CKD) remain uncertain. While dietary potassium is commonly restricted in CKD patients to mitigate hyperkalemia, there may be ill effects of this strategy by restricting healthy potassium-rich foods (fruits, vegetables).

We hypothesized that high-normal serum potassium levels are associated with better long-term survival in advanced non-dialysis dependent (NDD) CKD patients transitioning to dialysis.

Methods: Among 43,798 US Veterans with NDD-CKD transitioning to end-stage renal disease (ESRD) (mean age: 60.2 yrs, 10/2007-3/2015) an electronic health record cohort study was linked to United States Renal Disease System data. Associations of serum potassium levels (categorized as <3.5, 3.5–<4.0, 4.0–<4.5, 4.5–<5.0, and 5.0–5.5 mEq/L) with all-cause mortality were estimated using adjusted Cox models.

Results: In adjusted Cox analyses, high-normal serum potassium levels ranging from 5.0–5.5 mEq/L were associated with greater survival (HR: 1.07, 95% CI 1.04-1.10). In contrast, serum potassium concentrations at or below normal range were associated with higher death risk (OR 1.16, 95% CI 1.06-1.27). These findings are compatible with the hypothesis that within the normal range, high serum potassium levels may benefit survival among advanced CKD patients transitioning to dialysis.

Conclusions: Our study confirms that high-normal serum potassium levels is associated with improved long-term survival among advanced CKD patients transitioning to dialysis.

PO0482

High Serum Alkaline Phosphatase Predicts CKD Progression: Effect Modification by GFR

Francesca Mallama,1,2 Grazzella D’Arrigo,1 Francesco Marino,2 Grazzella Caridi,1 Giovanna Parlongo,1 Daniela Leonardi,1 Patrizia Pizzini,1 Sebastiano Cutrupi,1 Anna Pisano,1 Giovanni Tripepi,1 Carmine Zoccali,1 CNR-IFC, Reggio Calabria, Italy; 2Nephrology, Dialysis and Transplantation Unit, Reggio Calabria, Italy.

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±12 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, 290 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-by-AlkPhos interaction (p=0.007). Adjusted for age, gender, smoking, diabetes, cholesterol, BMI, systolic BP, CV comorbidities, hemoglobin, albumin, phosphate, and hs-CRP, did not modify this association.

Conclusions: In stage 3-5 CKD patients, AlkPhos within the normal range is associated with the progression to ESRD and the GFR is an effect modifier of this relationship. These findings are compatible with the hypothesis that within the normal range of this biomarker, the risk for CKD progression by AlkPhos is amplified by CKD severity. These data are in keeping with post-hoc analyses of SUSTAIN/ASSURE trials and support the hypothesis that interventions lowering AlkPhos may mitigate CKD progression.

Funding: Government Support - Non-U.S.

PO0481

Hyperkalemia, CKD, and RAAS Inhibition: A Triad with a Fine Balance to Prevent Mortality

Luis F. Goncalves, Mario R. Raimundo. Hospital Beatriz Angelo, Loures, Portugal.

Background: Hyperkalemia (HK) is a common and dangerous complication of CKD. HK is also a complication of beneficial therapeutic agents acting on the RAAS. Our goal was to investigate incidence, prevalence and clinical outcomes of at least one episode of HK in a CKD population outpatient setting. Additionally, we investigated the association of HK with changes in RAAS inhibition and mortality.

Methods: Retrospective analysis of all adult patients referred to a nephrology clinic over a 6 years period. We included CKD stage 3 patients with at least 24 months of follow up and 3 or more serum potassium determinations. The prevalence of HK at first consultation and incidence during follow up were assessed. Patients were split in two groups prior to analysis: A) Patients without any HK episode and B) Patients with at least one HK episode.

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 drugs was removed or not started in 200 (34.8%) and diuretic was initiated in 165 (26.8%). 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 vs 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 1.08-3.04); 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.

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

Underline represents presenting author.
PO0483

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. PMI was used as an indirect surrogate of arterial stiffness. Statistics were performed using R 3.6.2.

Results: The mean SBP was 158.8 ± 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 index was 17.5 (5.0-36.3) %. The PMI was 0.94 ± 0.23, the PMP was 21.6 ± 7.3 x 10⁶, and the BMI was 22.9 ± 4.7 kg/m². Both PMI and PMP 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, HbA1c, and blood pressure was not correlated with either eGFR or CKD stages.

Conclusions: We observed correlations between both PMI and PMP and kidney function. This study indicates that PMI and PMP may be possible makers of the relative risk of unhealthy obesity with CKD.

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.

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 (PMP) 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 PMP 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 by kidney biopsy. The PMI and the PMP were calculated from the following formula: PMI = BMI x resting heart rate (RHR) /1730. PMP = BMI x RHR x systolic blood pressure. We evaluated the clinicopathological findings associated with PMI and PMP.

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 index was 17.5 (5.0-36.3) %. The eGFR was 0.94 ± 0.23, the PMP was 21.6 ± 7.3 x 10⁶, and the BMI was 22.9 ± 4.7 kg/m². Both PMI and PMP 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, HbA1c, and blood pressure was not correlated with either eGFR or CKD stages.

Conclusions: We observed correlations between both PMI and PMP and kidney function. This study indicates that PMI and PMP may be possible makers of the relative risk of unhealthy obesity with CKD.
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 Trinetx 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 ≥90 days apart between January 2008 and March 2020. The index date was the first Hb measure (regardless of value) or anemia therapy (iron, ESA or blood transfusion) prescription 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 [females] or ≥14 g/dL [males] per WHO criteria. Baseline characteristics were summarized and stratified by presence of anemia.

Results: Preliminarily, of 709183 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, 36889 (16%) 8-10 g/dL and 6906 (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 ≥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 socioeconomic 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)

Based on the provided textual content, it appears that the document contains research findings related to chronic kidney disease (CKD), anemia, and risk factors for low eGFR. The studies were conducted in various settings and countries, with a focus on understanding the prevalence and factors associated with CKD and anemia. The research was aimed at improving clinical care and enhancing awareness of these conditions, particularly among certain populations such as individuals living with HIV. Various methods, including case-control studies and prospective cohort analyses, were employed to examine the incidence and risk factors for CKD, anemia, and low eGFR. The findings highlight the importance of addressing these conditions, as they are associated with adverse clinical outcomes and reduced quality of life.
Oxygen Kinetics and Microvascular Function in CKD

Natalie J. Bohmke,1 Meghan G. Ramick,2,3 David G. Edwards,2 Danielle L. Kirkman,1,3 Virginia Commonwealth University; Richmond, VA; 2University of Delaware, Newark, DE; 3West��University of Pennsylvania, West Chester, PA

Background: Patients with chronic kidney disease (CKD) have reduced cardiorespiratory fitness levels that are associated with reduced quality of life and mortality. Impaired oxygen uptake kinetics create a larger oxygen deficit that promotes fatigue. CKD related microvascular dysfunction may contribute to impaired oxygen uptake kinetics by hampering oxygen delivery to the working muscle. The purpose of this study is to investigate the relationship between oxygen kinetics and a measure of microvascular function in CKD.

Methods: 13 patients with stage 3-5 CKD (Mean±SD, Age 60±14 years; eGFR 48.5±10.3 ml/min/1.73m²) were included in the analysis. Peak oxygen consumption (VO₂peak) was measured via breath by breath expired gas analysis during a symptom limited graded cycle ergometry test. Oxygen kinetics were quantified as mean response time (MRT), the exponential time constant to reach 63% of steady state VO₂peak. Microvascular function was assessed as cutaneous vasodilation during local heating coupled with intradermal microdialysis, measured by laser Doppler flowmetry.

Results: VO₂peak was 20.36±8.7 ml/kg/min. A moderate inverse correlation was observed between oxygen uptake kinetics and microvascular function (Figure 1; p=0.056, p=0.02). Microvascular dysfunction may contribute to a larger oxygen deficit in CKD patients. Following further studies, microvascular function could serve as a potential treatment target to improve exercise tolerance in these patients.

Funding: Other NIH Support - Grant number: 1R01DK122343

Conclusions: Microvascular dysfunction may contribute to a larger oxygen deficit in CKD patients. Following further studies, microvascular function could serve as a potential treatment target to improve exercise tolerance in these patients.

Funding: Other NIH Support - Grant number: 17GRNT33670462

PO0491

Evaluating the Longitudinal Association of Marijuana Use and Adverse Kidney Outcomes

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Background: Marijuana use has increased for recreational and medicinal purposes, however, its long-term effects on the kidneys remain uncertain. We examined the longitudinal association of marijuana use and adverse kidney outcomes among adults living in Baltimore, MD.

Methods: We used data from the prospective Healthy Aging in Neighborhoods of Diversity across the Life Span study. Baseline exposure, defined as self-reported never, former, or current marijuana use, and covariates were obtained between 2004 and 2009. The primary outcome was measured using an eGFR <60 ml/min/1.73m². Rapid kidney function decline (defined as a ≥33% eGFR decline per year) among those with a baseline eGFR ≥15 and incident albuminuria (albumin-to-creatinine ratio [ACR] ≥30 mg/g) at follow-up was also assessed. Participant characteristics were evaluated using ANOVA or χ² tests. Multivariable-adjusted logistic regression was used to evaluate associations of marijuana use with kidney outcomes. Covariates included baseline eGFR, age, sex, race, education, poverty status; current cigarette, opiate, cocaine use; hypertension, diabetes, and body mass index (BMI).

Results: Among 1,529 participants, 54.5%, 31.8% and 13.7% reported never, former, or current marijuana use, respectively. Participants with current marijuana use were more likely to be younger, male, American, have lower BMI and concurrently use cigarettes, opiates and/or cocaine; but were less likely to have hypertension or diabetes. Mean follow-up time was 8.6 ± 0.9 years. Rapid kidney function decline occurred in 5% of the cohort, but there was no significant difference in deaths between marijuana exposure groups (Pearson χ², p=0.524). After adjustment, marijuana use was not significantly associated with incident reduced kidney function (OR 1.08 [95% CI, 0.49-2.36] among those with current use, and OR 0.90 [95% CI, 0.49-1.61] for former use). Marijuana use was not significantly associated with rapid kidney function decline (OR 0.73 [95% CI, 0.42-1.27] for current use) or incident albuminuria (OR 0.63 [95% CI, 0.11-4.83] for current use).

Conclusions: In this Baltimore-based cohort, there was no independent association of marijuana use and longitudinal adverse kidney outcomes.

Funding: Other NIH Support - National Institute on Aging

PO0492

Life’s Simple 7 and CKD Progression: Results from the Mexico Chronic Renal Insufficiency Cohort (MCRIC) Study

Magdalen Madero,1 Ana P. Hernandez Martinez,2 Ana K. Fernandez Yepiz,2 Jinsong Chen,1 Claire T. Larkin,1 Natalie Meza,1 Eunice Carmona,1 Christopher G. Viamonte,1 Carlos L. Morales Cruz,1 Zuleyma T. Vasquez Vasquez,1 Tania J. Ramos Estrada,2 Areli d. Avalos Galicia,1 Bernardo Moguel,2 Carlos Linares Kolofon,1 Ana C. Ricardo,1 James P. Lash.1 University of Illinois at Chicago, Chicago, IL; 2Instituto Nacional de Cardiologia Ignacio Chavez, Mexico, Mexico

Background: The American Heart Association developed the Life’s Simple 7 metric to promote cardiovascular health. We evaluated the association of this metric with chronic kidney disease (CKD) progression among individuals with CKD living in Mexico.

Methods: MCRIC is an ongoing, prospective observational cohort study of adults with CKD recruited in Mexico City, with entry estimated glomerular filtration rate (eGFR) ≥30 ml/min/1.73 m². Using data from 1,731 participants, we conducted a proportional hazards regression analysis to evaluate the association between Life’s Simple 7 (score range 0-14) and CKD progression (30% decline in eGFR from baseline).
Ideal cardiovascular health was defined as nonsmoker; body mass index ≤ 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.

(Po0493) Facilitators and Barriers to Self-Management of CKD
Sarah J. Schrauben,1 Eleanor Rivera,1 Sandra Amaral,2,1 Laura M. Dember,1 Harold I. Feldman,1 Frances K. Barg,1 1University of Pennsylvania, Philadelphia, PA, 2The Children’s Hospital of Philadelphia, Philadelphia, PA.

Background: Self-management is integral for the prevention and management of chronic kidney disease (CKD). Despite low adherence to self-management behaviors, few studies provide insight into barriers and facilitators of self-management from the perspective of patients. Methods: Semi-structured interviews were conducted with 30 participants who were purposively recruited for representation by CKD stage (3 or 4), age (≥65, 65 yrs), race (white, non-white), and sex. Interviews focused on patient experiences with CKD and efforts to follow treatment recommendations. They were recorded, transcribed, and entered into NVivo 12.0 for coding and analysis. Transcripts were coded inductively and analyzed thematically.

Results: We identified three key phases of CKD self-management behavior: prioritization, participation, and maintenance. Facilitators and barriers were organized according to these phases. Participants needed to prioritize the behavior to consider engagement, which was favorably influenced by optimism, stress management, and effective patient-provider communication. Prioritization was impeded by fatalism and competing priorities. One of the most widely reported impediments to behavior was presence of comorbid conditions that caused treatment burden and adverse symptoms. Notable facilitators of behavior performance included the presence of motivating factors, self-efficacy, social support, low cost, and convenience. For maintenance, participants’ ability to integrate and sustain behaviors in their lives was influenced by the aforementioned behavior performance factors, but also by behavior-specific factors, such as pets and physical therapy (for physical activity) and pharmacy assistance (for medication adherence). Key elements of effective maintenance included the use of memory aids, goal-setting, self-monitoring, and proactive preparation.

Conclusion: Individuals who adhered to CKD self-management behaviors viewed them as a priority, and developed strategies that fit their lifestyle to allow for behavior performance and maintenance. To increase self-management behavior prioritization, performance, and maintenance, we need to assess patients’ attitudes and beliefs, improve patient-provider communication, help patients overcome barriers such as high costs and conflicting treatment regimens, and leverage facilitators such as memory aids and goal-setting.

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 vasopressors. Results were stratified by CKD stage.

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 (1.01, 1.49), stage 4- 1.99 (1.72, 2.30)]. Hypertension and non-Hispanic 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.1 Multi-adjusted model for baseline characteristics

<table>
<thead>
<tr>
<th>Stage</th>
<th>Mean (SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 3a</td>
<td>12.7% (11.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>Stage 3b</td>
<td>21.2% (15.8)</td>
<td></td>
</tr>
<tr>
<td>Stage 4</td>
<td>35.6% (21.6)</td>
<td></td>
</tr>
</tbody>
</table>

1 p<0.001

Table 1. Usual Source of Care and Clinical Outcomes in Adults with CKD: Findings from the Chronic Renal Insufficiency Cohort (CRIC) Study

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 Thilda C. Tan,1 Jiang He,4 Raquel J. Green,1 Matthew R. Weir,1 Sarah J. Schrauben,1 Mildra S. Saunders,2 Ana C. Ricardo,1 James P. Lash,1 University of Illinois at Chicago, Chicago, IL; 2University of Pennsylvania, Philadelphia, PA; 3Kaiser Permanente, Northern California, Oakland, CA; 4Tulane School of Public Health and Tropical Medicine, New Orleans, LA; 5Johns Hopkins Medicine, Baltimore, MD; 6University of Maryland School of Medicine, Baltimore, MD; 7University 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 1% 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

Association between usual source of care (ER/urgent care vs. clinic/doctor’s office) and outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Observed</th>
<th>Expected</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incident ESRD</td>
<td>0.86 (0.40-1.82)</td>
<td>0.86</td>
<td>1.0</td>
</tr>
<tr>
<td>Cardiovascular Events</td>
<td>0.79 (0.47-1.35)</td>
<td>0.79</td>
<td>1.0</td>
</tr>
<tr>
<td>All-Cause Death</td>
<td>1.83 (1.39-2.37)</td>
<td>1.83</td>
<td>1.0</td>
</tr>
</tbody>
</table>

*p<0.05; Results adjusted for clinical center, age, sex, race, education, income, smoking status, physical activity, HbA1c<7%, statin, aspirin, ACEI/ARB, eGFR, urine protein.

PO0498

Healthcare Resource Utilization and Costs of CKD According to the 2012 KDIGO CKD Classification: A Report from the DISCOVER CKD Retrospective Cohort

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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 ≥1 UACR measure and ≥2 eGFR measures of 0-75/ml/min/1.73m² 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, 6,270 patients met the KDGO 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 KDGO 2012 defined population (Rate 100-PY[95%CI] 59.0[53.7-64.8] vs 26.4[25.5-27.3]) and mean length of stay 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

Figure 1. Summary of annual healthcare resource use and cost (US$)

PO0499


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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. Billing 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<50, 30–199, 200–5,000mg/g). The FR (CDR=200-5,000mg/g) population was categorized with significantly higher annualized per-patient healthcare costs, $39,222/yr (UACR 0–50mg/g) to $63,236/yr (UACR 200-5,000mg/g).
200-5000mg/g) vs. $19,547/yr (UACR <30mg/g). Persons in the highest UACR category were almost three times more likely to have a hospital admission compared to the lowest (rates 0.55/year vs. 0.20/year, respectively; see Table 1).

Conclusions: This analysis of a contemporary US healthcare system demonstrated that there exists a high disease burden in the DAPA-CKD-like population as seen by the substantial increase in healthcare resource utilization and costs compared to other cohorts of patients with a lower UACR. These results highlight the need for innovative therapies to improve patient outcomes in this high risk population.

Funding: Commercial Support - AstraZeneca

Table 1. Summary of healthcare resource utilization and costs by UACR category

<table>
<thead>
<tr>
<th>Category</th>
<th>UACR &lt;30mg/g</th>
<th>UACR 30-99mg/g</th>
<th>UACR 100-299mg/g</th>
<th>UACR &gt;300mg/g</th>
</tr>
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<tbody>
<tr>
<td>Average 12 mo spend</td>
<td>$15,547</td>
<td>$20,892</td>
<td>$28,022</td>
<td>$39,423</td>
</tr>
</tbody>
</table>

PO0500

Understanding Patterns of Medical Spend Informs Design of Upstream Intervention in CKD

Title: Srinivas. 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 no CKD diagnosed or evident by lab values vs. 19.1 percent of those with unrecognized Stage 3b to 4 CKD (n=31,435) vs. 18 percent among those with recognized Stage 3-5 CKD or ESRD (n=52,242; P < 0.001). No statistical difference was observed between wellness rates and stage 1 and stage 2 unrecognized CKD cohorts. Of annual spend in 2019, those with recognized CKD/ESRD, incurred 61.9 percent of spend in the inpatient setting vs. 25 percent among those with unrecognized CKD. The number of chronic condition increased from an average of 3.5 among those with Stage 3-5 unrecognized CKD to 10 among those with recognized CKD/ESRD. Average 12 mo spend was $ 6500 among those with unrecognized CKD stage 3b-5 and $ 22,978 among those with recognized CKD/ESRD (p<0.0001). A diagnosis of CHF was recorded in 13.1 %, 20.5 %, and 24.3 % of those with undiagnosed CKD stage 3a-5 vs. 46.9 percent of those with diagnosed CKD/ESRD (Chi square for trend <0.001).

Conclusions: CKD is often unrecognized clinically despite eGFR support of its existence in the medical record. Decompensation of unrecognized heart disease likely contributes to increased inpatient utilization and costs with clinical recognition of CKD. Wellness measures are unfortunately deficient in this population and systems of care triggered by eGFR values could inform care upstream of CKD decompensation to capture value.

Funding: Clinical Revenue Support

PO0501

Abstract Withdrawn

PO0502

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 Pecoiots-Filho, 4,5 Glen James, 1 Hiddo J. L. Heerspink, 1 Stephen Nolan, 1 Lam S. Carolyn, 6,7 Hungta (Tony) Chen, 1 Eiichiro Kanda, 1 Alyshah Abdul Sultan, 6 Naoki Kashiura, 6 Mikhail Kosiborod, 8,9 David C. Wheeler, 9,10 Carol A. Pollock, 10,11 AstraZeneca, Cambridge, United Kingdom; 1 Karolinska Institutet, Stockholm, Sweden; 2 AstraZeneca, Gothenburg, MD; 3 Arbor Research Collaborative for Health, Ann Arbor, MI; 4 Pontificia Universidade Catolica do Parana Escola de Medicina Campus Londrina, Londrina, Brazil; 5 Rijksuniversiteit Groningen, Groningen, Netherlands; 6 National Heart Centre Singapore, Singapore, Singapore; 7 Duke-NUS Medical School, Singapore, Singapore; 8 Kawasaki Ika Daigaku, Kurashiki, Japan; 9 Saint Luke’s Mid America Heart Institute, Kansas City, MO; 10 University College London, London, United Kingdom; 11 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 at least 2 years of follow-up, 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 61%, 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

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

Underline represents presenting author.
PO0503

Treatment Pathways of Patients with CKD: A Report from the DIS-COVER CKD Retrospective Cohort

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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 to at least 500 CKD patients including: RAAS, statins, diuretics and anti-hypertensives. We also described median time to first line therapy initiation.

Results: Preliminary, 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 data 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 their time on therapy.

Conclusions: Patients with CKD have high therapy burden, with varying time to initiation of therapies.

PO0505

Albuminuria Testing and Prevalence and Incidence of Elevated Albuminuria in the DISCOVER CKD Retrospective Cohort

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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 twice) was 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 48.9% (IQ: 32.5-58.3%) and 4.3% (IQ: 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% (IQ: 28.4-37.0%) and 21.9% (IQ: 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 median incidence of ACR≥30 mg/g at 5 years was 23.3% (IQ: 18.6-28.5%) and 21.7% (IQ: 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, IQ: 0.600-0.655, validation cohorts 0.635, IQ: 0.619-0.641) and in HTN only (median C statistic: development cohorts 0.649, IQ: 0.621-0.695, validation cohorts 0.665, IQ: 0.638-0.671).

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 focused efforts based on risk stratification may not improve clinical utility. 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

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Background: Urine albumin and serum creatinine (Scr) help define chronic kidney disease (CKD). Despite the fact that urine albumin and Scr are multiplicatively associated 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.

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

Underline represents presenting author.
Dipstick Urinalysis Can Identify Patients with Early CKD Who Lack a Quantified Proteinuria Measurement
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University of Texas Southwestern Medical Center at Dallas, Dallas, TX.

Background: Urine protein-to-creatinine ratio (UPCR)>0.15 g/g or albumin-to-creatinine ratio (UACR)>30 mg/g is the gold standard for identifying patients with stages 1-2 CKD with eGFR>60 mL/min/1.73m^2, but are not routinely obtained. Dipstick urinalysis semi-quantitative protein (DSP) is widely available and commonly measured.

Methods: To develop a pragmatic EHR tool to identify patients with stages 1-2 CKD, we investigated diagnostic utility of various DSP cutoffs (negative/trace, 30, 100, 300, or >500 mg/dl) against gold-standard proteinuria (UPCR>0.15 g/g or UACR>30 mg/g) using logistic regression. We also investigated whether addition of SG improved the diagnostic utility of DSP by comparing areas under the receiver-operating characteristic curves (AUC) for DSP with and without addition of SG. DSP was obtained from the EHR in 3,897 individuals with UPCR or UACR measured on the same date. A development model was created in a random sample of 2,728 (70%) using a bootstrap method and validated in the remaining 1,169 individuals.

Results: Mean age was 57±16.9 years, 51.7% were female, 25.6% Black, and 42.8% had an eGFR>60 mL/min/1.73m^2. Gold-standard proteinuria was present in 1,775 (45.5%). DSP cutoff=30 had specificity 81.1 (95% CI 79.0, 83.1), +LR=2.43 (95% CI 2.15, 2.75), -LR=0.67 (95% CI 0.63, 0.71). The combination of DSP and SG, taken continuously, performed better than DSP alone (Figure A). When including SG, a DSP cutoff of 30 had the best diagnostic accuracy vs. other cutoffs (Figure B). In the validation cohort, addition of SG to DSP also yielded a higher AUC than DSP alone, P=0.03. For DSP p>30 as a screening test, an SG of at least a 1.025 is needed. A more dilute urine, with a SG of 1.020, would be allowed if DSP p>100. A DSP cutoff of 30 had an AUC of 0.652 (0.621, 0.684), P<0.001, vs. a cutoff of 300 or 500. Using DSPs>30 identified an additional 141 individuals with CKD than use of eGFR≥60 alone.

Conclusions: Combining DSP and SG from a dipstick urinalysis can identify patients with early CKD who do not have a measured UPCR or UACR.

Funding: NIDDK Support

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

Underline represents presenting author.
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
Luis F. Goncalves, Adriana Fernandes, Mario R. Raimundo. Hospital Beatriz Angelo, Loures, Portugal.

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 65.5 mg/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 1.03 - 3.62) 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 Indicators vs. Risk-Based Triage for Nephropathy 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 nephropathy 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 nephropathy 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% [9.9-8.6%] in the referred group, compared to 1.3% [0.3-3.9%] in the unreferral 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, subspecialty 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 nephropathy 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 ≥18 years, with eGFR <60 mL/min/1.73 m² and concurrently measured serum albumin/creatinine ratio, who had an ambulatory encounter with a nephrologist from 1/1/2017-12/31/2018 using the Optum Labs® 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 health care 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.

206
PO0515
Classification of Cause of CKD Using ICD-9 and ICD-10 Codes
Jennifer Chen,1 Matthew F. Blum,1 Aditya L. Surapaneni,2 Yingying Sang,2 Alex R. Chang,2 Josef Coresh,2 Morgan Grams,1,2 Johns Hopkins University School of Medicine, Baltimore, MD; 3Johns Hopkins School of Public Health, Baltimore, MD; 4Geisinger Health, Danville, PA.

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 International 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 (13.6%), obstructive nephropathy (5.2%), and nephritic syndrome (4.9%). 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 determined by our classification algorithm. The most prevalent etiologies of CKD in patients with available ICD codes using electronic medical record data; however, validation suggests varying degrees of accuracy across different CKD etiologies.

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.

PO0516
Epidemiology of Patients with High-Risk CKD: A Demographic Evaluation of Patients Who Had Indications for SGLT2 Inhibitors and GLP-1
Huiwen Chen,1,2 Melanie R. Weltman,1 Manqi Cai,1 Jonathan Yabes,1 Thomas D. Nolin,1 Manisha Jhamb,1,2 Khaled Abdel-Kader.1 University of Pittsburgh, Pittsburgh, PA; 2University of Pittsburgh Medical Center, Pittsburgh, PA; 3Vanderbilt University Medical Center, Nashville, TN.

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, many patients with high risk CKD and indications for SGLT2is and GLP-1 are not on the 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 population health management approach to improve CKD care. The studied populations include patients with high risk CKD and indications for SGLT2is and GLP-1, who were not on the 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.

Results: Baseline demographics such as median age, gender, race, and BMI were compared. Comorbidities, the presence of endocrinology referral, laboratory values and whether or not patients have been on angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) were also compared. Clinicians’ characteristics were compared as well. Patients who had the indications for SGLT2is but were not on them were more likely to be older in age, had low GFR (around low 30 ml/min) and low hemoglobin A1C. Patients who had the indications for GLP-1 but not on them were likely to have high A1C and likely to have already been on insulin.

Conclusions: Identification of features of high risk patients who had clinical indications for SGLT2is and GLP-1 but were not on the medication would be helpful in finding better ways to provide nephrology recommendations regarding SGLT2is and GLP-1.

Funding: NIDDK Support

PO0517
Disparities in CKD Progression by Medicare Advantage Enrollees Clarissa J. Diamantidis,1 Lindsay Zepel,1 Virginia Wang,2 Valerie A. Smith,2 Sarah H. Scholle,4 Loida A. Tamayo,1 Matthew L. Maciejewski,1,2 Duke University School of Medicine, Durham, NC; 3HSRD, Durham VA HCS, Durham, NC; 4OptumLabs Visiting Fellow, Minnetonka, MN; National Committee for Quality Assurance, Washington, DC; Centers for Medicare and Medicaid Services, Baltimore, MD.

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, 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: 18.5-18.7) lower than levels 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.

Funding: Other U.S. Government Support

PO0518
Impact of the Race Multiplier in the Estimated Glomerular Filtration Rate Equation on Care Delivery Among African-American CKD Patients
Saliman Ahmad, Mallika L. Mendu. Brigham and Women's Hospital, Boston, MA.

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 reclassified 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.

Funding: Private Foundation Support

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

Underline represents presenting author.
PO0519
Prevalence of Diabetes, Hypertension, Anemia, and Hyperkalemia as Frequent Comorbidities in Patients with CKD Regardless of their KDIGO Staging
L. M. Perez-Navarro,1 Samantha Escoza Valdivia, Alberto Sigfrido Benitez Rentería,2 Rafael Valdez-Ortiz,1 Hospital General de Mexico De Eduardo Liceaga, Ciudad de Mexico, Mexico; 2AstraZeneca, Ciudad de Mexico, Mexico.

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% (693); 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 glycemia < 100 mg/dL; 53% with triglyceride >150 mg/dL and 29% with 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

PO0520
Cystatin C Use in Clinical Practice
Jennifer Torres,1 Jennifer L. Ennis,2 Rita L. McGill,1 ‘University of Chicago, Chicago, IL’; 2Laboratory Corporation of America, Burlington, NC; 3DaVita Inc, Denver, CO.

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 patients 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 provided, and relationships between serum cystatin C and creatinine levels were examined with correlation analysis and linear regression.

Results: We examined 87,803 cystatin C levels obtained among 55,360 patients, 51% (907) were women, the mean age was 50.2±11.5 years. 12% were on renal replacement therapy, 5% hemodialysis and 1% peritoneal dialysis. 87% (487) 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% (693); 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 glycemia < 100 mg/dL; 53% with triglyceride >150 mg/dL and 29% with 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

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 at 0.5, 1, 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. Medial levels of eGFR slopes were 1.5, 1, 0.5, 2 and 3yr 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 2yr. 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). 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
Alyshah Abdul Sultan,1 Ping Sun,1 Katarina Hedman,2 Xia Wang,3 Mark T. Houser,1 Dustin J. Little,2 Glen James.1 1AstraZeneca, Cambridge, United Kingdom; 2AstraZeneca, Gothenburg, Sweden; 3AstraZeneca, Gaithersburg, MD.

Background: Epidemiology 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 3, 4, 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 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 events</th>
<th>NDD CKD 3 Rate</th>
<th>NDD CKD 4 Rate</th>
<th>DD Rate</th>
</tr>
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<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>Pneumonia</td>
<td>7.8</td>
<td>12.2</td>
<td>15.2</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>U2I</td>
<td>7.1</td>
<td>12.6</td>
<td>9.8</td>
</tr>
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</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 SØrstadius,2 Stephen Nolan,2 Juan Jose Garcia Sanchez,2 HealthLumen, London, United Kingdom; 3AstraZeneca AB, Soderatle, Sweden; 4AstraZeneca 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 estimated 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
Alvash Abdul Sultan,1 Kirsty Rhodes,1 Michail Doulos,2 Irena Brookes-Smith,3 Joshua S. Faria,1 Jose D. Salazar,2 Glen James,1 Iain MacPhee,2 Robert J. Unwin,1 David Wright,1 Mishal Patel,1 Paul D. Metcalfe,1 Lutz Jermutus,1 1AstraZeneca, Cambridge, United Kingdom; 2AstraZeneca, Gothenburg, Sweden.

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 3-year observation period post-index date (date of 2nd eGFR measurement) were extracted. Patients were clustered based on 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: Preliminarily, 407,108 patients with 1.8 million eGFR measurements (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 progressing patients were 3 times more likely (Hazard Ratio (HR)=2.95; 95%CI:2.75-3.10) 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
PO0526

Using Autoencoders for Imputing Missing Data in eGFR Decline Trajectories of Patients with CKD

Davina J. Zamanzadeh,1 Panayiotis Petousis, Tyler A. Davis,1 Anders O. Garlid,1 Xiaoyan Wang,1 Keith C. Norris,1 Obidiugwu Duru,1 Katherine R. Tuttle,1 Alex Bui,1 Susanne B. Nicholas.1 CURE-CKD Registry Study Team 1University of California Los Angeles, Los Angeles, CA; 2Providence 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 removing 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. 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>
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</thead>
<tbody>
<tr>
<td>MCAR</td>
<td>0.80/1.1</td>
<td>0.65/1.1</td>
</tr>
<tr>
<td>MAR</td>
<td>0.83/0.6</td>
<td>0.67/1.1</td>
</tr>
<tr>
<td>CART</td>
<td>0.83/0.6</td>
<td>0.75/1.4</td>
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<tr>
<td>CURE</td>
<td>0.83/0.6</td>
<td>0.67/1.1</td>
</tr>
<tr>
<td>KB</td>
<td>0.83/0.6</td>
<td>0.75/1.4</td>
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</table>

PO0527

Machine Learning Prediction of ESKD and Death in CKD Patients: Electronic Medical Record-Based Cohort Study

Eijihiro Kando,1 Atsuyaiki Tokuyama, Seiji Itano, Hajime Nagasu, Naruki Kashihara. Kawasaki Medical School, Kurashiki, Japan.

Background: Chronic kidney disease (CKD) is a risk factor for end-stage kidney disease (ESKD) and death. An accurate prediction of these 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)

Results: The RF 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 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).

Conclusions: 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.

Funding: Other NIH Support - NIMHD

PO0528

Predicting Rapid eGFR Decline Using Electronic Health Record (EHR) Data Despite High Missingness in the CURE-CKD Registry

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Background: Patients with rapid eGFR decline tend to progress to kidney failure. Automated tools can identify individuals at risk of severe renal function 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 identifies patients 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 (Hb), and the diagnosis of hypertension, diabetes, and CKD. We selected patients with CKD (N=93,567) and at-risk for CKD (N=913,289) with eGFR > 140 mmol/L (72%), age 45-66 years (56%), DM (52%), and AIC > 8 (50%).

Conclusions: 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.

Funding: Other NIH Support - NIMHD

PO0629

A Machine Learning-Based Prediction Model for Trajectory of GFR in CKD Patients with Rapid Decline of GFR by Using a Big Database

Dajo Inaguma,1 Akimitsu Kitagawa,1 Ryosuke Yanagiya,1 Akira Koseki,2 Tomoyuki Fujimori,1 Michiharu Kudo,1 Shingo Fukuma,1 Naotake Tsuibo,1 Yukio Yuzawa,1 Fujita Health University School of Medicine, Department of Nephrology, Toyoake, Japan; 2IBM Research, Tokyo, Japan; 3Fujita Health University Bantane Hospital, Department of Nephrology, Nagoya, Japan; 4Fujita Health University, Division of Medical Information System, Toyoake, Japan; 5Kyo 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 0.95^days/deay parameter). The random forest algorithm and python code from 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

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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 deeply-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 promises 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.
CKD Health Services Research

PO0533

Mortality Following New Onset of CKD Among Veterans by Comorbid Conditions: Results from a US Large Incident CKD Population

Nikla Rios Burrows,1 Devasmita Choudhury,2 Wei Yu,1 Meda E. Pavkov,1 Robert Nee,2 Alfred K. Cheung,1,3 Keith C. Norris,4 Guofen Yan,5 Centers for Disease Control and Prevention, Atlanta, GA; 2 Salem VA Medical Center, Salem, VA; 3 University of Virginia, Charlottesville, VA; 4 Walter Reed National Military Medical Center, Bethesda, MD; 5 University of Utah Health, Salt Lake City, UT; 6 University of California Los Angeles David Geffen School of Medicine, Los Angeles, CA; 7 VA Salt Lake City Health Care System, Salt Lake City, UT.

Background: Data on mortality rates after CKD onset are scarce. Using a recently constructed national incident CKD cohort, we examined mortality rates following new-onset CKD for various subgroups with or without comorbidities.

Methods: We identified 1,074,238 individuals with new-onset CKD between 2002 and 2017 in the US Veterans Health Administration (VHA). CKD onset was defined as the first time when estimated GFR (eGFR, CKD-EPI equation) decreased to <60 mL/min/1.73 m² for >3 months. Individuals excluded were those in the VHA for <2 years prior to first eGFR <60, or had CKD stage 4 or 5, or end-stage kidney disease 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. All individuals were followed for death status from onset through June 30, 2018.

Results: CKD patients with and without comorbidities had similar mean eGFRs at onset (51 mL/min/1.73m²). Most (97%) were male and mean age at onset was 72 years. Hypertension (HTN) (90%), cardiovascular disease (CVD) (75%), and diabetes (46%) were the three most common comorbidities. For each comorbidity, mortality rate was substantially greater among those with compared to those without (Table). After adjustment for age, sex, race, ethnicity, and onset eGFR, mortality risks remained substantially greater among those with than those without the comorbidities, ranging from 12% greater with HTN to 100% greater with liver disease.

Conclusions: At time of CKD onset, mortality risk is greater in veterans with the presence of comorbidities. Intervention trials to examine the management and treatment of comorbidities on mortality in an incident CKD population might be warranted.

Funding: NIDDK Support, Other U.S. Government Support
PO0535

Impact of Variability in Estimated Glomerular Filtration Rate on Major Clinical Outcomes: A Nationwide Population-Based Study

Sooin Lee,1 Yeonhee Lee,1 Schoon Park,1 Yaerim Kim,2 Min woo Kang,1 Semin Cho,1 Yong Chul Kim,3 Kwon Wook Joo,1 Chun Soo Lim,2 Yong Su Kim,2 Dong Ki Kim.1 Seoul 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 ≥3 times between 2012 and 2016 were considered. Those with eGFR under 60 mL/min/m² were excluded. The fluctuation of eGFR was represented with variability independent of the mean (VIM) value, 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, 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 (NDD) CKD

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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 values 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 y increase)</td>
</tr>
<tr>
<td>CCI per 2-point increase</td>
</tr>
<tr>
<td>Hemoglobin per 2.5 g/dL increase</td>
</tr>
<tr>
<td>SQ not scaled (expressed normal)</td>
</tr>
<tr>
<td>Not surprised; neutral</td>
</tr>
<tr>
<td>Surprised; increases</td>
</tr>
<tr>
<td>Very surprised; increases</td>
</tr>
</tbody>
</table>

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Underline represents presenting author.
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 31, 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+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

<table>
<thead>
<tr>
<th>Hazard Ratio (95% CI)</th>
<th>All cause death</th>
<th>Cardiovascular death</th>
<th>Any hospitalization</th>
<th>CV death</th>
<th>CV Events</th>
<th>Renal Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR category with number (percentile)</td>
<td>0&lt;60 (N=75,162)</td>
<td>60-74.9 (N=133,323)</td>
<td>75-89.9 (N=107,563)</td>
<td>90-102 (N=27,062)</td>
<td>102+ (N=5,762)</td>
<td></td>
</tr>
<tr>
<td>0.42 (95% CI: 0.27-0.67)</td>
<td>0.55 (0.39-0.78)</td>
<td>0.41 (0.30-0.54)</td>
<td>0.50 (0.34-0.70)</td>
<td>0.42 (0.28-0.63)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* 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 CKDops
Manfred Hecking,1 Charlotte Tu,2 Jarcy Zee,2 Brian Bieber,2 Sebastian Hödlmoser,3 Benedicte Stengel,4 Helmut Reichel,5 Kunihiro Yamagata,6 Ricardo Sesso,7 Friedrich K. Port,2 Bruce M. Robinson,2 Roberto Pecoto-Filho.8 On behalf of CKDops and CKD REIN investigators 1Medical University of Innsbruck, Division of Internal Medicine, Innsbruck, Austria; 2Arbor Research Collaborative for Health, Ann Arbor, MI; 3Medical University of Vienna, Department of Epidemiology, Vienna, Austria; 4CESP, Insern U104, Kidney and Heart Team, Villejuif, France; 5Nephrologisches Zentrum Villingen-Schwenningen, Villingen-Schwenningen, Germany; 6University of Tsukuba, Ibaraki, Japan; 7Escola Paulista De Medicina, Unifesp, Sao Paulo, Brazil.

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 (CKDops) participants.

Methods: Using data of 5682 CKDops 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 CKDops 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 (5.2 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.

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Risk of Bleeding after Renal Biopsy: By Comorbidity

<table>
<thead>
<tr>
<th>Chronic Kidney Disease</th>
<th>Relative Risk</th>
<th>95% CI Lower Limit</th>
<th>95% CI Upper Limit</th>
<th>P-value</th>
<th>Standard Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>1.00</td>
<td>0.89</td>
<td>1.03</td>
<td>0.22</td>
<td>0.06</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>1.607</td>
<td>1.400</td>
<td>1.756</td>
<td>&lt;0.001</td>
<td>0.068</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.000</td>
<td>0.980</td>
<td>1.020</td>
<td>0.085</td>
<td>0.012</td>
</tr>
<tr>
<td>Pericardial Effusion</td>
<td>1.060</td>
<td>1.040</td>
<td>1.080</td>
<td>&lt;0.001</td>
<td>0.014</td>
</tr>
<tr>
<td>Renal Vascular Disease</td>
<td>1.055</td>
<td>0.870</td>
<td>1.269</td>
<td>0.723</td>
<td>0.012</td>
</tr>
<tr>
<td>Female Gender</td>
<td>1.000</td>
<td>0.980</td>
<td>1.020</td>
<td>0.085</td>
<td>0.012</td>
</tr>
<tr>
<td>Weight Loss</td>
<td>1.000</td>
<td>0.980</td>
<td>1.020</td>
<td>0.085</td>
<td>0.012</td>
</tr>
</tbody>
</table>

| Age                     | 1.000         | 0.980              | 1.020              | 0.085   | 0.012          |

Table1. PO0542

Evaluation of Thromboelastometry and Multiple Electrode Aggregometry in ESRD

Alvina Abdelmaquid,1,2 Lara N. Roberts,3 Jennifer R. Joslin,4 Kiran H. Parmar,1 Kate Bramham,1,3 ’King’s Kidney Care, King’s College Hospital, London, United Kingdom; 2Alexandra University, Medical Research Institute, Alexandria, Egypt; 3King’s Thrombosis Centre, Department of Haematological Medicine, King’s College Hospital NHS Foundation Trust, London, United Kingdom; 4Thrombosis and Haemostasis Centre, Guy’s and St Thomas’ NHS Foundation Trust, London, United Kingdom; 5Department of Women and Children’s Health, King’s College London, London, United Kingdom.

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 antithrombin (TAT), alpha-2 antiplasmin, d-dimer and Interacellular 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).

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))

PO0543

During P2Y_12 Antiplatelet Therapy, Treatment of Anemia Was More Frequent Among Peripheral Artery Disease Patients with Lower eGFR: The EUCLID Trial

Judith Hsia,1,3 Sarah T. Kavanagh,1 Charles W. Hoptie,2 Marc P. Bonaca,1,3 William R. Hiatt,1,3 CPC Clinical Research, Aurora, CO; 2Dartmouth College, Hanover, NH; 3University of Colorado School of Medicine, Aurora, CO.

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 vs ≥60 mL/min/1.73m^2 (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.
**PO0546**

Magnetic Resonance Imaging-Based Renal Function Estimation Using a Machine Learning Approach

Daichi Fukaya,1 Tsutomu Inoue,1 Eito Kozawa,2 Masahiro Ishikawa,3 Yusuke Watanabe,2 Hiroaki Arano,3 Naoki Kobayashi,2 Mamoru Niitsu,2 Hirokazu Okada.1 Department of Nephrology, Faculty of Medicine, Saitama Medical University, Iruma-gun, Japan; 2School of Clinical Engineering, Faculty of Health and Medical Care, Saitama Medical University, Hidaka-shi, Japan; 3Division of Dialysis Center and Department of Nephrology, Saitama Medical University International Medical Center, Hidaka-shi, Japan.

**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 hemodynamic 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 from 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 F1-score of the confusion 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, 0.86, 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 model 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 hypertension, 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 selective serotonin reuptake inhibitors (SSRIs) in patients with chronic kidney disease.

**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), Opioid oral morphine milligrams equivalent (MME)) & QOL (LASA-6, PHQ-9 & SF-8) were obtained. The Wilcoxon test was used. ERA using an open irrigation ablation catheter was performed in a spiral manner distal to proximal 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 redos) in 20 patients, with female:males, 14:6; median age 40y. 12 patients (60%) had Loin 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 8.5m (n=12/20;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).

**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**

**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. Brief pain inventory (BPI), opioid oral morphine milligrams equivalent (MME) & QOL (LASA-6, PHQ-9 & SF-8) were obtained. The Wilcoxon test was used. ERA using an open irrigated ablation catheter was performed in a spiral manner distal to proximal 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 redos) in 20 patients, with female:male; 14:6; median age 40y. 12 patients (60%) had Loin 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 8.5m (n=12/20;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).

**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

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**Background:** Kidney function is globally evaluated by estimated glomerular filtration ratio (eGFR) based on serum creatinine (Crea). Since Crea is influenced by body muscle mass, there is serious concern of overestimation of eGFR among elderly people with higher muscle volume due to frailty. In this study, eGFR based on Crea (eGFRc) and Crea×(fat mass of the Crea×fat mass of the body) were analyzed in association with psoas muscle mass index (PMI) by CT image among CKD patients whose kidney function was accurately evaluated by measured GFR (eGFRc) computed from inulin clearance (Cin).

**Methods:** Study design: Single-center, cross-sectional retrospective study. Study subjects were consecutive 184 CKD patients (123 males) at Nagoya university hospital whose Crea and abdominal CT were examined within 1 year between 2009 and 2013. New eGFR formula based on Crea and PMI (eGFRc×PMI) were developed in 122 patients and validated in 62 patients, which were randomly determined to each cohort. 20%
accuracy for Cini was analyzed by eGFRcreat and eGFRcys calculated by eGFR formulae for Japanese. The performance of eGFRcreat-PMI was assessed by means of bias (eGFRcys/mGFR), accuracy (percentage of estimates within 20% of mGFR), root mean square error, and correlation coefficient. In PMI tertile subgroups and GFR(Cini) subgroups (<30, 30-60, >60%), the performance of each formulae was assessed.

Results: Patients’ characteristics (n=184, mean±SD) or median[Q1,Q3] were: age: 62 [50, 70], eGFRcreat: 58.5 (25.5), eGFRcys: 59.4 (25.9), Cini: 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 logCys in univariate analyses, and with age, gender and log-BMI in multivariate analysis. New eGFR formula (eGFRcreat-PMI) was well correlated with Cini. 20% accuracies for Cini was the highest in eGFRcreat-PMI (74.5%), compared to eGFRcreats (67.9%) and eGFRcreat (68.5%), which was more prominent among low PMI tertile group (77.4% in eGFRcreat-PMI, 67.7% in eGFRcys, and 71.0% in eGFRcreat) and high PMI tertile group (73.8% in eGFRcreat-PMI, 59.0% in eGFRcys, and 67.7% in eGFRcreat).

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.

PO0550
Incidence and Predictors of Non-Alcoholic Fatty Liver Disease in CKD
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Background: The prevalence of non-alcoholic fatty liver disease (NAFLD) is increasing due to 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 (eGFRcreat <60 ml/min/1.73 m2) a median follow-up time of 4.7 years 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 in 2005, 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

PO0551
Alterations of Gray Matter Volumes and Connectivity in Patients with CKD Compared to Healthy Subjects
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Background: Our previous study demonstrated that patients in End stage renal disease had decreased structural and functional brain connectivity, and there was significant association between brain connectivity and cognitive function. The aim of this study was to evaluate the alterations of structural and functional connectivity using graph theoretical analysis in the neurologically asymptomatic patients with relatively early stage chronic kidney disease (CKD).

Methods: We prospectively enrolled neurologically asymptomatic 20 patients with CKD stage 3 and 20 healthy controls, and all of the subjects underwent diffusion tensor imaging (DTI) and resting state functional MRI (rs-fMRI). Using data from the structural and functional connectivity matrix built on DTI and rs-fMRI, we calculated network measures, including global efficiency, local efficiency, mean clustering coefficient, characteristic path length, and small-worldness index, and investigated the differences between patients with CKD and healthy controls.

Results: The patients with CKD had altered global structural connectivity and preserved functional connectivity compared to healthy controls. All of the measures of global structural connectivity were significantly different between the patients with CKD and healthy controls. However, all of the measures of global functional connectivity in the CKD patients were not different from those in healthy participants. In the CKD patients, the functional betweenness centrality of the right insular cortex, right occipital pole, and right thalamus was significantly different from that in healthy subjects. The structural betweenness centrality of the left hippocampus, right posterior cingulum was significantly different from that in healthy subjects.

Conclusions: There were significant alterations of global structural connectivity between patients with CKD and control. However, functional connectivity of brain network was preserved in contrast to ESRD patients.

PO0552
CKD and Metabolic Risk Factors: A Cross-Sectional Study Based on 398,120 Adults in China
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Background: Chronic kidney disease (CKD) has become a worldwide health problem. The prevalence of CKD varied within countries by different socio-demographic characteristics and economic status. Elderly people are particularly susceptible to kidney damage from age-related decline in glomerular filtration and chronic disease states, such as diabetes mellitus (DM) and hypertension (HTN). It is necessary to understand the epidemiological features and the association risk factors of CKD in adults, especially in these elderly populations.

Methods: We did a cross-sectional survey based on the records of universal health examinations of the residents in Binhai county of China in 2018. A total of 398,120 participants aged a 18 years in this study had underwent blood test, body measurements and routine urinalysis. Those 51.6% of subjects who aged ≥65 years (n=37,533) were randomly selected to complete the routine urinalysis. Chronic renal insufficient (CRI) was defined by eGFR < 60 ml/min/1.73 m2(CKD-EPI), while CKD was defined by CRI or presence of proteinuria. We analyzed the epidemiological features and the association between CKD and relevant covariates by logistic regression models in the general and elderly population.

Results: The age- and gender- standardized prevalence of CRI was estimated to be 1.10% (95% CI, 1.07%-1.13%) in Chinese adult population. It was 0.86% among men (95% CI, 0.82%-0.90%) and 1.34% among women (95% CI, 1.29%-1.39%). Female, aging, central obesity, elevated triglycerides, systolic blood pressure, fasting blood glucose (FBG) and heart rate were independent risk factors for CRI in the general adults. Rates of CRI increased significantly by age, especially when people aged ≥60 years. Furthermore, the prevalence of CKD was 17.7% (95% CI, 17.5%-18.1%) in the elderly. Aging, HTN, elevated triglyceride and FBG were still found to be independent risk factors for CKD in this subgroup. Elevated FBG had the strongest correlation with CKD, gender was no longer association with CKD in the elderly.

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PO0553
Are There Any Further Modalities for Prediction of Subclinical Volume Overload in Advanced Stages of CKD?
Ahmed H. Bakri, Hazem Mansour. Ain Shams University Faculty of Medicine, Cairo, Egypt.

Background: Subclinical volume overload is commonly seen in our daily practice which represents a debatable issue. These patients respond favorably to diuretics despite lacking clinical signs of volume overload. Therefore a proper assessment of the volume status in Chronic Kidney Disease (CKD) patients leads to a better control of their medical condition and prevents further deterioration of their clinical situation into the well-known sequelae. Although many tools were used to detect volume overload in such patients as biomarkers, ultrasonography, bio-impedance, echo, and blood viscosity, many non-specific results were due to presence of concomitant comorbidities. The use of Bio Impedance Spectroscopy (BIS) is a recent tool increasingly used due to its appealing features that make it non-invasive. BIS is an objective fluid status assessment method, which is shown superior to classical methods such as BP monitoring and weight control in many studies. Combining some of these tools may improve their accuracy and specificity. Inferior vena cava collapsibility index (IVCVC) with Brain Natriuretic Peptide (BNP) can be considered for more specificity and assessment.

Methods: To assess the usage of combined IVCVC and BNP level in CKD patients to predict subclinical volume overload, 110 patients with CKD (stage 4&5) & not on dialysis and having normal LV systolic function were included with exclusion of the following: 1) patients who suffered other causes of raised BNP than volume overload (i.e. anemia and heart failure). 2) Patients on diuretics. Complete history, clinical examination and basic laboratory were done for all included patients. IVCVC, BNP serum level were evaluated. By using BIS, we estimated Fluid overload (FO) and extracellular water (ECW). The patients were subdivided a FO >15% were considered as volume overloaded.

Results: Among the 110 cases, we found that 26 patients (23.6%) had subclinical hyperervolemia as diagnosed by FO/ECW ratio >15. IVCVC ≥38% had higher diagnostic
performance than BNP ≥24 pg/mL. Combining both IVCCI ≥38% and BNP ≥24pg/mL increased the specificity and negative predictive value for detection of subclinical hyperparathyroidism.

Conclusions: Combined elevated BNP level and decreased IVCCI could be more precise tools for subclinical volume overload detection in CKD patients.

PO0554
Sensitivity of Urinary N-Terminal Osteopontin-to-Creatinine Ratio in Predicting Renal Function Loss
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Background: Osteopontin (OPN) is a multifunctional protein that gets cleaved to create N-terminal OPN (ntOPN). ntOPN has been reported in urine in kidney diseases 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 years. Serum and urinary levels of the ntOPN were quantified by ELISA. Using estimated glomerular filtration rate (eGFR), UACR and urine albumin excretion (UAE) 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 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.

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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: Fenofibrates 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 fenofibrates’ 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 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 triglyceride 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.

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

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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 intravenously (IV) twice a week and cinacalcet 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 antoxidative 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 arteriolar walls, internal 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±82.4 months and one patient had no chronic kidney disease. Six patients were taking warfarin, with an average of 46 months on anticoagulation. The mean pre-diagnostic serum calcium product was 42 mg^2/dL^2 with an average of 46 months on anticoagulation. The mean pre-diagnostic serum calcium product was 42 mg^2/dL^2 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.

PO0559
Role of Adipose Tissue-Derived Mesenchymal Stem Cells in CKD: A Phase 1 Study Assessing Safety and Clinical Feasibility
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Background: Chronic kidney disease (CKD) is a most common progressive disorder associated with high mortality and huge socio-economic burden globally. We hypothesize that allogeneic adipose tissue mesenchymal stem cells (hASCs) are renotrophic and may retard CKD progression through anti-apoptotic, anti-fibrotic, and anti-inflammatory effects. In this study, we will assess the safety and tolerability of a hASCs infusion in CKD patients with various underlying etiologies.

Methods: We performed a single-arm phase I clinical trial with a 6-month follow-up. This study enrolled 12 eligible CKD patients with an estimated glomerular filtration rate (eGFR) of 15-44 mL/min/1.73m^2 (mL/min). Patients were allocated to receive low, moderate, or high dose of allogeneic cultured hASCs infusion. We investigated the safety issues and kidney function during the follow-up visit.

Results: There was no patient lost to follow-up. We observed two treatment related adverse events (AE) in high dose group. One subject experienced grade 1 slow speech immediately after hASCs infusion, which was resolved on the next day and completely normal afterwards. The AE was considered possibly related to study treatment and met dose-limiting toxicity (DLT). Another subject experienced grade 1 bradynia after the infusion, and the situation was resolved during the following 9 days, however, this AE was not considered as DLT. One SAE was reported in moderate dose group, who was hospitalized for persistent heavy proteinuria, and later proved as diabetic nephropathy stage 4 by renal biopsy. No significant reduction in mean systolic blood pressure was observed in all treated patients, and specifically an improvement in eGFR was noted among those with baseline eGFR<30mL/min. No significant reduction in proteinuria was noted.

Conclusions: This trial demonstrated the safety and tolerability of allogeneic hASCs infusions in various stages CKD patients. Patients with reserved renal function (e.g. Backlund, S., Hoffstedt, J., Smid, E.F., et al. J Am Soc Nephrol 31: 2020

PO0605
Pegunigalsidase Alfa, Novel Pegylated Enzyme Replacement Therapy, Evaluated in Fabry Patients with Progressing Kidney Disease: A Randomized Clinical Trial Study Design
David G. Warnock,1 Derrylam Hughes,2 Sari Alon,3 Raul Cherkoff,3 Einat Almon,3 Raphael Schifflmann,4 UAB Medicine, Birmingham, AL; 2LSDU, Institute of Immunity and Transplantation, Royal Free London NHS Foundation Trust, London, United Kingdom; 3Protalix Biotherapeutics, Carmiel, Israel; 4Baylor Institute of Metabolic Diseases, Baylor University Medical Center, Dallas, TX.

Background: Fabry disease (FD) is an X-linked multisystem lysosomal storage disorder, affecting males and females caused by the deficient of α-galactosidase-A (α-Gal-A) activity. Long-term disease manifestations include progressive renal failure, hypertrophic cardiomyopathy, cardiac rhythm disturbances, stroke, and death. Two enzyme replacement therapies (ERT) and oral chaperon therapy are commercially available. The clinical benefit of available treatments may not be as robust as anticipated, especially in the subset of males with ‘classic’ Fabry disease. In the context of ERT, a combination of factors including dose, dosing interval, presence of anti-drug antibodies, estimated glomerular filtration rate (eGFR), and age at the time of ERT initiation, and proteinuria could explain the less than optimal responses achieved by the currently available ERT. Pegunigalsidase alfa is a novel PEGylated homo-dimer ERT which is more stable, has a favorable safety profile, potentially less development of anti-drug antibodies, and enhanced pharmacokinetic profile (~80 hours half-life and higher AUC) compared to other available ERT.

Methods: Adult FD patients (males and females) deteriorating in kidney function with annualized eGFR < -2 mL/min/1.73 m^2/year while on agalsidase beta have been enrolled into BALANCE, a phase-III double-blind active control study (NCT02795676), and were randomized (2:1 ratio) to pegunigalsidase alfa or continue agalsidase beta for 2 years at 1 mg/kg every other week. The primary outcome is the difference in the mean annualized slope of eGFR between the study between the two groups.

Results: Description of the baseline characteristics for approximately 75 patients enrolled at 29 US and European study sites by: age, sex, enzymatic activity, genetic mutations, FD symptoms, previous FD treatment length, kidney function (eGFR, eGFR slope and UPCR), Lyso-Gb3, and anti-drug antibodies pre-treatment status.

Conclusions: This trial demonstrated the safety and tolerability of allogeneic hASCs infusion in various stages CKD patients. Patients with reserved renal function (e.g. Backlund, S., Hoffstedt, J., Smid, E.F., et al. J Am Soc Nephrol 31: 2020

PO0606
Pegunigalsidase Alfa, Novel Pegylated Enzyme Replacement Therapy, Evaluated in Fabry Patients with Progressing Kidney Disease: A Randomized Clinical Trial Study Design
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Background: Fabry disease (FD) is an X-linked multisystem lysosomal storage disorder, affecting males and females caused by the deficient of α-galactosidase-A (α-Gal-A) activity. Long-term disease manifestations include progressive renal failure, hypertrophic cardiomyopathy, cardiac rhythm disturbances, stroke, and death. Two enzyme replacement therapies (ERT) and oral chaperon therapy are commercially available. The clinical benefit of available treatments may not be as robust as anticipated, especially in the subset of males with ‘classic’ Fabry disease. In the context of ERT, a combination of factors including dose, dosing interval, presence of anti-drug antibodies, estimated glomerular filtration rate (eGFR), and age at the time of ERT initiation, and proteinuria could explain the less than optimal responses achieved by the currently available ERT. Pegunigalsidase alfa is a novel PEGylated homo-dimer ERT which is more stable, has a favorable safety profile, potentially less development of anti-drug antibodies, and enhanced pharmacokinetic profile (~80 hours half-life and higher AUC) compared to other available ERT.

Methods: Adult FD patients (males and females) deteriorating in kidney function with annualized eGFR < -2 mL/min/1.73 m^2/year while on agalsidase beta have been enrolled into BALANCE, a phase-III double-blind active control study (NCT02795676), and were randomized (2:1 ratio) to pegunigalsidase alfa or continue agalsidase beta for 2 years at 1 mg/kg every other week. The primary outcome is the difference in the mean annualized slope of eGFR between the study between the two groups.

Results: Description of the baseline characteristics for approximately 75 patients enrolled at 29 US and European study sites by: age, sex, enzymatic activity, genetic mutations, FD symptoms, previous FD treatment length, kidney function (eGFR, eGFR slope and UPCR), Lyso-Gb3, and anti-drug antibodies pre-treatment status.

Conclusions: This trial demonstrated the safety and tolerability of allogeneic hASCs infusion in various stages CKD patients. Patients with reserved renal function (e.g. Backlund, S., Hoffstedt, J., Smid, E.F., et al. J Am Soc Nephrol 31: 2020

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PO0561 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 globotriasylceramide (Gb3). Reduction in histological Gb3 burden in renal peritubular capillaries (PTCs) is considered an indicator of treatment efficacy and patients with severe renal involvement are likely to benefit the most. Previous studies demonstrated that treatment with PEGylated α-Galactosidase-A significantly reduced renal lyso-Gb3 burden.

Methods: The phase I/II (NCT01678898) dose-ranging studies (0.2mg/kg; 1 mg/kg; 2mg/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 quantitively assess patients' renal involvement, and was reduced to a mean of 0.83 after 6 months (-67.8% in the three dose groups. Mean BLISS score at baseline was 4.23, proving an important indicative of clinical improvement.

Results: Renal biopsies were available and evaluated in 13 out of 16 patients allocated to the highest tolerable dose of angiotensin-converting enzyme inhibitor (ACEI) or angiotensin II receptor blocker (ARB) for at least 8 weeks. They received amiodarone 5 mg twice daily or triamterene 50 mg twice daily for 8 weeks. All the patients then entered a washout phase for 4 weeks, followed by a crossover to the other trial drug for 8 weeks. Weight, blood pressure, metabolic panel, urine studies, and 24-hour urine protein excretion were frequently monitored. Patients with serum potassium >5.5 or an increase in serum Cr >30% one week after the treatment were withdrawn.

Conclusions: These results show a potential benefit of pegunigalsidase-alfa on renal function for FD patients currently treated with agalsidase alfa, to be confirmed by long-term data.

Funding: Commercial Support - Chiesi USA, Protalix Biotherapeutics

PO0563 Tolerance for Potassium Supplementation in Patients with CKD
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Background: Recent studies have shown an association between higher potassium (K+) intake and better kidney outcomes in patients with chronic kidney disease (CKD). However, K+ supplementation in CKD may be limited by the risk of hyperkalemia (>5.5 mEq/L). The primary aim of this study was to patients with CKD with the aim of determining whether it is safe to use Potassium supplementation in patients with progressive CKD and hypertension.

Methods: In 151 patients (67±11 years, 74% males, eGFR 32±9 mL/min/1.73 m2, 83% on renin-angiotensin inhibitors), K+ supplementation (40 mEq/day) increased urinary K+ excretion from 73±24 to 106±28 mEq/day, WKBI from 4.3±0.5 to 4.7±0.5 mEq/L, and plasma aldosterone from 294 (210-447) to 366 (271-504) pg/mL (P<0.001 for all). The majority of patients (n=138, 91%) remained normokalemic upon K+ supplementation, despite the use of renin-angiotensin inhibitors. K+ supplementation increased renin-angiotensin system activity (156±62 to 155±68 mEq/day, systolic blood pressure (132±15 to 132±15 mmHg), or eGFR (32.9±32.8 mL/min/1.73 m2).

Conclusions: This short-term study illustrates the feasibility of investigating the renoprotective potential of K+ supplementation in patients with CKD and provides the characteristics of patients in whom K+ is safe.

Funding: Private Foundation Support

PO0656 The Effect of Amiloride and Triamterene on Proteinuria in Patients with Proteinuric Kidney Diseases
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Background: Proteinuric kidney diseases are associated with a significant risk of developing stage renal failure. Treatment options after maximizing the renin-angiotensin-aldosterone system (RAAS) inhibition are limited. Amiloride, a diuretic inhibiting epithelial sodium channel (ENaC), has been reported to have antiproteinuric effects in animal studies independent of its action on ENaC. This study was designed to specifically examine the effect of Amiloride and triamterene in patients with significant proteinuria.

Methods: It is a cross-over pilot trial where each patient acted as his/her own control. Patients with proteinuria more than 1.0g/day, eGFR >30mL/min/1.73m2, and on the drug of interest was given one of angiotensin-converting enzyme (ACE) or angiotensin receptor blocker (ARB) for at least 8 weeks. They received amiodarone 5 mg twice daily or triamterene 50 mg twice daily for 8 weeks. All the patients then entered a washout phase for 4 weeks, followed by a crossover to the other trial drug for 8 weeks. Weight, blood pressure, metabolic panel, urine studies, and 24-hour urine protein excretion were frequently monitored. Patients with serum potassium >5.5 or an increase in serum Cr >30% one week after the treatment were withdrawn.

Results: A total of 12 patients were enrolled and completed the study. Amiloride reduced 24-hour urine protein by 25.4% (P=0.00435), UPCr by 31.6% (P=0.0104), UACR

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Hyperparathyroidism (SHPT) in CKD
Comparison of Extended-Release Calcifediol (ERC), Immediate-Release Calcifediol, Cholecalciferol, and Paricalcitol for Treating Secondary Hyperparathyroidism (SHPT) in CKD

Background: 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 ≥ 150 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) 1 mcg 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 (6.8) ng/mL and 154 (99) pg/mL, respectively. No differences were observed at baseline between treatment groups (14-17 subjects each). The mean change in serum 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.

Funding: Commercial Support - OPKO Health, Inc; Vifor Pharma

Renoprotective Effects of Febuxostat and Allopurinol in Patients with Hyperuricemia and CKD: A Meta-Analysis

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, 1.75; P = 0.0003) 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 = 0.0003). 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.

Funding: NIDDK Support

CKD Is Associated with Attenuated Plasma Metabolome Response to Oral Glucose Tolerance Testing

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) >60 ml/min per 1.73 m² 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 taurome metabolism, phenylalanine, tyrosine and cryptoporphyrin 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 mitochondrial 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 agonists.

Funding: NIDDK Support

Funding: Commercial Support - OPKO Health, Inc; Vifor Pharma
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 urate-to-creatinine ratio ≥2.50 mg/g or eGFR decrease ≥0.90 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 (normouricemia and hyperuricemia [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.

Conclusions: In CKD patients at risk of progression, the effect of allopurinol on eGFR decline was not modified by baseline serum urate.

Funding: Government Support - Non-U.S.

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 ≥40%, and composite 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 in a modified Cox model to predict time from study entry to the hard outcome of KRT. Potential surrogate endpoints were compared by number of events and prediction accuracy (integrated area under the time-varying receiver operating curve [AUC]).

Results: N = 5242 patients had median (IQR) baseline eGFR of 26.8 (20.7-35.5) and 1448 KRT events over a median (IQR) follow-up time of 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. 0.73-0.73). 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.

Funding: Commercial Support - AstraZeneca

Figure: PRISMA diagram

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

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Poster PO0568

Poster 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 ≥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.

Funding: Commercial Support - AstraZeneca

Figure: PRISMA diagram
PO0571

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.

PO0572

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 and 25% of “Yes” patients had a hospital encounter by 12 months (HR 1.85, CI[0.927, 3.689]).

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

PO0573

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 non-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 Biomediicine 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.

PO0574

Telenephrology Care for Veterans in the COVID-19 Pandemic
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Background: Chronic kidney disease (CKD) affects 37 million adults in the United States. Since 2013 our Nephrology section has carried out a telenephrology clinic and implemented electronic consults (E-consults). During the COVID-19 pandemic, we implemented changes to evaluate patients with kidney disease. The aim of this study is to report our experience.

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

Underline represents presenting author.
Methods: This is a single-center, retrospective chart review study, which evaluated the outcomes of our telenephrology clinic (video-on-demand and telemedicine clinic visits), as well as E-consults. Between January 2013 and 2020, 410 patients were seen at telemedicine clinic visits, and 1020 E-consults were evaluated. During the COVID-19 pandemic, between March 2020 and May 2020, 40 patients were assessed through video-on-demand.

Results: For telemedicine, a total of 169 patients were included, 99.4% were males, and 87% were white. The mean age was 66 ± 10 years, 92% had hypertension, and 41% diabetes mellitus. The baseline eGFR was 45 ± 14 mL/min/1.73m2. A one-way analysis of variance showed a statistically significant difference on the systolic (SBP) and diastolic (DBP) blood pressure (p-value < 0.000), and improvement in potassium and bicarbonate levels (p-value = 0.000). Phosphorus levels did not show a significant difference (p-value 0.37). There was a significant association between attendance to ≥3 telenephrology visits and SBP control (p-value=0.027), DBP control (p-value=0.002) and potassium improvement (p-value=0.013). The overall decrease in GFR was 1.2 ± 1.1 mL/ min/1.73 m2 (95% CI -0.41 to 2.95), lower than the reported natural progression of CKD (1.03 mL/min/1.73 m2/year). A survey for the video-on-demand patients showed 100% satisfaction, reflecting that patients felt their renal care needs were fulfilled. E-consults were covered in less than 24 hours, with 100% satisfaction from primary care physicians.

Conclusions: This is the first study evaluating the use of telenephrology in patients with kidney disease during the COVID-19 pandemic. In our cohort, telenephrology interventions improved SBP, DBP, bicarbonate, and potassium control. All three options improved health outcomes and guaranteed safety during the COVID-19 pandemic, at a reduced cost for the patient and the institution.

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 as 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 compliance, and clinical data were recorded. Data on blood pressure control was collected. 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 4.5 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 setting 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 sample showed mild-to-moderate CKD progression consistent with previously reported 10 years, 92% had hypertension, and 41% diabetes mellitus. The baseline eGFR was 45 ± 14 mL/min/1.73 m2. A one-way analysis of variance showed a statistically significant difference on the systolic (SBP) and diastolic (DBP) blood pressure (p-value < 0.000), and improvement in potassium and bicarbonate levels (p-value = 0.000). Phosphorus levels did not show a significant difference (p-value 0.37). There was a significant association between attendance to ≥3 telenephrology visits and SBP control (p-value=0.027), DBP control (p-value=0.002) and potassium improvement (p-value=0.013). The overall decrease in GFR was 1.2 ± 1.1 mL/ min/1.73 m2 (95% CI -0.41 to 2.95), lower than the reported natural progression of CKD (1.03 mL/min/1.73 m2/year). A survey for the video-on-demand patients showed 100% satisfaction, reflecting that patients felt their renal care needs were fulfilled. E-consults were covered in less than 24 hours, with 100% satisfaction from primary care physicians.

Conclusions: This is the first study evaluating the use of telenephrology in patients with kidney disease during the COVID-19 pandemic. In our cohort, telenephrology interventions improved SBP, DBP, bicarbonate, and potassium control. All three options improved health outcomes and guaranteed safety during the COVID-19 pandemic, at a reduced cost for the patient and the institution.

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 provide telenephrology care via videoconferencing to PCPs 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 18.3 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. Qualify 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 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.

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: CKD3B & 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 ≤42, the mortality benefit was observed with 1 or more nephrology visit, p<0.005. 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.

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 ESKD 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 SGLT2 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 (IDC), 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 IDC 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 IDC, but receipt of IDC was limited by resource availability.

Results: Of the 329 incident ESRD patients included in our study, the mean age was 59.6 years (SD 13.3), 47% were female, and 86% were African American or Hispanic. The baseline characteristics were similar between the groups, except the IDC 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 IDC 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 IDC was associated with a higher odds (OR 3.9 [95% CI 2.0 – 7.8]; P<.0001) of kidney transplant listing compared to usual care alone after adjusting for sociodemographic and clinical factors. Other outcomes also favored IDC 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 randomized controlled studies are needed to determine the effectiveness of IDC 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 2015 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 only one Renal Program in the region. The results may not be generalizable to different populations, health care systems, or predictive models. Further research is needed to establish the optimal KFRE criterion upon which MCKC funding eligibility can be based.

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. Of these patients, 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 disease, calculated by the Kidney Failure Risk Equation (KFRE), greater than 10%. The disease, calculated by the Kidney Failure Risk Equation (KFRE), greater than 10%.

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 veterans prescribed one or more doses of patiromer between 10/2015 and 11/2019 at the Veterans Affairs Northeast Ohio Hospital System (VANEOHS), 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 209 (SD 3-1597) 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 had either increased RAAS inhibitor dose over the study 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). We performed 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 G2, 1.44 [0.78–2.65] for G3a, 4.06 [2.17–7.37] for G4 and 8.44 [4.53–16.5] for G5, respectively, compared with patients in the lowest category (G1) as the reference value. In the higher glomerular filtration rate (GFR) category (>G3b), 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 than those in the lower GFR category (≤G3a). In addition, aldosterone blockers, biguanides, fibrates, 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 more to pay attention to prescribe medicines according to renal function.

A Pilot and Feasibility Randomized Controlled 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 and for increased RAAS inhibitor dose over the study period. 15 (29%) veterans either maintained or increased RAAS inhibitor dose over the study period. 228 veterans with hyperkalemia were included for analysis. Mean age was 69 ± 13 years, 42% were women. 5%, 38%, 43% and 14% had CKD stages 2, 3A, 3B/4 and ESKD, respectively. Sedentary and stepping durations did not change in the SOC group. In the SLIMM group, the maximum decrease in sedentary duration, increase in stepping duration, and the number of steps per day were observed at week 20 but attenuated at week 24 (Fig1). In separate linear mixed effects models (Table 1), overall treatment effects of the intervention on sedentary duration, stepping duration and the number of steps were not significant. The SLIMM intervention significantly reduced baseline sedentary duration by 14% at week 24.

Conclusions: It is feasible to reduce sedentary duration and increase stepping duration in CKD but additional measures along with SLIMM intervention may be needed to sustain its effect on sedentary behavior.

Funding: NIDDK Support

The Effects of Allopurinol on the Progression of CKD According to 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 glomerular filtration rate in patients with CKD stage 3 or 4, no history of gout, and who were at risk of progression (identified by urinary albumin-to-creatinine ratio ≥265 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 ≥4.

Methods: At baseline, 1,982 (23%) 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 23.1 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 (-0.33 mL/min/1.73 m²/year, 95% CI -1.18 to 0.11) and placebo (-0.76 mL/min/1.73 m²/year, 95% CI -1.18 to 0.17). 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 and 3500 mg/24h and estimated glomerular filtration rate (eGFR) 30 to 90 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 primary outcome was proteinuria change from baseline to week 8. The main secondary outcome was change in inoxel measured GFR (mGFR).

Results: Fifty-eight patients were screened of whom 53 patients were randomized. Median baseline proteinuria was 1110 mg/24h (IQR 730, 1560) mg/24h; mean mGFR was 58.3 (SD 23) 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 primary outcome was proteinuria change from baseline to week 8. The main secondary outcome was change in inoxel measured GFR (mGFR).

Conclusions: Six week treatment with dapagliflozin does not affect proteinuria in patients with chronic kidney disease without diabetes, but did induce acute and reversible decrease in mGFR, body weight reduction, and increased hemoconcentration.

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) was 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 hypothetical cohort of similar demographic and chronic kidney disease characteristics. Outcomes were measured as cumulative CKD stages with standard eGFR decline (<0.5 mL/min/1.73 m2 annually) and one with rapid eGFR decline (4.20). Models were populated using best available literature. Results: CKD patients with rapid eGFR decline had a reduced life expectancy of 9.1 years compared with 6.4 years in those with standard mGFR 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 with dapagliflozin in patients with eGFR decline (5.5 versus 7.9) and an additional 493.7% 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 previous published studies. The improved diagnosis thresholds of CKD may reduce the 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. Zamilpimab (IC50 0.2nM, Kd 120pm), a humanized mAb specific for human TG2, is under investigation for the treatment of fibrosis. Application of zamilpimab in a primary human cell model of renal fibrosis had positive results; however due to human specificity, zamilpimab efficacy cannot be tested in rodent in vivo models.

Methods: A unilateral ureteric occlusion model of CKD was developed in aged cynomolgus monkeys. Zamilpimab was applied prophylactically immediately following model induction. TG2 activity was measured using an in-situ activity assay, and zamilpimab 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 that correlated to an increased TGFβ1 dimer, leading to end-stage renal failure. At this time point, zamilpimab intervention in a 4-week study, 7 days post final dose, TG2 activity and TGFβ1 dimer were completely inhibited at a high dose level of 3 mg/kg. At 6 months post final dose, at a low dose. However, both zamilpimab doses ameliorated the level of renal fibrosis by pathology score, computerized determination of fibrin index and hydroxyproline.

Conclusions: Our primate model of CKD demonstrated that zamilpimab can effectively block TG2 activity and prevent renal fibrosis. A Phase 1/2 study of zamilpimab for the treatment of post-renal transplant fibrosis is ongoing (NCT04335578).

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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 PINK1-mediated mitophagy in experimental and human kidney fibrosis.

Methods: Pnk-1−/−, myeloid-specific Mfn1 (LysM-Cre−/−Mfn1fl/fl), Mfn2 (LysM-Cre−/−Mfn2fl/fl) null mice and corresponding controls were subjected to unilateral ureteral obstruction (UUO) (17, 20 days) or adenine diet (AD, 28 days). Kidneys, renal macrophages (MRMs), bone marrow-derived macrophages (BMDMs), PBMCs, and plasma were analyzed by western blot, qPCR, Mito stress test, ELISA, immunohistochemistry, flow cytometry, confocal and electron microscopy. Patients with renal biopsy-proven interstitial fibrosis & tubular atrophy (IFTA, n=6) and severe CKD (GFR 30 mL/min, n=15) were compared to controls (no IFTA, n=9) and mild/moderate CKD (GFR >30 mL/min, n=8).

Results: MFN1 and MFN2 expression decreased in kidneys after UUO or AD, and BMDMactivated TGF-β1 treatment AD-fed LysM-Cre−/−Mfn1fl/fl/but not LysM-Cre−/−Mfn2fl/fl mice displayed increased renal expression of CD11b+F4/80+ macrophages than AD-fed controls. Increases in fibronectin, CD206, galectin-3, and TGF-β expression in the kidneys and RMs were higher in AD-fed LysM-Cre−/−Mfn1fl/fl 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−/−Mfn2fl/fl RMs and BMDMs than LysM-Cre−/−Mfn1fl/fl and controls. The reduction in colocalization of MFN2 but not MFN1 with renal mitochondria after UUO was higher in Pnk-1−/− mice. PBMCs 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 PINK1 expression in IFTA-treated human RMs was associated with increased fibrotic response.

Conclusions: This study is the first to suggest that myeloid-specific MFN2 but not MFN1 by regulating 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

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only; Underline represents presenting author.
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 pharmaceutical blocking EZH2 (Enhancer of Zeste Homolog 2), a histone H3 lysine 27 histone 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 mice 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 models of chronic kidney disease (CKD) induced by UUO and 5/6 nephrectomy (SNx).

**Results:** Global inhibition of EZH2 by administration of gambogic 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 vitro. Moreover, pharmacological and genetic inhibition of EZH2 suppressed expression of Notch-1, Notch-3, Jagged-1 and HES-1 and HEV-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-κB as well as expression of multiple profibrogenic cytokines/chemokines and renal macrophtage 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 (RNL5) 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 RNL5 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. RP181MNP or empty MNP was administered weekly for 4 weeks. Reduced renal cell death was evaluated by immunohistochemistry and plasmacytoid (Cr). The mechanism of action of RP181MNP was investigated using single cell RNA sequencing (scRNAseq) of whole kidney cells.

**Results:** MNP were retained intracellularly by TKPTS cells and were localized to proximal tubules in vivo. RP181MNP protected TKPTS cells from CP-induced cytoxicity: cell viability was enhanced 3.5-fold, n=6, p<.05, compared to empty MNP. Naked RP81 increased cell viability 1.72-fold, n=6, p<.05 over BSA control. Compared to WT, CP in KO caused more severe AKI (Cr: 0.61 mg/dl ± 0.05 vs. 0.13±0.03 in WT, n=3, p<.05), higher mortality (45% death at 4 weeks vs. 20%, p<.005), and more severe CKD (Cr: 0.16 ± 0.02 mg/dl ± 0.1 ± 0.05, n=5, p<.05). In KO given CP, RP181MNP ameliorated AKI (Cr: 0.30 ± 0.05 mg/dl vs. 0.64 ± 0.14 in control, n=5, p<.05) and CKD (increased kidney weight: 176% ± 7.0 vs. 145± 2.4, decreased plasma Cr: 0.10± 0.01 vs 0.16±0.02, and KiM:1-124.3±15.1 pg/ml vs 227±23.4). RP181MNP significantly reduced plasma cytokines IL-1β, IL-2, IL-6, KC, and TNFα and inhibited regulated necrosis. SCRNAsseq revealed that RP181MNP preserved tubule and vasculature cell mass and decreased infiltrated immune cells caused by CP.

**Conclusions:** We conclude that RP181MNP attenuates CP-induced CKD by diminishing cell death pathways and inflammation activation by CP. These data suggest that RP181MNP may be an effective therapeutic agent to prevent CKD in patients treated with repeated doses of cisplatin.

**Funding:** NIDDK 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 shikim) suppressed renal fibrosis in the mouse model of unilateral ureter obstruction (UUO). Interestingly, in vitro the inhibitors suppressed fibrogenic 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-flox mice were bred with Pax8-xT/A1C 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 littermates. 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 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 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 littermates.

**Conclusions:** Together, these results indicate a pathogenic role of glycolysis in maladaptive kidney repair. Importantly, PKM2 and associated metabolism contribute to the degeneration of renal tubules after acute kidney injury.

**Funding:** NIDDK Support, Veterans Affairs Support

PO0595

**Proximal Tubule-Specific DPP4 Deletion Slows Kidney Disease Progression in Obese Mice**

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**Background:** Obesity is a major risk factor for Chronic Kidney Disease progression to End Stage Renal Disease and/or Dialysis. Increased absorption of fats and/or sugars from Western Diet (WD) likely leads to kidney tubular injury in obesity. We observed that whole body dipeptidyl peptidase 4 (DPP4) deletion as well as inhibition in WD-fed mice results in decreased kidney injury which, in turn was associated with a decrease in proximal tubule DPP4. Therefore, we hypothesized that proximal tubule (PT) DPP4 activation leads to injury and progression of kidney disease.

**Methods:** PT-KO and WT littermates were fed a WD starting 4-6 weeks of age and continued for 2 years. GFR and albuminuria were monitored periodically. Tissue histology was performed at select intervals. GeLC-MS was used to separate kidney peptides and Scaffold 4/Pathway guide used to analyze the Proteomics data.

**Results:** WD-fed WT mice gained 150-200% weight of chow-fed (CD) mice and had a greater decline in GFR than CD-fed animals over 2 years (50% vs. 20%, p<0.05). WD-fed PT-KO mice had a lesser decline (~35%) when compared to WT mice. This was true for both male and female mice. Concomitantly, there was an increase in albuminuria in WD-fed WT mice that was mitigated in PT-KO mice. PAS/PSR stained sections showed worsening fibrosis, tubular dilatation and glomerulomegaly, tubular vacuolization in WD-fed WT mice that was mitigated in PT-KO mice. Oil Red O staining showed increased fat accumulation in glomeruli and tubules of WD-fed WT mice that was mitigated in KO mice. Proteomics analysis followed by immunoblots showed that WD-feeding led to an increase in cell adhesion proteins and ribosomal machinery that was significantly suppressed by KO. In addition, there was a shift towards reduction in gluconeogenesis and improved fatty acid oxidation in KO mice.

**Conclusions:** Obesity without diabetes can lead to rapid decline in GFR in both male and female mice. DPP4 inhibition may slow decline if started early in the course of developing obesity and/or insulin resistance.

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The PAR-1 Antagonist Vorapaxar Protects Against AKI to CKD Transition

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Background: Protease-activated receptor-1 (PAR-1) has been reported as a key 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 vorapaxar, an FDA-approved drug for reducing thrombotic cardiovascular events, has any renoprotective effect in a robust AKI mouse 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 kidney injury marker-1 (KIM-1) in UIRI kidneys. Mice treated with vorapaxar showed less intrarenal accumulation of ECM proteins including fibronectin, α-smooth muscle actin and collagen I via TGF-β1/Smad signaling after UIRI. IR-induced endothelial dysfunction and macropage infiltration were also decreased by vorapaxar treatment. In NRK-52E cells, PAR-1 expression was activated under a hypoxia milieu associated with upregulation of TGF-β-induced ECM protein accumulation.

Conclusions: Vorapaxar diminishes renal fibrosis through TGF-β1/Smad signaling in UIRI model, and protects against tubular injury during AKI to CKD transition. A PAR-1 targeted strategy by vorapaxar 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. C7081-16C), and Hong Kong Society of Nephrology/ HK Foundation for Research Grant 2018.

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 Sphn2 or Mfn2d, and then reacts with SIP receptors (SIPR1-5) to affect various cell functions. We recently showed that SphK2–/– mice were protected from renal fibrosis when compared to wild type or Sphk1–/– mice (PMID: 27799486). We hypothesized that Sphk2 deletion in renal perivascular cells confers the protection from progressive kidney fibrosis.

Methods: Male Fosl/Cre Sphk2fl/fl and Fosl/Cre Sphk2fl/fl (control) mice were used. For unilateral ischemia-reperfusion injury (IRI), left kidney was clamped for 30 min; right nephrectomy was performed at day 13. For bilateral IRI, both kidneys were clamped for 30 min. Mice were euthanized at day 14 to evaluate kidney fibrosis (unilateral IRI) and at day 1 to evaluate the extent of acute kidney injury (bilateral IRI). Primary kidney perivascular cells were isolated from kidneys of Fosl1Cre Sphk2fl/fl and control mice.

Results: In the unilateral IRI model, Fosl1Cre Sphk2fl/fl mice demonstrated better kidney function (plasma creatinine, less kidney fibrosis (histology)) with less macropage infiltration, and suppressed expression of fibrosis-related genes (Acta2, Colla1, Col3a1) in the kidneys compared with control mice but there was no difference in plasma SIP between the groups. In contrast, in the bilateral IRI model, there was no difference between the groups in kidney function, kidney Haver1/En2 expression, and histology at day 1. In vitro studies, Sphk2-deficient perivascular cells expressed less inflammatory cytokines, such as Ccl2, Itgav, Clec11, after LPS stimulation compared with control perivascular cells. Sphk2-deficient and control perivascular cells robustly expressed Smad2, but not Mfn2d, and S1pr1-3 among the five SIP 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 SIP production by Sphk2 is exported through Sphn2 and reacts with S1PR1 to enhance the inflammatory signal in these cells, leading to immune cell infiltration and subsequent fibrosis in the kidneys.

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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 (RRK-48F) 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, UUO and UUO. Pharmacological inhibition of JMJD3 with GSKJ4 completely blocked the expression 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 (TGFB1), Smad3, Notch1, Notch3 and Jagged1. Inhibition of JMJD3 by GSKJ4 or specific siRNA also resulted in the similar responses in cultured NRK-49F and mTECs exposed to serum or TGFB1. 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

Induction of CKD by Gene Deletion of Canonical Transient Receptor Potential 1 (TRPC1) Channels Independent of Hypertension and Nepheromalgy 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 relationships has been established. Since null mice are obese, hyperterylyceridemic 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 (CI) 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 Cr. Systolic (S) & diastolic (D) BP was measured by arterial (A) cannulation.

Results: Null mice were hyperglycemic from the 3rd mon & developed diabetes in 6 to 22 mon by standard IP glucose tolerance test. Nepheromalgy was absent in null mice since kidney volume by US (0.38 vs. 0.46 at 7 mon & 0.4 vs 0.5 ct at 11-20 mon) was 16% smaller & kidney (K) to body (B) weight (W) (1.2 vs 1.5 7 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 echogenicity at 20 mon, though normal at 7 or 11 mon. Urine albumin/Cr ratio in null mice rose barely (64-71%). At 17 mon, CrCl fell by 30% (p<0.01) in null & by 46% (p<0.01) in null vs. GFR at 22 mon corroborated stage III CKD as inulin C1 fell by 45-48%, whether expressed per mouse, per g KW, 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 torr), DBP (77 vs 86 torr), & MABP (89 vs 98 torr). Since TRPC1 was implicated in cardiac hypertory 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 dysfunction, compromises homodynamics and produces hypohypertensive 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
The Novel Soluble Guanylyl Cyclase (sGC) Activator Runcaciguat Induced Renal Vasodilation and Reduced Kidney Damage in a Rat CKD Model

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Background: CKD progression is associated with impaired NO/sGC/cGMP-signaling, low cGMP production and increased oxidative stress. Oxidative stress modifies the native sGC to oxidized, heme-free apo-sGC which cannot be activated by NO anymore. Runcaciguat is a novel potent and selective sGC activator that binds and activates heme-free sGC independently of NO and restores NO/sGC/GMP signaling. We investigated the effects of Runcaciguat on intrarenal hemodynamics and in a rat model of T2D-associated CKD.

Methods: Hemodynamic effects were analyzed ex vivo in isolated renal afferent/effluent arterioles and in perfused kidneys. Effect of Runcaciguat on kidney protein expression was evaluated in diabetic and proteinuric rats. ZSF1 rats (12w, male, n=6/gp) were implanted with telemetry systems and treated daily orally for up to 12 weeks with Runcaciguat, Enalapril or placebo. Key parameters included proteinuria, kidney structural changes, biomarkers, kidney gene expression, systemic hemodynamics, and substance plasma exposures.

Results: Runcaciguat dilated renal afferent/effluent arterioles under NO depletion and increased blood flow, GFR and cGMP production in NO-depleted, isolated perfused kidney slices under ZSF1 rat conditions dose-dependently reduced proteinuria (~17%, ~50%, ~85% (p < 1, 3.10 mg/kg/bid) without changing mean arterial pressure at steady-state. The reduction of proteinuria was significantly higher than with Enalapril (-39%, -63% (p < 0.2, 60 mg/kg/d) at doses significantly reducing systemic blood pressure. Runcaciguat reduced kidney injury parameters, albuminuria and liver and kidney weight. Runcaciguat restored reduced whole blood hemoglobin and plasma triglycerides while Enalapril did not. Metabolic improvement was accompanied by gene expression changes suggesting improvement of vascular and endothelial functions independently of interaction with the Renin-Angiotensin-Aldosterone system. Runcaciguat plasma concentration was dose-proportional after acute and chronic dosing.

Conclusions: Runcaciguat prevented further decline in kidney function and structure independent of blood pressure in CKD rats. Our data suggest that the novel sGC activator Runcaciguat represents a promising treatment option for CKD patients.

Funding: Private Foundation Support

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 surface-exposed, high-afﬁnity receptor for tubular lipid uptake, is upregulated in response to 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 cells were cultured 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 palmitic 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 >14,000 compounds and tested for its anti-fibrotic ability.

Results: KIM-1 expression in DKD patients was positively correlated with tubulointerstitial inﬁltration 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 increasedH2AX 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. JB1 reduced the pro-fibrotic effect of conditioned media from FA-treated human primary cells and tubuloids.

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 KIM-1 as a therapeutic target for chronic kidney disease including DKD and our work introduces a new candidate therapeutic agent.

Funding: NIDDK Support, Commercial Support - Boehringer Ingelheim

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: 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 proliferation of Smad3, Smad7, 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 differentiation 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 TGFβ/β1 and eGFR signaling.

Funding: NIDDK Support, Other NIH Support · National Natural Science Foundation of China

Critical Role of STAT6 Signaling in Renal Fibrosis

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Background: Kidney fibrosis is a pathologic characteristic of chronic kidney disease, resulting in progressive loss of kidney function to end-stage kidney failure. We have recently demonstrated that bone marrow-derived fibroblasts contribute to the pathogenesis of kidney fibrosis. In this study, we investigated the role of STAT6 in activation of bone marrow-derived fibroblasts and development of renal fibrosis in folic acid nephropathy.

Methods: To investigate the role of STAT6 in myofibroblast activation and kidney fibrosis, we used STAT6 knockout mice or treated wild-type mice with AS1517499, a STAT6 inhibitor. Wild-type mice treated with vehicle were used as controls. Folic acid was administered at 250 mg/kg intraperitoneally to induce kidney fibrosis. Kidneys were harvested 2 weeks after folic acid injection.

Results: Folic acid injury led to activation of STAT6 in the interstitial cells of the kidney, which was abolished by treatment with AS1517499. Wild-type mice treated with AS1517499 accumulated fewer bone marrow-derived fibroblasts compared with vehicle-treated mice. AS1517499 treatment significantly inhibited myofibroblast activation, reduced total collagen deposition, and suppressed expression of extracellular matrix proteins with folic acid injury. Compared with wild-type mice, mice with STAT6 deficiency exhibited fewer myofibroblast and myofibroblasts and expressed less α-SMA protein in the kidneys following folic acid injury. Furthermore, genetic deletion of STAT6 significantly reduced total collagen deposition and ECM protein production in the kidneys with folic acid nephropathy.

Conclusions: Our results demonstrate that STAT6 signaling plays an important role in the development of bone marrow-derived fibroblasts during the development of renal fibrosis in folic acid nephropathy.

Funding: NIDDK Support, Veterans Affairs Support

The Role of HNF4α in CKD Progression

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Background: Acquired kidney mitochondrial dysfunction is a prominent feature of Chronic Kidney Disease (CKD), and is associated with onset and progression of CKD. HNF4α is a transcription factor highly expressed in proximal tubules which controls the expression of genes involved in critical metabolic pathways. As a result, mutations in HNF4α are associated with mitochondrial defects. We previously found that Hnf4α is reduced in the kidneys of Col4α3KO mice with progressive CKD and it correlated with hyperphosphatemia. Here, we tested the hypothesis that kidney Hnf4α is reduced in response to hyperphosphatemia and that Hnf4α decline in CKD contributes to mitochondrial dysfunction and CKD progression.

Methods: We fed WT mice a control (Ctl) and a high phosphate diet (HPi) for 6 weeks. We confirmed that phosphate intake was reduced in the kidneys Col4α3KO mice by RT-PCR and next performed RNA sequencing (RNAseq) to identify genes and molecular pathways affected by HNF4α reduction in CKD. Finally, to further evaluate the causal role of Hnf4α reduction in CKD progression, we treated Col4α3KO mice with a daily dose of 30mg/g of I.P. IEs4α (700mg/kg) for 5 days.

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

Underlines represent presenting author.
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 KO 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 (~30%) are regulated by HNF4α. Pharmacological inhibition or HNF4α in Col4a3 KO 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 fibrocollagen, 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 225/150 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, COL I (PRO-C1), III (PRO-C3), VI (PRO-C6), and fibronectin (FBN-C) formation were assessed in the medium by enzyme-linked immunosorbent assays developed at Nordic Bioscience.

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 and 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 fibrocollagen 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 fibrocollagen. 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-β-stimulated human proximal tubular epithelial cell (HK-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 pathological assessment via hematoxylin and eosin staining. Immunohistochemistry, western blots, and qPCR were used to determine the expression levels of FoxM1, Collagen I, E-cadherin, α-SMA, and Snail1.

Results: FoxM1 inhibition could ameliorate RIF and reduce the deposition of Collagen I. H&E staining revealed that renal structural damage, inflammatory cell infiltration, and ECM deposition were significantly attenuated by thiostrepton treatment in the UUO rats. FoxM1 downregulation significantly suppressed EMT, as evidenced by decreased protein and mRNA expression levels of α-SMA and Snail1 and a significant increase in protein and mRNA expression levels of E-cadherin.

Conclusions: FoxM1 inhibition could be a novel therapeutic strategy for the treatment of RIF.

PO0607
The Macrophage Recruitment in the Unilateral Ureteral Obstruction Is Associated with the Raise of MCP-1 and Is Dependent of Lipocalin 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 chemotactarctant protein-1 (MCP-1) raise. In addition, studies in patients have demonstrated that neutrophil gelatinase-associated lipocalin (NGAL, also called Lipocalin-2), it 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 macrophages 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 C3HBL/6 Wild type (WT) y Nyal-KO mice (8-12 weeks) were used for experiments. Male Sham surgery (control group) or sham surgery (control group) was performed to determine the effect of CaSR in the 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 Mgl reabsorption. CaSR may play a key role for the mg loss-related renal fibrosis.

PO0610
Fibroblast-Specific LRP-1 Promotes Renal Fibrosis
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Background: LRP-1, a scavenger receptor up-regulated during obstructive nephrathy, has been shown to mediate the actions of multiple profibrotic factors including αIPα, TGF-β1, and CTGF. However, in the 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 the podo-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.

Funding: NIDDK Support, Private Foundation Support

PO0611
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 in renal tubules of 5/6Nx rats at all measured time points and stained for the presence of kidney fibrosis 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.

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 13 weeks following 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. Protopic 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, cubilin, and mitochondrial VDAC.

Conclusions: Loss of important tubule proteins through production and urine excretion of previously unidentified LRT-EVs may represent a hitherto unappreciated aspect of chronic renal insufficiency.

Funding: Other NIH Support - NHLBI

PO0612
Indoleamine-2, 3-Dioxygenase Activates Wnt/B-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. In addition, 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 occlusion. Two weeks after 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. Protopic 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, cubilin, and mitochondrial VDAC.

Conclusions: Loss of important tubule proteins through production and urine excretion of previously unidentified LRT-EVs may represent a hitherto unappreciated aspect of chronic renal insufficiency.

Funding: Other NIH Support - NHLBI

PO0608
Enabled ICOS-RTE-Tresps Proliferation Is Involved in the Pathogenesis of Active Systemic Lupus Erythematosus (SLE)

Kathleen Kälble, Christian Nusshag, Frida Steinborn-Kroehl.1 Christian Steinborn-Kroehl.2

Background: Dysfunction of CD4+ regulatory T-cells (Treg) and CD4+responder T-cells (Tresps) is an important trigger in the development of active systemic lupus erythematosus. But decreased in active SLE patients compared to healthy control patients. In contrast, proliferation of ICOS+RTE-Tresps is medically inhibited in SLE but increased differentiation of ICOS+RTE-Tregs via resting MN-Tregs into CD31−recent RTE-Tresps is not inhibited but enabled in SLE.

Methods: To determine differences in the differentiation of inducible costimulatory molecule (ICOS)− and ICOS+Tregs/Tresps, their percentages of CD45RA CD3− recent thymic emigrant (RTE)-Treg/Tresps and CD45RA/CD3+ mature naive (MN)-Treg/Tresps as well as CD45RA CD3+ and CD45RA/CD3− memory-Treg/Tresps (CD3+ and CD3−-memory Tregs) within total Tregs/Tresps were calculated. Additionally, subsets were stained for the proliferation marker Ki67. 124 healthy control patients and 234 SLE patients in remission show 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-Tresps into CD31−memory-Tresps is inhibited. Similarly, active SLE patients show an increased differentiation of ICOS+RTE-Tregs 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-Tresps differentiation compared to healthy control patients. Therefore, 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-Tresps is medically inhibited in SLE remission patients. In active SLE patients, proliferation is enabled decreasing the ICOS+Tregs/ICOS−Tresps ratio.

PO0609
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 the development of renal interstitial fibrosis along with the down regulation of Myo-transporting molecules, suggesting that CaSR plays an important role in the development of renal damage associated with Mg deficiency. We report here an analysis of the effects of calcimimetics administration on renal fibrosis models.

Methods: The left kidneys of 8-week-old SD rats were ligated to create unilateral ureteral obstruction (UUO) model and studied after 7 days. Cinacalcet 1.0 mg/day, a calcimetics, was administered to a part of UUO animals. Experiments were performed in three groups of sham group, UUO group and UUO+Cinacalcet group (n=5). Fibrosis was evaluated by the Trichrome and analysis of the histopathological fibrosis-related molecules. We also studied on mRNA expression of Mg-transporting molecules. Results: It was confirmed from immunohistochemistry and gene expression that CaSR expression was remarkably decreased by UUO (RT-PCR: sham 1.01±0.09 vs UUO 0.04±0.03, n=5). Cinacalcet treatment partially rescued the expression in the remaining 30-50% compared to UUO group. In Azan staining, an increase in the fibrosis area and a decrease in the non-damaged tubules were apparent in UUO, however, Cinacalcet treatment partially rescued. mRNA expression of TGF-beta and MCP-1 was not significantly decreased by Cinacalcet treatment as compared to UUO group.

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

**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 well 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, Angiotsensin-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. This 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 (CKDu): Is the Problem Dehydration, Water Contamination, or Both?**

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**Background:** An increasing number of people of Central America develop CKDu. The disease is characterized by chronic tubulo-interstitial nephritis. Occasionally, it presents as an acute kidney injury (AKI). 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 > 6000 workers (11/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 AKI 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 CKDu remains to be determined.

**PO0615**

**Effects of Chronic Intermittent Hypoxia on umod-/- Rats’ Model Link to Alterations of Gut Microbiota**

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**Background:** Previous studies showed that both obstructive sleep apnea and uromodulin (UMOD) were associated with gut microbiota regulation. Here we explored the interaction effects of chronic intermittent hypoxia (CIH) and UOMD expression on variation of gut microbiota and association with phenotype.

**Methods:** umod−/− and wild type (WT) Sprague Dawley rats were attributed into 4 groups (N=10 in each group), umod−/− and WT under CIH, umod−/− and WT under normal air. All four groups were fed with same chaw for 10 weeks. All rats were anesthetized to collect fecal samples from large intestine directly and blood at the end of weeks feeding. The bacterial composition was analyzed based on 16S ribosomal DNA pyrosequencing. Bioinformatics tools, including sequence alignment, abundance, and taxonomic diversity, were used in microbiome data analyses. Correlation analysis between differential genera and changed biochemical indicators were measured.

**PO0616**
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±0.2mmol/L, P=0.04). Under normoxia environment, the α-diversity of gut microbiota decreased in umod\(^{-}\) group compared with WT group (Chao1 index, 301.8±30.2 vs 374.3±55.3, 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=0.043). 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-Anaerotruncus (P=0.008) increased and g-Flavonifractor (P=0.008) and g-Anaerostipes (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 CD improve renal function by affecting intestinal microbiome in CKD3-5 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 ribosomalRNA(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 = 0.002). CD can increase the abundance of some short chain fatty acid(SCFA) producing bacteria and decrease the abundance of some enteric 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 Glut9loxlox 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 in vitro. 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.

Funding: Government Support - Non-U.S.
PO0618

Serum Lysyl Oxidase Is a Potential Diagnostic Biomarker for Kidney Fibrosis
Xiaojin Zhang, Chen Yu. Department of Nephrology, Tongji Hospital, Tongji University, Shanghai, China, China.

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 in kidney fibrosis models.

Results: Serum LOX levels were higher in patients with kidney fibrosis than in those without 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=0.44, p<0.001) and the prediction of kidney fibrosis (5.06, p<0.001). ROC curve analysis of serum LOX showed an AUC of 0.80 (95% CI 0.74 to 0.86). The optimal serum LOX level cutoff point was 253.34 µg/ml for the prediction of kidney fibrosis and 306.36 µg/ml for the prediction of moderate-severe renal fibrosis. LOX expression was significantly upregulated (2.3-2.6-fold and 6-fold, respectively) in vitro and in vivo in 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 has potential to be a noninvasive 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.

PO0619

Tubulointerstitial Fibrosis and Markers of Kidney Tubule Secretion
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Background: Tubular secretion plays an important role in the efficient elimination of endogenous solutes and medications, and lower secretory clearance is associated with risk of kidney function decline. We evaluated whether the biopsy measurement of tubular secretory clearance even after adjusting for eGFR and albuminuria.

Methods: Among 418 persons, the mean age was 53 years, 51% were women, 64% were White and 18% were African American. The mean eGFR was 50 ml/min/1.73m² and median album/creatinine ratio was 890 mg/g. Compared to individuals with no IFTA, those with IFTA had a 15% lower eGFR (p<0.001), 27 to 76% lower UPR for the all 9 solute markers (p<0.001, respectively). ROC curve analysis of serum LOX showed an AUC of 0.80 (95% CI 0.74 to 0.86). The optimal serum LOX level cutoff point was 253.34 µg/ml for the prediction of kidney fibrosis and 306.36 µg/ml for the prediction of moderate-severe renal fibrosis. LOX expression was significantly upregulated (2.3-2.6-fold and 6-fold, respectively) in vitro and in vivo in interstitial fibrosis models.

Results: Serum LOX levels were higher in patients with kidney fibrosis than in those without 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=0.44, p<0.001) and the prediction of kidney fibrosis (5.06, p<0.001). ROC curve analysis of serum LOX showed an AUC of 0.80 (95% CI 0.74 to 0.86). The optimal serum LOX level cutoff point was 253.34 µg/ml for the prediction of kidney fibrosis and 306.36 µg/ml for the prediction of moderate-severe renal fibrosis. LOX expression was significantly upregulated (2.3-2.6-fold and 6-fold, respectively) in vitro and in vivo in 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 has potential to be a noninvasive 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.

PO0620

Proximal Tubule Albumin Uptake: Potential Role for Endothelin System in Sickle Cell Disease Patients
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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<sub>α</sub> 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<sub>α</sub> receptor antagonism preserves albuminuria by preserving the expression of proximal tubular albumin-associated transporters in proximal tubule (PT) cells.

Methods: Male C57BL/6 and 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 8 decreased megalin (53% reduction) and doubled NHE-3 expression. Pre-treatment with the ET<sub>α</sub> antagonist, BQ123 (1 µM), preserved megalin expression and had no effect on NHE-3. Moreover, selective ET<sub>α</sub> 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 ET<sub>α</sub> 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 trafficking. We suggest that PT ET-1 receptor signaling contributes to albuminuria in SCD.

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Underline represents presenting author.

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APOL1 Risk Variants Mediate Increased Oxidative Phosphorylation Complexes Biogenesis and Mitochondrial Dysfunction

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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 functionality was assessed in targeted 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 APOL1-6xHis 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 HEUPECs) when compared to G0/G0 carrying HEUPECs. We observed reduced mitochondrial function in the presence of increased OXPHOS complexes in G1/G2 HEUPECs. Using TEM, reduced mitochondrial matrix density and increased mitochondrial area were detected in G1/G2 HEUPECs. Hyperbranched mitochondria in G1/G2 HEUPECs were identified 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 6xHis tagged APOL1 expression. We found the mRNA level of cardiolipin synthase (CRLS1) was significantly increased in G1/G2 HEUPECs, which is consistent with the overexpression of OXPHOS complexes in G1/G2 HEUPECs.

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.

NIDDK Support, Private Foundation Support

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 hyperkalemia, especially in patients with kidney disease. The cellular mechanism behind mineralocorticoid action and interrelated function has recently been developed with pronounced antibiotic activity at doses which have only limited effect on the potassium homeostasis. The exact molecular transcriptional targets of spironolactone and finerenone, however, remain unknown. Since there are more than 20 different receptor subtypes in vivo, single cell RNA and single cell epigenome (ATAC) analysis can help to define transcriptional targets.

Methods: We treated uninephrectomized, Sprague-Dawley rats injected with DOCA and spironolactone group. Single-nuclei open chromatin and gene expression analysis highlighted transcriptional targets of aldosterone, spironolactone and finerenone.

Funding: NIDDK Support, Commercial Support - Bayer AG

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 epigenomic 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 integrated the epigenetic annotation to identify causal variants and target genes which were further tested by CRISP techniques in zebrafish.

Results: We identified genome-wide functional elements and thousands of interactions between the distal elements and target genes. The results revealed that risk variants for renal tumor and chronic kidney disease were enriched 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.

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 cardiomypathy. We have recently demonstrated that adipocyte dysfunction and uremic cardiomyopathy developed in partial nephrectomy mouse model, were significantly ameliorated by adipocyte-specific expression of NaKtide, 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 in vitro studies, mouse adipocytes were subjected to oxidized LDL (oxLDL) or index suflate (IS) with or without pNaKtide treatments. Partial nephrectomy was performed in C57Bl6 mice in order to produce experimental uremic cardiomyopathy. Specific expression of NaKtide 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 with 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 drug-induced apoptosis and drug metabolism contribute the profound impact on the pathogenesis of uremic cardiomyopathy. The overall analysis showed a widespread normalization of gene expression by pNaKtide/adipose specific NaKtide treatments that were altered in uremic cardiomyopathy.

Conclusions: The study provides a detailed genome-wide molecular information about adipocyte function in relation to uremic cardiomyopathys 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

Transcriptomic Profiling Identifies Potential Mediators of Tubular Injury Sensitization of Glomeruli to Subsequent Second 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: 1 expressing human CD25 receptor on podocytes and Diphtheria toxin receptor on proximal tubular cells) and Nep25/DTR (n=5 per group) were used. Tubular injury was induced by injecting diphtheria toxin, followed by uninephrectomy (Nx) 4 weeks later and induction of glomerular injury

Funding: Private Foundation Support
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+ vs Nep25/DTR-. GO of biological processes showed involvement in 13 processes, 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 (Serpine1), alpha-1-antitrypsin 1-2 (Serpin1b), protein Z-dependent protease inhibitor (Serpine10) and complement C4b (C4b).

In addition, members of the non-canonical Wnt signalling pathway Wnt-9a (Wnt9a) and Wnt-10a (Wnt10a) and their interactors latent transforming growth factor beta binding protein 2 (Ltbp2) and VANGL planar cell polarity protein 2 (Vangl2) 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+

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=0.0014) without a significant change in Ang II levels (272 vs. 299 fmol/mg protein). To verify the kidney uptake of our ACE2 variant SPECT/Micro-CT imaging was performed. After the injection of radiolabeled ACE2-ABD kidney uptake was clearly seen (red) (Figure).

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.

Results: Injury to the kidney increased MLL1 and menin expression and H3K4 monomethylation (H3K4me1) in renal tubular epithelial cells and fibroblasts. Administration of MI-503, a highly selective inhibitor of the MLL1/menin complex, attenuated renal fibrosis and expression of α-smooth muscle actin, fibronectin and collagen I. Treatment with MI-503, MLL1 siRNA or menin siRNA also inhibited TGFβ1 and serum-induced activation of epithelial-mesenchymal transition (EMT) in vitro. Moreover, UUO injury induced epithelial expression of phospho-histone 3 at Serine 10 and expression of profibrotic factors, TGFβ1 and connective tissue growth factor; and blocking the MLL1/menin complex with MI-503 inhibited these responses. Finally, MLL1 inhibition reduced expression of snail and twist, two transcription factors involved in the development of EMT and renal fibrosis and the expression of proliferating cell nuclear antigen, cyclin D1 and p27 in fibroblasts.

Conclusions: Our data suggest that targeting disruption of the MLL1/menin complex can attenuate renal fibrosis through inhibition of EMT and fibroblast activation/proliferation.

Funding: NIDDK Support, Other NIH Support - National Natural Science Foundation of China
PO0629

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 (Erdj1, Gp2), cytoskeletal/extracellular matrix fibers (Lamal, Ctnbp2) and signal transduction (Camkb2, Ppren2). 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 TALs cells towards a fibrosis program. These findings may contribute to understanding the pathogenesis of CKD progression.

Funding: NIDDK Support, Veterans Affairs Support

PO0630

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 retrobulbar anaesthesia with ADR and 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 maximizing 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 changed during the first 24h of culture, after which they declined. Metabolic rates for glutamate, 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 perturbed intracellular metabolic levels: nucleosides adenosine (+159%), and inosine (+171%), increases in 1,3-BPG (+194%), and changes 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 arachidonate (+107%), as well as the depletion of several phosphatidylethanolamine 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

Table 1. Body weight, hematocrit, and blood chemistry results

Data are presented as the mean ± SD.

* p < 0.05 vs. the sham group

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

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

Anti-Interleukin 22 Antibody Relieves Angiotensin II-Induced Renal Injury in Mice Through Inhibiting NLRP3 Inflammasome Activation

Rong Tang, Xiaoying Hospital Central South University, Changsha, China.

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 via inhibiting NLRP3 inflammasome activation in angiotensin II (Ang II) induced hypertensive renal damage in 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 injected intraperitoneally every other day with saline, recombinant mouse IL-22 (rIL-22; 20 μg/kg), mouse anti-IL-22 monoclonal antibody (anti-IL-22 mAb; 1.25 μg/mouse) or isotype IgG. So mice were divided into 5 groups: control, Ang II, Ang II+rIL-22, Ang II-anti-IL-22, Ang II-IgG. 28 d after Ang II infusion, all mice were euthanized. Blood pressure, urinary albumin/creatinine ratio, serum creatinine (Scr) and renal histopathology were measured. NLRP3, cleaved caspase-1 and IL-1β in kidney were detected by western blot. Renal inflammatory factors were detected by ELISA, IL-22 and IL-22R1 in kidney were detected by western blot.

Results: IL-22 and IL-22R1 Levels were elevated in kidney of Ang II-induced mice. Anti-IL-22 mAb therapy ameliorated proteinuria excretion, Scr and renal pathological damage in mice with established hypertensive renal injury. Blood pressure in Ang II-infused mice was also decreased after the treatment of anti-IL-22 mAb. In addition, anti-IL-22 mAb reduced NLRP3, cleaved caspase-1, IL-1β, TNF-α and IL-6 expression in kidney, along with inhibition of renal fibrotic related factors expression.

Conclusions: Anti-IL-22 antibody can reduce renal inflammation and fibrosis in Ang II-induced hypertensive mice, which may be through suppression of NLRP3/caspase-1/IL-1β pathway, suggesting it might exert therapeutic potential for the treatment of hypertensive renal injury.

Funding: Government Support - Non-U.S.
interaction between NKA-α and CD40 that was enhanced by activation of the NKA-α (c-Src signaling) and sUA through expression level and endocytosis of NKA-α and CD40 might be involved to control signaling strength.

**Funding:** NIDDK Support

**P00636**

**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 inflammation in gouty arthritis, soluble uric acid (sUA) in this context is discrepant. 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 vitro, Alb-creERT2; Glut9lox/lox and Glut9creERT2; Alb-creERT2; Glut9lox/lox control mice were injected with tamoxifen and placed on a Chow diet with no sUA 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 microrystal contaminants triggering IL-1β release. Solubilizing UA with NaOH avoided such artifact. This microrystal-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, Alb-creERT2; Glut9lox/lox mice with HU (serum UA of 9-11mg/dL) showed a suppressed inflammatory response to MSU crystals compared to Glut9lox/lox controls without HU.

**Conclusions:** We unravel a technical explanation for discrepancies in the published literature on monocyte responses 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 without HU.

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

**P00637**

**PP2A Increases 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 PP2ACre ablation.

**Results:** We observed a significantly increased induction of PP2Acre in macrophages. We then generated mice with macrophage-specific deletion of PP2Acre. These mice developed less renal fibrosis as indicated by less macrophage accumulation, tubular atrophy or extracellular matrix deposition. In cultured cells, the deficiency of PP2Acre in macrophages resulted in decreased cell motility by inhibiting the activity of Rap1. Furthermore, TNFα production was downregulated in macrophages with PP2Acre-deficiency and co-culture of PP2Acre-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.

**P00638**

**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-arrestins signaling in renal fibrosis process and the role of lysyl oxidase (LOX) in the AT1R-β-arrestin pathway. Moreover, in normal rat kidney tubule epithelial cells (NRK-52E) treated with SII in vitro, inhibition of JMD3 activity reduced EC proliferation and migration. Suppression of JMD3 enhanced the level of histone H3K27me3 promoting its binding to the promoter of EC markers (VE-cadherin and eNOS). These responses resulted in EndMT and VSMC proliferation. Moreover, the expression of JMD3 is reduced through TGFβ1/β-arrestin-1 signaling pathway. In AVFs from ESRD patients, the decreased expression of JMD3 in ESRD patients 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/β-arrestin-1/JMD3 signaling exist in AVFs which epigenetically regulates EC differentiation and barrier function leading to neointimal hyperplasia of AVF in CKD.

**Funding:** NIDDK Support

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

Underline represents presenting author.
**PO0640**

Renal Macrophage Infiltration Precedes Macrophage to Myofibroblast Transition and 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 (MPT) 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 macrophage activity and MPT in the kidney.

**Methods:** We used a clinically relevant, repeated low dose model of CDDP-KI to characterize the immune response and MPT in the kidney following cisplatin treatment.

**Results:** Flow cytometric analysis revealed significantly increased numbers of renal infiltrating CD68+ inflammatory monocytes and F4/80+ infiltrating macrophages 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+ CD286+ 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 MPT. 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

**PO0641**

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) discarded due to incompatibility (n=7). Renal microvasculature (MV) was studied in vitro using micro CT after infusing contrast agent into the renal artery. Kidneys were also compared for angiogenic gene and protein expression.

**Results:** Age and sex were comparable between RVD and DK. RVD had reduced density of medium-sized (0.2-0.3mm) MV vs. donor kidneys (Fig. A-B, p=0.04), whereas density of small (0.02-0.2mm) and large (0.3-0.5 mm) MV was similar. Vascular tortuosity ratio was higher in RVD vs DK (Fig. C, p=0.05). The number/tubule of peritubular capillaries (PTC) was significantly lower in RVD, as was CD31+ area, whereas numbers of new angiogenic vessels (β3 integrin+, Fig. D) and pericytes were higher. Renal fibrosis and MV remodeling (media/lumen) were greater in RVD, as were oxidative stress and angioptin-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. Angioptin-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.

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*Underline represents presenting author.*
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 cyclodextrin, 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 nephrapathy 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 ADP and progammed ADR challenged mice, Cpd A and G reduced ACR by 8% and 30-fold, respectively, compared to controls. In Col4A3 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 the kidney cortex of ADR challenged mice strongly correlated with albuminuria. In both the FSGS and Alport mouse models, Cpd G significantly reduced proteinuria, kidney histology, kidney and heart biomarkers and kidney gene expression.

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 - Hoffmann-La Roche, Boehringer Ingelheim, Private Foundation Support

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: Adipin-induced 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 adömine 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, during 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 6.0 ± 0.3 mg/dl (week 7) 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 9 (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 9 (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 9 and 23% lower at week 9 in metformin-treated CKD rats compared to vehicle treatment (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 kidney-induced CKD. Our data do not present new evidence for a beneficial effect of canagliflozin on progression of non-diabetic CKD.

Funding: Commercial Support - Bayer AG

PO0645
The Novel Soluble Guanylyl Cyclase (sGC) Activator Runcaciguat Attenuates Hypertensive Cardiorenal Rat Diseases
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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 heme-independent 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=13/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-NNAME 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 cardiorenal 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

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
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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 pathways. Finerenone has direct anti-fibrotic properties resulting in reduced kidney fibrosis in vitro as well as in vivo. Here, we investigated potential 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 (C57Bl/6j, 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 empagliflozin (10 and 30 mg/kg), or in a direct comparison of both drugs. Intersitial myofibroblast accumulation was quantified via alpha-smooth muscle actin (αSMA) and interstitial collagen deposition via Sirius red fast green staining. Secondary analyses included kidney mRNA expression of inflammatory and fibrotic markers and pathways.

Results: Myofibroblast accumulation was dose-dependently reduced in finerenone-treated mice (-22% @ 3 mg/kg, p=0.1; -41% @ 10 mg/kg, p=0.002) as well as collagen deposition (-22% @ 3 mg/kg, p=0.1; -44% @ 10 mg/kg, p=0.001). These anti-fibrotic effects of finerenone on protein level were matched on mRNA expression level (including collagens type III and IV). In contrast, treatment with SGLT2 inhibitor strongly increased urinary glucose excretion but had neither significant effects on kidney myofibroblasts (0% @ 10 mg/kg, p=0.7; -10% @ 30 mg/kg, p=0.99) nor on collagen deposition (-6% @ 10 mg/kg, p=0.9; -9% @ 30 mg/kg, p=0.8). In finerenone-treated mice reduced kidney fibrosis was parallelly by reduced kidney PAI-1 expression (-19% @ 3mg/kg, p=0.3; -41% @ 10 mg/kg, p=0.002).

Conclusions: Finerenone has direct anti-fibrotic properties resulting in reduced myofibroblast and collagen deposition in a mouse model of progressive kidney fibrosis.

Funding: Commercial Support - Bayer AG
PO0647
The Novel Potent and Selective Vasopressin V1a Antagonist BAY237949 Blocks Arginine Vasopressin-Mediated Decline of Renal Blood Flow and Tissue Oxygenation

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Background: Hypoxia is a major contributor to kidney disease progression. Arginine vasopressin (AVP) potentially induces renal medullary vasoconstriction via vaso-vascular receptors resulting in reduced renal blood flow (RBF). Here we characterized the kidney-protective properties of a recently identified, potent and selective V1a receptor antagonist.

Methods: BAY237949 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 BAY237949 for human V1a receptor (IC50 1:1.2 nM, IC50 1:170 nM). BAY237949 mediated dose-dependent relaxation (IC50 = 3.1 nM) of isolated rat A. renalis vessel rings precontracted by AVP. BAY237949 improved the AVP-mediated reduction of perfusate venous flow (figure) without affecting urinary volume. In vivo, infusion of AVP significantly increased mean arterial pressure (CON: 97±1, AQP: 135±12, means±SD) which was normalized by BAY237949 in a dose-dependent manner (90±5; p<0.0001). Infusion of AVP reduced both renal perfusion (CON: 1008±8, AQP: 758±107) and tissue oxygenation (CON: 27±4, AQP: 17±4). BAY237949 dose-dependently restored RBF (960±30; p<0.0001) and increased pO2 (25±4; p<0.0001).

Conclusions: BAY237949 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 & endothelial dysfunction in patients with cardiovascular disease (CVD) & chronic kidney disease (CKD). Apabetalone is an inhibitor of BET proteins - epigenetic readers modulating gene expression in pathological VC & inflammation. We studied apabetalone’s impact on tissue non-specific ALP (TNALP) expression in cell culture, then analyzed serum ALP in phase 2 trials.

Methods: Expression of TNALP (gene symbol APLP) was measured in primary hepatocytes, HepaRG, HepG2, primary mesangial cells (MC), vascular smooth muscle cells (VSMC) & vascular 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 ALP 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 ALP expression & TNALP enzyme activity (p<0.001). ALP was suppressed 50-70% in 3 vascular endothelial cell types with apabetalone. In VSMCs, apabetalone lowered ALP 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 (-0.001), in reducing patients in the CKD subgroup (p<0.001). Notably, 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<0.0091-13DUL); similar associations were observed at 24-26 weeks (HR 0.66 per 1-SD ALP 95% CI 0.43-0.99 p=0.045, 1-SD=14UL).

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 renal IR.

Methods: To induce severe chronic TID after renal IR, unilateral renal ischemia and reperfusion for 60 min was performed via clamping of right renal pedicle using four types of male mice; wild type mice (hL-FABP+/+AT1a+), human L-FABP chromosomal transgenic mice (hL-FABP+/+AT1a+), AT1a knockout homo mice (hL-FABP+/+AT1a−), and generated hL-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 hL-FABP+/+AT1a+, hL-FABP+/+AT1a− and hL-FABP−/− AT1a− mice, the degrees of both atrophy and TID were significantly ameliorated in the IR-kidneys of the hL-FABP+/+AT1a+ mice. Systolic blood pressure levels in the hL-FABP−/− AT1a− mice were similar to 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 (SB) medicine for the treatment of EH, designated as SYNB8802.

Methods: SYNB8802 is an engineered bacteria derived from Escherichia coli Nissle 1917 (EcN) that has been engineered to metabolize oxalate to formate and CO2 in vivo.

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.
A Novel Small Molecule Modulating the Mitochondrial NEET Proteins Improves Inflammation and Fibrosis in Kidneys of Nonalcoholic Steatohepatitis Mice


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 picrosirisin 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 peritubular 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.

PO0653

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 uric acid from CKD patients impairs cardiomyocyte (CM) relaxation and contraction by inducing endothelial cell dysfunction and that 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 uric acid 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.

PO0652

SIRT3 Deacetylates PDH1α 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 (PDH1α) 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 (IR) 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 PDH1α were transfected into PTCs.

Results: Acetylation showed that the majority of proteins were hyper-acetylation after UUO. GO enrichment analysis revealed that PDH1a was the most obviously enriched GO term. Immunoprecipitation analysis confirmed that PDH1α acetylation was enhanced after UUO or IR operation. Activation of SIRT3 by HKL could block the hyper-acetylation of PDH1α, restored PDH enzyme activity, and inhibited the phosphorylation of PDH1α in mice with UUO or IR. On the contrary, Sirt3 KO mice had more acetylated PDH1α, more phosphorylated PDH1α and defective PDH enzyme activity. In vitro, increased PDH1α acetylation was accompanied by reduced PDH enzyme activity and increased PDH1α phosphorylation in PTCs after TGF-β1 stimulation. Activation of SIRT3 by HKL repressed the effect of TGF-β1. Inhibition SIRT3 activity by 3-TYP or SIRT3 siRNA transfaction have the same effect as TGF-β1. K149, K267, K385 were identified as the main potentially lysine acetylated sites in PDH1α.

Conclusions: In summary, our data showed that mitochondrial proteins involved in regulating energy metabolism were acetylated and targeted by SIRT3 in PTCs. The deacetylation of PDH1α at lysine 385 by SIRT3 plays a key role in metabolic reprogramming in renal fibrosis.

Funding: Government Support - Non-U.S.
differences in whole kidney analysis of inflammatory cytokine qPCR between them, renal macrophage CD148KO mice showed high expression of 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 the LRG1 expression to the TGF-β signaling in RTECs leading to renal fibrosis progression.

Methods: We examined the expression of LRG1 in the tubulointerstitial 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, Lrp1−/−, and Pan-LRG1−/− 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 NF-κB 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 Lrg1 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-understood in 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 Extraction kit (Cellular Dynamics). The purified nuclei were microdissected in the proximal tubular segments and used for snRNA-seq. The sequencing libraries were generated using Illumina NextSeq 550. Downstream bioinformatics analyses used Seurat.

Results: A total of 23,885 nuclei were analyzed. PTC’s 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, dedifferentiated-intermediate, dedifferentiated-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 processes 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 responses, and suggest potential therapeutic targets in specific cellular populations in renal fibrosis.

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 datasets. 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 drugability, in line with AstraZeneca’s 5R framework. We are undertaking in vitro studies via genetic modification in selected cell types to generate target-specific CKD-linked readouts. Subsequently, we will employ in vivo studies to confirm the mechanism of action for targets that had shown successful in vitro readouts. Eventually, we will progress targets with compelling novel biology within our renal portfolio.

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 with robust but selective deletion of Twist1 mRNA >90% vs. WTs in CD4- T cells, and >85% vs. WTs 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 WTs as quantitated by western blot for Col1 (0.75 ± 0.06 vs 1.0 ± 0.05; p = 0.02) and αSMA (0.65 ± 0.01 vs 1.0 ± 0.08; p = 0.01) and by RT-PCR for Col1 (0.69 ± 0.08 vs 1.0 ± 0.10; p = 0.048), fibronectin (0.76 ± 0.07 vs 1.0 ± 0.06; p = 0.03), TGFβ1 (0.73 ± 0.08 vs 1.00 ± 0.04; p = 0.004) and PAI-1 (0.47 ± 0.06 vs 1.0 ± 0.09; p = 0.001).

Twist1 TKO mice also showed attenuated kidney injury as indicated by NGAL mRNA expression (0.55 ± 0.06 vs 1.0 ± 0.16; p = 0.04). Twist1 can suppress pro-inflammatory mediators such as TNFα and IL17A in T cells, and expression of these cytokines was significantly lower in Twist1 TKO kidneys compared to WTs.

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 adults in the US have CKD. In 40% of cases, CKD leads to irreversible loss of kidney function, end-stage renal disease. Pre-biotic bacterial 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 sub-groups (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 BlaszGZO 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. The pathway of indole metabolism and have immunostimulatory effects. Experiments to validate effect of Lactobacillus in germ-free mice are underway.

Conclusions: Resistant starch slows down the progression of chronic kidney disease in 5/6 nephrectomy model. For the first time we demonstrate decrease in kidney fibrosis during RS supplementation. Metaproteomics allows to discover molecular mechanisms and bacterial species responsible for beneficial effects of RS. MST2 analysis allows for clear visualization of the most important connections within the bacterial co-abundance network.

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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 (SDM c and cortex (SDM c and medulla (SDM m) and medulla (SDM m). First, we report significantly higher membrane potential in SDM compared to SDF (p < 0.001). H2O2 levels were elevated in both the cortex (SDM c) and medulla (SDM m) mitochondria compared to SDF (p < 0.01). Interestingly, mitochondrial superoxide production was increased in the medulla compared to the cortex for both SDM c and SDM m, while SOD2 expression was lower (p < 0.001). Antioxidant capacity was lower in SDM c tissues compared to all other groups, which is consistent with higher H2O2 levels (58 ± 7 vs. 35 ± 1 pg/mg protein, p < 0.001). Ex vivo analysis showed similar lipid peroxide radical levels in males and females, but detected different renal 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 may affect the predisposition to kidney disease development later in life.

Funding: Other NIH Support - NIHBI, Commercial Support - Dialysis Clinics Inc

PO0661
Renal Involvement in Coronavirus Disease 2019 (RECORD): 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 14.5% 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 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.
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 analyzed the available literature to develop a national model of CRRT demand and capacity to estimate shortage. In sensitivity analysis, we varied parameters influencing CRRT demand and capacity. To estimate non-COVID-19 CRRT demand, we applied the prevalence of acute kidney injury (AKI) requiring CRRT, and the AKI incidence 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

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 tubules. However, involvement of SARS-CoV-2 in acute kidney injury (AKI), however involvements of SARS-CoV2 in tubular injury has not been fully understood. 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, FDNB, α1-MG, and L-FABP) 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), α1-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 (0.37 vs non-severe: 0.14g/gCr), α1-MG (33.3 vs 10.1U/L), β2MG (17134.4 vs 1168.5ug/L), α1-MG (63.6 vs 12.4mg/L), L-FABP (57.9 vs 7.5ug/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.
0.067 mcg/kg/min (95% CI 0.047-0.101). Intradialytic hypotension (SBP decrease ≥20 mmHg) occurred in 10 (9.7%) of 104 PIRRT procedures, and 13/101 (13%) PIRRT were discontinued due to severe hypotensive episodes, with 2 patients switched to CRRT. System clotting was a frequent event during the first three weeks of March (7 events in the first 30 PIRRT procedures) until concomitant enoxaparin (0.5 mg/kg/day) and regional anticoagulation (unfractionated heparin 500 U/h) were employed. During follow-up, 3 patients (36%) recovered from AKI and respiratory failure, 3 (21%) died, and 6 (43%) are still hospitalized at the time of this report. In those who recovered renal function (9/14), the median number of PIRRT sessions was 6 [IQR 5-8]. Table shows changes in our PIRRT protocols during the COVID-19 outbreak.

Conclusions: PIRRT therapy was feasible and appropriate in most patients who exhibited an exuberant inflammatory response, severe hemodynamic instability, and hypercoagulability.

PO0666
COVID-19 AKI: Risk Factors and Markers of Disease from a Large UK 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. A 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, increasing with stage of AKI (p<0.001). AKI was associated with ICU admission (27% vs 10% p<0.001), requirement of non-invasive ventilation (14% vs 4%) (both p<0.001). Prior diabetes (18% vs 8%), hypertension 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.

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 pathogenic 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.

PO0667
High C-Reactive Protein and D-Dimer on Admission Predict the Development of AKI in Patients Hospitalized with COVID-19
Sandeep Venkataraman, Zhiying You, Jessica B. Kendrick. University of Colorado Denver School of Medicine, Aurora, CO.

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 diagnosis 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 on 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. Ninety-five 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 ACE/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 FEU 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 nephrotoxic medications and close monitoring for the development of AKI.

PO0668
Hematuria and Elevated Lactate Dehydrogenase Are Associated with AKI in Hospitalized COVID-19 Patients
George Thomas, Georges Nakhoul, Jonathan J. Taliercio, Tushar J. Vachharajani, Sevag Demirjian. Cleveland Clinic, Cleveland, OH.

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 with no 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 pathogenic 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.
patient had BMI greater than 35 kg/m² and a history of appendectomy. Median duration of
follow-up from time of PD catheter placement was 37 days (IQR 32-37.5), death-censored
median follow up was 35 days (IQR 30-37.5). The median time from AKI to death was
17 days (IQR 14-22). Median time from AKI to renal recovery was 34 days (IQR 21-40).

Conclusions: In our AKI-PD cohort, the mortality rate was noted to be 36% and 45%
for patients with renal recovery observed. Two of our patients converted from CRRT to PD due to repeated filter
clogging. We did not observe any bleeding complications in our cohort. We hypothesize
that hypercoagulable COVID-19 patients may be excellent candidates for PD potentially
due to lower risk of bleeding complications.

Table 1.

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 severe personnel shortages related to illness. Studies have shown no difference in
clinical outcomes between HD and PD for AKI. We describe our rapid adoption of an
acute PD program during the COVID-19 surge.

Case Description: At Montefiore Medical Center (MMC), in Bronx, NY, the first patient with COVID-19 was admitted on March 11, 2020. As the number of patients with AKI 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 MMC. From April 1st to April 22nd, 30 patients were initiated on PD with the help of surgery and interventional radiology who placed Trenchhoff catheters at bedside and under fluoroscopy, respectively. Of those 30 patients, 14 died, 8 were discharged, and 8 were still hospitalized as of May 14, 2020. Of the 8 patients discharged, 3 were still on PD and 5 had renal recovery (all were able to stop dialysis and 4 returned to baseline creatinine). Of the 8 patients still hospitalized, 4 patients were switched to IHD (3 due to fluid retention and 1 due to PD catheter malfunction), and 4 patients had renal recovery and were able to stop dialysis. Challenges to this program included lack of nurse training, difficulty securing supplies and irregular therapy provision and underdosining due to staffing shortages. Patients on medical wards received more frequent exchanges and did not have significant volume overload and metabolic derangements like those patients requiring intensive care.

Discussion: Despite challenges, we demonstrate the feasibility of acute PD as an
alternative to HD in patients with COVID-19-associated AKI. In this single-center experience, we found that acute PD was more effective for stable patients on the wards than for patients with severe illness requiring intensive care.
Results: The 20 patients initiated early RRT after 6.4±3.6 days from ICU admission. The median time of renal pathology was 50±42.2 hours, 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 cumulative risk of death of early RRT patients was lower than control group (50.5% vs 66.7%, p=0.040). Univariate analysis and Cox proportional hazard regression also confirmed that early initiation of RRT was an independent risk factor (HR 0.21, 95% CI 0.06-0.74, p=0.014) for in-hospital all-cause death of severe Covid-19 after adjusting by SpO2, lymphocyte proportion, albumin, LogNT-proBNP, LogInterleukin-6, mechanical ventilation and use of glucocorticoid. A figure that shows the course of disease indicates that early initiation of blood purification may decrease the death without multiple organs injury (39% vs 0%, p=0.037).

Conclusions: Early initiation of blood purification could probably reduce the mortality of severe Covid-19. It was implied that it could delay occurs and reduce degrees of target organs injuries by cutting the peak load of cytokine storm. Further research in basic and clinical were needed to clarify the mechanism of blood purification in cytokine storm-related diseases.

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: Early reports of acute kidney injury (AKI) associated with COVID-19 have claimed high incidence of proteinuria. If so, it may suggest an AKI pathogenesis not solely related to ischemic acute tubular injury (ATI). We hypothesized that those claims result from observation bias. Therefore, we sought to investigate the rate of de novo proteinuria in AKI associated with COVID-19 (CoV-AKI) compared to that of AKI in the pre-COVID-19 era (non-CoV-AKI).

Methods: Hospitalized patients with CoV-AKI entered the cohort (n=161). As a control-CoV-AKI group (n=186), we accessed a database of patients with AKI who underwent urinary sediment microscopy due to suspicion of an intrinsic cause of AKI (Sedi-AKI cohort, 2017-2019). We examined the incidence of proteinuria of any degree (S umoji ≥1+ dipstick), significant [urine protein-to-creatinine ratio (UPCR) ≥0.5-3.0 g/g or ≥3+ dipstick] or overt [UPCR ≥3.0 g/g + 3+ dipstick].

Results: In CoV-AKI and non-CoV-AKI, respectively, Women were 62% and 63% (p=0.56). Black race was more common in CoV-AKI (75% vs. 35%; p=0.0001). ATI (ischemic and/or toxic) was the presumed cause of AKI in 75% and 71% of CoV-AKI and non-CoV-AKI, respectively. Incidence of de novo significant or overt proteinuria were 123/148 (83%) vs. 8/186 (4.3%), respectively. Incidence of any, significant or overt proteinuria were 123/148 (83%) vs. 37/186 (20%) respectively.

Conclusions: Early initiation of blood purification may decrease the death without multiple organs injury (39% vs 0%, p=0.037).

PO0675
AKI due to COVID-19 in the Intensive Care Unit: Analysis of a Brazilian Center


Background: The kidney may be affected by coronavirus (COVID-19) in the setting of acute kidney injury (AKI) or glomerular diseases. Data about AKI in Intensive Care Unit (ICU) patients of Latin-America are scarce. The aim of this study is evaluate the risk of AKI, dialysis (HD) and death in ICU patients diagnosed with COVID-19 in a brazilian center.

Methods: Analysis from medical records of ICU patients with diagnosis of COVID-19 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-19 were analyzed. There was predominance of male (64.2%), median age of 66.3 years. The previous diagnosis of hypertension, diabetes, smoking, high cholesterol, 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 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 one's 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=0.05), 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-19 patients, it was related to hypertension, support therapies and use of hydroxychloroquine. 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 Desiree Garcia Anton,2 Diana Aguirre, Denisse Arellano-Mendez,3 Franco H. Cabeza Rivera,4 Julio A. Gutierrez-Prieto,5 Blanca Martinez-Chagolla,6 Sonia Rodriguez Ramirez,7 Carmen Velasco-Casado,8 GlomCon Latin America Working Group 1Especialidad de Nefrologia, Hospital General Regional 46, Guadalajara, Mexico; 2University of Mississippi Medical Center, Jackson, MS; 3Hospital General de Mexico, Mexico; 4Unidad Medica de Atencion Ambulatoria 254, IMSS, Morelia, Mexico; 5Hospital Central del Estado de Chihuahua, Chihuahua, Mexico; 6Hospital General "Dr. Miguel Silvia ", Morelia, Mexico; 7Multi-Organ Transplant Program, University Health Network, Toronto, ON, Canada; 8Pathology Department, University Health Network, Toronto, ON, Canada.

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. Between May 20-27, 2020 from sixteen Spanish speaking Latin American countries divided into 6 categories. We present the results for the AKI category.

Results: 430 responses were obtained of which 360 (84%) were considered for analysis. Of the participants, 54% reported the prevalence of AKI to be <5%, while 32% estimated it at 6-10%. The majority of AKI in these patients was stage 3 according to 31% of the respondents. Roughly half of the nephrologists witnessed new onset proteinuria which was almost exclusively (96%) sub-nephrotic. The majority (64%) reported no hematuria. Half of the participants (59%) reported that renal replacement therapy (RRT) was never or rarely required. Intermittent hemodialysis was the main RRT used reported by 88% of those surveyed followed by continuous renal replacement therapy (33%), peritoneal dialysis (24%) and prolonged intermittent hemodialysis (19%). The most common complications during RRT were hypotension (60.3%) and circuit clotting (36.6%). Over one third of the participants (35%) estimated the mortality of patients with AKI and COVID to be <20%.

Conclusions: Our survey highlights potential differences in the presentation, management and outcomes of AKI in patients with COVID-19 in LA; among those, a lower prevalence, higher need for RRT and lower mortality. More studies are warranted to better understand AKI in hispanic COVID-19 patients as well as its distinct characteristics compared to the rest of the world.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
**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 any increase in risk factors places 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 preadmission CD4 count and HIV viral load. AKI was defined and staged using KDIGO criteria. Fisher and Wilcoxon tests were used to compare differences in 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 was 47 years and 83% had a suppressed HIV viral load (<40 copies/mL). After excluding 11 with ESKD, AKI incidence was 50%. Those with AKI were older (63 [SD 9.5] 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 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 the evidence about the etiology of COVID-19 encountering acute kidney injury (AKI) is unknown. Moreover, the efficacy of different treatments that COVID-19 patients undergo needs to be explored. In this study, we aimed to explore these questions.

**Methods:** A single-center, retrospective study was conducted in which 96 patients with COVID-19 were enrolled. Epidemiological, clinical, and laboratory characteristics, as well as treatments and patient outcomes were described. Characteristics were compared between severe cases and critical cases. Relevant factors of AKI were filtrated, and the treatment efficacy was also evaluated. Results: A total of 6 patients (6.3%) died during hospitalization. Four patients (4.2%) developed AKI, among which 3 patients (75%) died. Statistical analysis indicated that AKI was not common in COVID-19 patients without underlying kidney disease, but was related to mortality. Age, severity of disease, procalcitonin, C-reactive protein and interleukin-6 were correlated with AKI onset in COVID-19 patients, while lymphocyte count and estimated glomerular filtration rate at admission were inversely related to the development of AKI.

**Conclusions:** In conclusion, AKI is not common in COVID-19 patients without underlying kidney disease but related to mortality.

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

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**PO0679**

Acute Peritoneal Dialysis with Percutaneous Catheter Insertion for COVID-19-Associated AKI in Intensive Care: Experience from a UK Tertiary Centre

Dandisobra B. Braidie-Azikiwe, Elaine Bowes, Kate Bramham, Caroline Tuley, Eirini Lioudaki, Hugh Cairns, Claire C. Sharpe. King’s College Hospital, London, United Kingdom.

**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 hemodiafiltration therapies (CVVHFD) 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 Seldinger 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 percutaneous insertion was 90.2% (IQR 77.5, 100).

**Conclusions:** PD provides a safe and effective alternative to CVVHFD 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**

- 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

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**PO0680**

Adding Heparin to Citrate in Continuous Renal Replacement Therapy May Extend Filter Lifespan in COVID-Related AKI


**Background:** COVID may predispose patients to thrombosis and lower filter lifespan. Association between D-dimer level and DD. There are considerable challenges providing RRT for large numbers of patients with COVID-19 and alternatives to continuous veno-venous hemodiafiltration therapies (CVVHFD) 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 Seldinger 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 percutaneous insertion was 90.2% (IQR 77.5, 100).

**Conclusions:** PD provides a safe and effective alternative to CVVHFD 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**

- 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

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

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filter clotting per patient-day. ACD/Hep also presented less clotting than ACD group (ACD:Hep: 41% vs ACD 106% p < 0.05). In COVID patients, median TFC was 33.5 h [17.0;72.0]. ACD:Hep [0.90 [13.68-65.5], 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;68.0], ACD/Hep low DD: 67.0 h [26.0;72.0]). Figure 1. There was statistically significant correlation in between DD and TFC in ACD patients, but not in ACD/Hep group.

Conclusions: Hemox may extend filter lifespan in CRRT, and this benefit seems to be greater in high DD patients.

Funding: Government Support - Non-U.S.

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 COVID19 has not been well described. AKI has been associated with increased mechanical ventilation times. Recent publications have shown a strong association of COVID19-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 more 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 in creatinine from within 48 hours). AKI stage was defined by KDIGO criteria (0.3 mg/dL increase in creatinine from baseline). Total MV time was measured from initiation to extubation/continuous renal replacement therapy. Ventilator days were calculated using Hospital Episode Submission Data. AKI was defined per KDIGO criteria (0.3 mg/dL increase or greater than a 50% increase from the baseline Cr) between the current and baseline Cr. AKI stage was defined as per KDIGO criteria (0.3 mg/dL increase). AKI stage was defined by KDIGO criteria (0.3 mg/dL increase or greater than a 50% increase from the baseline Cr) between the current and baseline Cr. AKI stage was defined as per KDIGO criteria (0.3 mg/dL increase). AKI stage was defined by KDIGO criteria (0.3 mg/dL increase or greater than a 50% increase from the baseline Cr) between the current and baseline Cr. AKI stage was defined as per KDIGO criteria (0.3 mg/dL increase or greater than a 50% increase from the baseline Cr).

Results: Over 5000 AKI alerts were generated for this period for 4390 unique admissions. 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: We analyzed 318 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).

Funding: NIDDK Support

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 running to 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 1 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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PO0685

Characteristics and Outcome of AKI Needing Dialysis with COVID-19 Infection


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 hemodialysis (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, other organ injuries, length of stay & outcome, dialysis session details: blood flow rate(BFR), dialysis flow rate(DFR), ultrasound 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.


Conclusions: AKI needing HD in COVID-19 infection is associated with significant multiorgan injury and high mortality, making management difficult. 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

Claire Avillach, Megan E. Feeney, Mohamed T. Hassan Kamel, Hassan Mahmoud, Aileen W. Zhen, Natasha Awais, Sandeep Ghai. Boston Medical Center, Boston, MA.

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 64.3 ± 15.9 years. During the study period, patients showed markers of inflammation with a median CRP of 239.6 (IQR 123-391.5), fibrinogen 609mg/dl (431-693), d-dimer 4.036 ng/ml (1.777-15.558), CVVH was conducted in predilution 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). Ten 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: 15h with curative heparin vs 11.25h 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 coagulization of the filter in patients with hypercoagulable state. The fatality rate was 76.9% with a median time of 22.5 days (1-87 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, admissions 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 19, 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, and 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 56(62%) and only 6 patients were discharged, 5 of whom remained RRT dependent. Heavy proteinuria (3+) or urinary protein were initial C-reactive protein (CRP) were higher in those with AKI who died (21.1 [IQR 14.3-29.6] versus 6.6 [3.2-16.3], 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 AKI patients in a university hospital.

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. 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.

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 (99.4%) 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, anemia 62.5% 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 RDRW (14.7 ± 1.3, 13.3 ± 1.6; p<0.08), need of MV (88%) and vasopressive anine (90%), RRT (88%) and higher mortality (87%). We used serum creatinine, BFR, RDW, mechanical ventilation and vasopressor anine in model of regression. We observed that MV (OR 10.26 [CI95%, 1009-1038; p<0.001) and age (OR 1030 [CI95%, 1004-1056; p=0.002) were independently associated with AKI.

Conclusions: AKI is associated with high rates of RRT and death. Higher age and need of mechanical ventilation were associated with AKI in COVID19 patients.

Funding: Government Support - Non-U.S.
Rigoberto with severe COVID-19 disease and associated multiorgan failure. Although more comorbidities were present in CA-AKI, outcomes were better for CA-AKI. Among patients with AKI, 92 (56%) died, 49% in the CA-AKI vs. 63% in the HA-AKI therapy. Recovery from AKI was more frequent in the CA-AKI group 66% vs 44% for RRT initiation. In general, AKI was associated with higher severity of COVID-19 Stage 3. Stage 3 was more frequently observed in HA-AKI (p<0.001). RRT was provided parametric ANOVA.

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 - May 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 37% of patients associated to volume depletion were rehospitalized 26 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 with severe COVID-19 disease and associated multiorgan failure.

Is AKI in COVID-19 Patients Associated with Increased Mortality? Vasantha Muthuppalanappan, Jennifer Ng, Phoebe Sharratt, Kristi Sun, Mark Harber. Whittington Hospital, London, United Kingdom.

Background: Acute kidney injury(AKI) affects 22% of hospitalised patients and is associated with a 21.9% increased risk of mortality in non COVID-19 admissions. Based on reports from China the rate of AKI in patients hospitalised with COVID-19 is 3-9%. The study’s objective was to identify AKI prevalence in COVID-19 patients and associated adverse outcomes.

Methods: This is a retrospective observational cohort study of patients admitted to hospital with positive COVID-19 PCR testing from 14th February to 7th May 2020. Demographic data, past medical history and blood results were obtained from health records. AKI was defined according to KDIGO criteria.

Results: 383 patients (220 Male) were included in the final analysis, with an age range of 18-99 yrs (median 69 yrs). AKI occurred in 153(39.9%) patients (103 male), with a median age of 74 years. 111(72.5%) patients had AKI on admission, 42(27.5%) developed AKI while hospitalised. Average clinical conditions were more (CFs) in the CA-AKI group was 4. Median creatinine kinase in the AKI group was 231u/L (IQR 149-1260). Of all 153 AKI patients,100(65.4%) were in Stage 1, 29(19%) in Stage 2 and 24(15.7%) in Stage 3. 140(92%) patients required renal replacement therapy (RRT) with 7(30%) becoming dependent on dialysis. 3 patients died associated to COVID-19 and 4 deaths occurred among specialist units for treatment whilst on RRT. Mean peak serum creatinine of 246mmol/L was observed on Day 5 of admission and Day 11 of symptoms on average. 90/153(58.5%) patients had recovery of renal function. 40/76(53%) patients who required CPAP or mechanical ventilation respiratory support had evidence of AKI compared to 113/304(37%) of non-ventilated patients. Of all 153 AKI patients, 65(43%) deaths occurred compared to 43/228(19%) in the non-AKI group. This difference was significant, p<0.01, OR = 2.89 (95% CI: 1.81, 4.58) suggesting that patients with AKI had a 74% chance of increased death. Univariate analysis showed that age, males, baseline eGFR, albumin, CFS and Charlson comorbidity index were predictors of AKI. Multivariable analysis showed that independent predictors of AKI included males, Black and Asian race, baseline eGFR and albumin. An increase in baseline eGFR by 1ml/min in COVID-19 patients was associated with a 2.4% risk reduction in death, p<0.01, OR = 0.976 (95% CI: 1.02, 1.03).

Conclusions: AKI is a common finding and a poor prognosticator in patients with COVID-19.
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 (Sao 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 was assessed 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 (≤ 2 days from COVID symptoms) lasted 5.6 ± 4.0 days (vs 11.9 ± 9.2 days in later AKI presentation, p = 0.05). Both COV+ and COV- patients showed sCr and sU drop during 5-Dr, except for diuretic users, who presented sCr drop without sU drop. COV+ patients presented negative overall FB during 5-Dr, while COV- patients presented positive FB (516.2 ± 2730 vs 225.5 ± 5868 ml/24h). In COV+, sNa rose through 5-Dr (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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PO0695
Filter Clotting, Anticoagulation, and Duration of Sustained Low-Efficiency Dialysis in Patients with COVID-19 and AKI
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Background: There have been anecdotal accounts of shortened duration of renal replacement therapy (RRT) due to filter clotting in patients with COVID-19 and acute kidney injury (AKI) (CoV-AKI) requiring RRT (AKI-RRT). Thus, we examined the duration of runs of RRT in patients with CoV-AKI as well as in patients with AKI-RRT in the pre-COVID-19 era.

Methods: Among 161 patients with CoV-AKI, we identified patients with CoV-AKI who underwent RRT by sustained low efficiency dialysis (SLED) for 2 days (n = 52) (March-April 2020). As a control, we included patients with AKI without COVID-19 diagnosis who underwent SLED (n = 24) (non-CoV-AKI) in December of 2019, pre-COVID-19 era. We quantified the duration of RRT under various protocols of anticoagulation (AC) [no AC, citrate (CIT), regional heparin (rH), minimally intensive heparin (mIH), systemic low intensity heparin (sLH), systemic high intensity heparin (sHH), and sHH plus CIT (sHH+CIT)] by computing the duration (hours) of each SLED session (hrs of SLED/start) and the percentage of short SLED runs (< 6 hours).

Results: In CoV-AKI, the median hrs of SLED/start under each AC protocol were 6.1 for no AC, 5.4 for CIT, 10.6 for rH, 11.6 for mIH, 11.4 for sHH, and 14.6 for sHH+CIT. As the AC intensified, the duration of SLED increased (ohrs for trend, p = 0.014). Pre-COVID-19, standard AC for non-CoV-AKI were no AC or CIT and had a median longer RRT duration compared to CoV-AKI under either no AC or CIT (10.2 vs 5.5 hrs of SLED/start, for non-CoV-AKI vs CoV-AKI, respectively, p = 0.021). Similarly, the proportion of patients with short runs was greater in CoV-AKI (under no AC or CIT) vs non-CoV-AKI (55% vs 19%, p = 0.01). When comparing the 3 more aggressive AC protocols (sLH, sHH and sHH+CIT) in CoV-AKI with non-CoV-AKI, the duration of RRT was similar (12.2 vs 10.2 hrs of SLED/start, p = 0.11) and the percentage of short SLED runs were also similar (10% vs 19%, p = 0.25).

Conclusions: RRT in CoV-AKI was associated with shorter duration of SLED compared to non-CoV-AKI, likely driven by increased filter and/or catheter clotting. Aggressive AC protocols with sHH with or without CIT in CoV-AKI were successful in restoring the duration of RRT back to that observed in patients with AKI-RRT in the pre-COVID-19 era.
Impact of Renal 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 renal replacement therapy (RRT) modality on prognosis is undetermined. Patients with kidney transplant exhibit treatment-induced immunodepression, while patients 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 two 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 multivariate analysis, adjusted HR for 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.

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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 needing 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 patients. 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 was unreliable 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 69% 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). 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.

PO0697

Lower Continuous Venovenous Hemodialysis Replacement Rate and Its Effect on Patient Outcome in the COVID Crisis Time

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Background: Acute kidney injury (AKI) is a common problem encountered in COVID positive patients with incidence close to 23% and mortality close to 60% in this cohort of patients. Continuous Veno-Venous Hemodialysis (CVVHD) plays a primary role in management of these patients. Nephrologists nationwide have been facing a compelling supply/demand mismatch dilemma. Lowering the rate of replacement fluid flow rate (RFRF) is one strategy that was used by our practice to mitigate this issue in selected patients. We hypothesize there is no difference in clinical outcome between the patients receiving high RFRF vs low RFRF.

Methods: This is a retrospective observational study from a single center experience. We analyzed data from March 2020 till the end of May 2020. We included patients with confirmed coronavirus disease 2019 (COVID-19) who required CVVH during their hospitalization. Patients were divided into two groups i.e Group 1 (=20ml/kg/hr RFRF) vs Group 2 (<20ml/kg/hr RFRF). Patients 18 years or older with at least 3 days of CVVH during their hospital stay were included. We compared percentage drop of blood urea nitrogen (BUN) and phosphorus as well as hospital stay and mortality between the 2 groups. We used ANOVA, t-test and Chi square for analysis, as appropriate.

Results: We enrolled 36 patients in the study, 20 in group 1 and 16 in group 2. Eighty percent of the patients enrolled were men. Mean weight was 100 ±8 kg in group 1 vs 107 ±8 kg in group 2. There was no statistically significant difference in percentage reduction of blood urea nitrogen (BUN) or phosphorus (P0) >0.2k & 0.5 respectively (Means 25.4 vs 21.7 & 18.4 vs 17.1). Mean filtration fraction was similar between the two groups (17.9% vs 17%). Frequency of line clotting events was compared in the two groups using Chi square with P value 0.8. Mortality was not significantly different between groups, although it was actually lower in the groups treated with the lower RFRF.

Conclusions: Although our data analysis is still evolving, we found no difference in mortality, toxin clearance and frequency of line clotting between the two studied groups. No randomized control trial has assessed using a lower than 20ml/kg/hr RFRF in CVVH. Our study, thus far, showed no difference between the two groups. This finding needs to be further validated in a randomized control study.

PO0698

Markers of Inflammation and Risk for AKI and Need for Dialysis in Patients with COVID-19


Background: Acute kidney injury (AKI) is a reported manifestation of COVID-19 (CoV-AKI). Release of inflammatory cytokines has been recognized as a characteristic feature of SARS-CoV-2 and is linked to severity of illness. However, it has not been clearly determined if levels of serum markers of inflammation are associated with risk for development of AKI or its severity.

Methods: We conducted an observational study in patients hospitalized at Ochsner Medical Center over 1-month period with COVID-19 and diagnosis of AKI. We examined the relationship between the blood level of ferritin, C-reactive protein (CRP), procalcitonin (proCal), D-dimer and lactate dehydrogenase (LDH) and the incidence of AKI, as well as AKI requiring renal replacement therapy (AKI-RRT), by assessing comparison of means and safety of LMWH vs UFH in preventing ECC, during their hospital stay were included. We compared percentage drop of blood urea nitrogen (BUN) or phosphorus as well as hospital stay and mortality between the 2 groups. We used ANOVA, t-test and Chi square for analysis, as appropriate.

Conclusions: Although our data analysis is still evolving, we found no difference in mortality, toxin clearance and frequency of line clotting between the two studied groups. No randomized control trial has assessed using a lower than 20ml/kg/hr RFRF in CVVH. Our study, thus far, showed no difference between the two groups. This finding needs to be further validated in a randomized control study.
Morbid Obesity, Hypertension, and Male Sex Are Associated with Greater Risk for AKI in Patients with COVID-19

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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 644 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. Vasopressors and/or mechanical ventilation was required in 105 (65%) of them. In-hospital 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% (64/91). 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 13%, 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.

COVID-19: AKI and Outcomes

Poster

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

259
PO0704
Refractoriness of Hyperkalemia and Hyperphosphatemia in Dialysis-Dependent AKI Associated with COVID-19
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Background: There have been anecdotal accounts of an unusual incidence of persistent hyperkalemia (hyperK) and hyperphosphatemia (hyperP) 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 hyperK and hyperP 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 hyperP [serum phosphate (sP) ≥ 4.5 mg/dL], moderate hyperP [sP ≥ 10.0 mg/dL] and severe hyperP [sP ≥ 15.0 mg/dL] and severe hyperK [sK > 5.5 mEq/L], moderate hyperK [sK > 6.5 mEq/L], hyperK [sK ≥ 7.5 mEq/L], as % SLED-days, and by severity of hyperK and hyperP 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 correlated with sK and sP correlated 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
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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 3/13/20-5/7/20.

Methods: Patients admitted with COVID-19 confirmed by SARS-CoV2 PCR test were screened for AKI. Univariate and multivariate logistic regression was used to identify our risk 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) ± 15 (15) 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 ACE/ARB use did not differ between groups. Patients with AKI had higher CRP, median (IQR) 102 (44-161) vs. 59 (21-116) mg/L, p=0.009, and LDH on presentation, 365 (265-493) vs. 317 (228-385) U/L, p=0.04. Ferritin, IL-6, and D-dimer was similar between groups. A higher percent with AKI had received steroids, 42% ± 16%, p=0.001. Ticloplatinum was administered in 15% of AKI vs. 5% of non-AKI groups, p=0.08 while rates of hydroxycytroloquin 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. Nourreddine, Lisa M. Antes, Sreedevi kopissetti Jenigiri, Maria T. Story, Mecnakshi Sambharthi, 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 unblinded 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 90 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 who died and 253 adult COVID-19 positive inpatients who died. We analyzed COVID data on patients in a related unblinded 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 90 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
wise AKI mortality was AKI1 25.7% (27), AKI2 10.4% (11) and AKI3 20% (21). 66.6% haemorrhage patients 23% (25) AKI patients died with non-renal creatinine. Mortality in CKD patients as co-morbidity was 64%. All renal transplant patients survived without having AKI. 7.7% (19) patients required continuous positive airway pressure, 42.1% (8) patients developed AKI of these 75% (6) patients with CPAP died. A further 24 (9.75%) required mechanical ventilation with 62.5% (15) of these developed AKI with mortality of 80% (12).

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,1,2 Mitchel,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 (RRT) 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 RDG 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>Characteristic</th>
<th>Total Participants, n=42</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65.6 (7.2)</td>
</tr>
<tr>
<td>Sex, Male/Female</td>
<td>31(73%) / 11(27%)</td>
</tr>
<tr>
<td>Hospital</td>
<td>79(18%)</td>
</tr>
<tr>
<td>White</td>
<td>121(29%)</td>
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<tr>
<td>History</td>
<td>39(9%)</td>
</tr>
<tr>
<td>DM</td>
<td>28(67%)</td>
</tr>
<tr>
<td>HLD</td>
<td>26(62%)</td>
</tr>
<tr>
<td>CAD</td>
<td>15(37%)</td>
</tr>
<tr>
<td>CHF</td>
<td>6(14%)</td>
</tr>
<tr>
<td>COPD (20%)</td>
<td></td>
</tr>
<tr>
<td>Asthma (5%)</td>
<td></td>
</tr>
<tr>
<td>Baseline (100%)</td>
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<tr>
<td>Charlson Comorbidity Index</td>
<td>7.3(3.19)</td>
</tr>
<tr>
<td>Smoking, Never</td>
<td>15(36%)</td>
</tr>
<tr>
<td>Gender, Male/Female</td>
<td>31(73%) / 11(27%)</td>
</tr>
</tbody>
</table>

PO0709
The Clinical Presentation of AKI Complicating COVID-19: Observations from Elmhurst Hospital, New York City
Nasser M Alzahrani,1 Demetrios Papademetriou,2 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 anaylzed. 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 CKP) 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 interstitial nephritis as an underlying pathology as described earlier.

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

Underline represents presenting author.

PO0710
Incidence of AKI in Hospitalized Patients with COVID-19
Lili Chan, Kumandeep Chaudhary, Aparna Saha, Kinsuk Chauhan, Akhil Vaid, Barbara T. Murphy, John C. He, Girish N. Naddkar, 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. 538 (96%) of all patients had any urinary abnormalities of proteinuria, hematuria, or leukocyturia. 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) and 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.

PO0711
SARS-CoV-2 Infection and Outcomes in Chronic Dialysis Patients
Eduardo K. Leschen,1,2 Gideon N. Aweh,1 Vladimir Ladić,1 Harold J. Manley,1 Carol Stewart,1 Doug Johnson,1 Dialysis Clinic Inc, Nashville, TN; 2Tufts University School of Medicine, Boston, MA.

Background: The SARS-COV-2 pandemic (COVID) impacted ERD patients on dialysis, categorized by the CDC as immunocompromised. We describe the characteristics and outcomes in patients treated by a non-profit dialysis provider.

Table 1 Baseline and Presenting characteristics of the cohort

<table>
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<tr>
<th>Characteristic</th>
<th>N/A (n=398)</th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65.6 (7.2)</td>
</tr>
<tr>
<td>Sex, Male/Female</td>
<td>220 (55%) / 178 (45%)</td>
</tr>
<tr>
<td>Race, White/Non-White</td>
<td>300 (75%) / 98 (25%)</td>
</tr>
<tr>
<td>History</td>
<td>398 (100%)</td>
</tr>
<tr>
<td>History, Male/Female</td>
<td>220 (55%) / 178 (45%)</td>
</tr>
<tr>
<td>History, Race, White/Non-White</td>
<td>300 (75%) / 98 (25%)</td>
</tr>
<tr>
<td>History, History, Male/Female</td>
<td>220 (55%) / 178 (45%)</td>
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<td>History, History, Race, White/Non-White</td>
<td>300 (75%) / 98 (25%)</td>
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<td>History, History, History, Male/Female</td>
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</tr>
<tr>
<td>History, History, History, History, Race, White/Non-White</td>
<td>300 (75%) / 98 (25%)</td>
</tr>
</tbody>
</table>
Methods: From 2/17 to 5/29, 2020, Dialysis Clinic Inc. had identified 422 COVID+ patients from 98 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.

PO0713

Trends in Fever and Respiratory Illness in Hemodialysis Patients During the COVID-19 Pandemic
Sheetal Chaushri,1 Hao Han,1 John W. Larkin,1 Len A. Usvyat,1 Dinesh K. Chattoo,1 Jeffrey L. Hymes,2 Michael A. Kraus,2 Allan J. Collins,2 Franklin W. Maddux,3 1Fresenius Medical Care, Global Medical Office, Waltham, MA; 2Fresenius Medical Care, North America, Waltham, MA; 3Fresenius Medical Care AG und Co KGaA, Bad Homburg, Germany

Background: Hemodialysis (HD) patients are vulnerable to the 2019 coronavirus disease (COVID-19) due to older age and common coexistence of comorbidities. Fever and respiratory illness (RI) are common symptoms of COVID-19. In order to create a disease surveillance tool and anticipate areas of COVID-19 outbreak, we aimed to assess the trends in fever and RI symptoms in HD patients treated at a national dialysis provider network in the United States during the pandemic.

Methods: We used data from HD patients actively treated between Jan 1 2018 ad May 16 2020 at a national dialysis provider network of large integrated health care company. If the body temperature of the patient either before or after the treatment was greater than 100 degrees Fahrenheit, then the patient was identified as exhibiting the symptom of fever. If the patient complained of shortness of breath, wheezing, runny nose, bloody cough, dry cough or purulent cough, then in this analysis the patient was identified as exhibiting the symptom of RI.

Results: The total patients count ranged from 196,774 to 209,475 per week while the total count of HD treatments ranged from 413,477 to 454,215. For the year 2020, a clear increase in trend for number of patients was observed after week 11 (03/08-03/14/2020) for RI as well as fever. Both increasing trends spike at the week 15 (04/05-04/11/2020) and decline thereafter. At the end of the study period (May 16 2020) the trends in RI symptoms significantly increased while for fever such increase was observed post-week 11.

Conclusions: HD patients appear to exhibit a different trend in RI and fever symptoms during the year 2020 compared to concurrent periods in 2018 and 2019. Both increasing trends spike at the week 15 (04/05-04/11/2020) and decline thereafter. Surveillance of dialysis patients may allow early identification of COVID-19 outbreaks.

Funding: Commercial Support - Fresenius Medical Care
Implementation of Strategies for Prevention and Control of SARS-CoV-2 Infection at Dialysis Units in Latin America: Experience from GlomCon Latin America Working Group (L.GlomCon) 

Denisse Arellano-Mendez,1 Julio A. Gutierrez-Prieto,2 Javier Soto-Vargas,3 Blanca Martinez-Chagolla,4 Franco H. Cabeza Rivera,5 Desiree Garcia Antonio,6 Diana B. Sepulveda,7 Sonia Ramirez-Avila,8 Carmen Avila-Casado,9 GlomCon Latin America Working Group 1Unidad 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; 6Hospital General de Mexico, Mexico; 7Mexico City; 8Multi-Organ Transplant Program, University Health Network, Toronto, ON, Canada; 9Pathology 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 May 26 and June 20, 2020. Answers from 866 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 (77.8%) or shifts (68.7%) 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 a shortening 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) cohousing 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%) only 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.
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, Yariana 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 ESKD 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. 16/29 (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 orARB at the time of admission. 25/29 (86%) were dialyzed via arteriovenous fistula or graft. The most common presenting symptoms were dyspnea (85%), cough (60%) and fever (28%). All initial 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. 13 patients (10%) were readmitted during the period of observation. 

Conclusions: The observed lack of increased mortality in ESKD does not align with the outcomes of significance of serum ferritin in ESKD has to be done with caution. Furthermore, the rate was seen despite higher levels of ferritin, suggesting that the interpretation of the similar mortality to non-ESKD [2125 vs 633 ng/mL, p = 0.0019). p = 0.65]. Median serum ferritin level was significantly more elevated in ESKD compared to non-ESKD (BMI) were 32 vs 27 kg/m2 (p = 0.11) for those admitted to ICU vs wards, respectively. 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. 16/29 (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 orARB at the time of admission. 25/29 (86%) were dialyzed via arteriovenous fistula or graft. The most common presenting symptoms were dyspnea (85%), cough (60%) and fever (28%). All initial 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. 13 patients (10%) were readmitted during the period of observation. 

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COVID-19: Dialysis Patients

PO0722
COVID-19 Incidence and Outcomes in Hemodialysis Patients in Mexico
Juan M. Ardavin Iturrate, Alicia Pineira, Juan Carlos Rodriguez. 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 triangle; 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 Chi’ 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 1276 pts; Of 102 suspects 25 (24%) had PCR and 16 (64%) were(-), 13 (12%) -test were not 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 (1.35% 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 (13.8%), 11 (35%) 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
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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

Background: COVID-19 remains a major public health emergency and in-center dialysis providers have multiple opportunities for its spread. Elderly immune-impaired hosts 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, distributions 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 (92.9%) 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), 5/10 (50%) of the positive patients were MWF (24h) shift. On multivariate analysis, this effect approached significance (p=0.051); however, there was no interaction of COVID-19 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.

Chronological Distribution of COVID-19 Cases

PO0725
COVID-19 Infections in a Small Dialysis Organization in New York City
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Background: COVID-19 infected more than 1.6 million Americans (0.48%) and more than 15,000 of the 500,000 (3%) Americans with chronic kidney disease treated by dialysis. The Rogosin Institute operates nine dialysis centers in New York City (NYC), the epicenter of the COVID-19 US Public Health Emergency (PHE). We followed guidance from the Centers for Disease Control and Prevention and the New York State Department of Health throughout the PHE. We screened all patients and staff for signs and symptoms of COVID-19 by measuring temperature and inquiring about symptoms on presentation to the dialysis centers. Infected patients who did not require hospitalization were treated in our centers on a dedicated shift by dedicated staff. We used a symptom-based approach to discontinuing isolation.

Methods: We created a COVID-19 tool in REDCap to track the spread of Coronavirus. We surveyed our Electronic Health Record weekly using a direct data connection and automated scripting to identify patients infected with COVID-19. We reviewed demographic and clinical data for each infected patient. We used descriptive statistics to analyze our population of infected patients.

Results: On February 28, 2020, 1,559 patients received dialysis at our centers. By May 11, 241 (15.5%) had been infected. Our mortality rate was 22.8% compared to general populations in NYC (10-12%), US (6.0%) and worldwide (6.5%) and rates for dialysis patients reported between 7-20%. We had a disproportionate occurrence of COVID-19 among residents of Brooklyn (49% of infections, 44% of patients) and Queens (29%; 25%). Most of the infected patients were male (53%) and Black (51%). Common co-morbidities included hypertension (98%), diabetes mellitus (60%), heart failure (25%) and coronary artery disease (25%). Common outpatient medications included statins (64%) ACE inhibitors/ARBs (80%) and calcium channel blockers (65%). Fever was the only common presenting symptom (94% of patients). A significant proportion (12%) of patients were in the hospital within 14 days prior to diagnosis of COVID-19 infection.

Conclusions: COVID-19 infection was common and associated with high mortality rate in our NYC population of dialysis patients despite adherence to governmental guidelines for control of disease spread. We hypothesize community spread was common in our patients residing in the epicenter of the US COVID-19 PHE.

Funding: Clinical Revenue Support

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

265
COVID-19 Outbreak and Experience in a Dialysis Unit in the Philippines
Ma. Anna Angelica PO0726

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/OPSI-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 (c) adequate personal 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

PO0727

Demographic and Clinical Characteristics of Patients with CKD and SARS-CoV-2 Undergoing Hemodialysis Treatment
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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.

Methods: Retrospective, observational, single-center study in Mexico. We analyzed the clinical manifestations and outcomes of all maintenance HD patients hospitalized with COVID-19 from April 9th to May 31st, 2020 as confirmed by real-time polymerase chain reaction.

Results: 20 patients followed in our hospital with median age of 45.2±13.8 years, 50% were men. All the patients have HTA (100%), DM (50%), the most common symptoms at admission were asthenia (75%), dyspnea (65%), cough (55%) followed by myalgias (50%) and fever (45%). Poor oxygen saturation (<95%) breathing room air was observed in 18 patients (90%) with mean oxygen saturation of 77±9%. Lung abnormalities on initial chest X-ray were observed in all patients. Peripheral ground-glass opacities, the typical radiologic pattern, were bilateral in 13 patients and unilateral in 7. Laboratory studies with lymphopenia in 85% of patients with a mean of 0.7±0.38. There were no differences baseline leukocyte or lymphocyte from patients who survived vs from those who died. The mortality rate (40%) was much higher than that observed in the general population (8%). Mortality was higher in women.

Conclusions: The impact of this virus on patients with CKD is poorly understood. The evaluation of the nephrologist must be very detailed, most of the patients had mild dyspnea, however on physical examination, desaturation and radiological images were suggestive of infection by SARS-CoV2. The current situation provides a unique opportunity to gather vital information to process and learn from the experience worldwide. These results will allow us to treat them in a timely manner and reduce lethality in dialysis patients.

Effect of COVID-19 on Dialysis Practices on the Ground: Early Results from an International DOPPS Program Survey
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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, DOPPS, PD), Peritoneal (PDOPPS) Dialysis Outcomes and Practice Pattern 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% reported being on the late phase of the COVID-19 curve. 40%, 23%, 100% of MDs were more likely to recommend home dialysis; 19%, 5%, 29% reported an increase in missed dialysis treatments; 30%, 24%, 50% were more likely to prescribe potassium binders; and 75%, 60%, 83% had greater challenges obtaining vascular access interventions. Among NMs, 30%, 9%, 40% reported current limitations in access to COVID-19 testing; and 61%, 51%, 29% reported having, or risk of, shortage in staffing.

Conclusions: Early results indicate many clinics in Europe and US have had COVID-19 cases, but sites in the three DOPPS-China cities have avoided COVID-19 to date. 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.

PO0729
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>
<thead>
<tr>
<th>Variable</th>
<th>p-value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 65 years</td>
<td>0.001</td>
<td>2.3 (1.4-3.7)</td>
</tr>
<tr>
<td>Malegender</td>
<td>0.02</td>
<td>1.5 (1.0-2.3)</td>
</tr>
<tr>
<td>Race White</td>
<td>0.004</td>
<td>2.7 (1.5-4.7)</td>
</tr>
<tr>
<td>Albumin</td>
<td>0.007</td>
<td>0.4 (0.2-0.8)</td>
</tr>
<tr>
<td>Vintage</td>
<td>0.007</td>
<td>2.1 (1.3-3.2)</td>
</tr>
<tr>
<td>Dialysis (unsure)</td>
<td>0.01</td>
<td>2.8 (1.4-5.6)</td>
</tr>
<tr>
<td>Comorbidities (≥2)</td>
<td>0.01</td>
<td>2.4 (1.4-4.0)</td>
</tr>
</tbody>
</table>

a: Significant in the multivariable model; b: Significant if age, sex, and/or race were not forced into the model.

PO0730
Fighting COVID-19: Experience from a Chinese Hemodialysis Center
Qian Zhang, Mengjing Wang, Jing Chen. Huashan Hospital Fudan University, Shanghai, China.

Background: COVID-19 has ravaged China and spread throughout the rest of the world. Since there is no effective treatment available at present time, patients with ESRD feel anxious and uncomfortable to come to dialysis center and receive dialysis treatments.

Methods: To help the patients deal with their anxiety without interrupting their treatments, we developed emergency response plans and offered following instructions during the pandemic of COVID-19.

Results: 1) We have immediately adopted a comprehensive epidemiological screening and symptom evaluation for all hemodialysis patients, family members and medical staff. Confirmed and suspected COVID-19 patients will be quarantined in the designated places for 14 days after they are cured and discharged from hospitals. 2) We emphasize scientific education and teach our patients about the scientific evidence-based protection measures. 3) Patients shall wear masks throughout the treatment and avoid gathering and talking. They are trained how to wash hands in the correct way. They are required to wash their hands before entering the hemodialysis center and after returning home. 4) Before entering the hemodialysis center, everyone shall scan the QR code and register his or her health information. Medical staff will screen patients and perform the risk stratifications as seen in figure 1. Medical staff will check the patients’ temperature before, during and after dialysis treatment. 5) The environmental cleaning and disinfection measures will be strengthened for hemodialysis facility. The spaces between dialysis stations will be increased and the isolation curtains will be installed to keep social distance. Isolation treatment area will be set up to reserve for suspected COVID-19 hemodialysis patients.

Conclusions: Since we adopted above-mentioned instructions, we have zero infection case during the pandemic of COVID-19.
PO0732
Impact of Undertaking Safeguards to Limit Exposure and Prevent COVID-19 Infection in Ambulatory Dialysis: A Single-Center Experience
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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 FBKC (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.

PO0734
Outcomes of ESKD Patients Hospitalized with COVID-19
Jia Hwei Ng, Jamie S. Hirsch, Rimda Wanchoo, Mala Sachdeva, Susana Hong, Vipulbhai Sakhya, Kenar D. Jhaveri, Steven Fishbane. on Behalf of Northwell Nephrology Covid-19 Research Consortium Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY.

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.

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 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 PU and eventually tested positive for C19. The remaining 187 patients were C19 positive by nasopharyngeal 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 30a34 ml/kg/m'. 84 AKI patients required dialysis during their hospitalization (53%).

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 comorbidities, hospitalized C19 AKI 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 inflammation and hypercoagulability. However, to our knowledge, little is known about the level of inflammation and hypercoagulability among non-hospitalized in-center hemodialysis patients with COVID-19. We collected inflammatory and coagulation markers from 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 group 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 these elevated markers associate with cardiovascular and thrombotic events (dialysis circuit and vascular access clotting, sudden cardiac death) is needed.

Funding: NIDDK Support, Clinical Revenue Support

PO0737

Network Analysis of In-Center Spread of COVID-19: A Single Dialysis Center Experience

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1 Renal Research Institute, New York, NY; 2 Icahn School of Medicine at Mount Sinai, New York, NY.

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 Euclidean 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. 1b) 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
**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 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 ward of hospital admission. Multivariate analysis was performed to test the association of ESRD with mortality after adjustment for age, diabetes, hyperlipidemia, stroke, coronary artery disease, and congestive heart failure.

**Results:** 122 ESRD patients were included in this study. ESRD patients had 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 a significant difference 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 initiation 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 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 regions 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. 20% of personal protective equipment (PPE) were unavailable in 13% of facilities, staff, and housekeeping. HD units in the same zip code of an epicenter in New York regions emerged.

**Conclusions:** These data suggest that during current COVID-19 pandemic, half of HD units have significantly increased their adherence to hemodialysis prescription in order to fear of contacting the SARS-CoV-2 virus. Retrospective studies have suggested that patients are avoiding seeking medical care due to fear of contracting COVID-19. We therefore evaluated the effects of the COVID-19 pandemic on patient adherence to their dialysis prescription.

**PO0740**

Outpatient Initiation of Dialysis for AKI Requiring Dialysis Following Diagnosis of COVID-19

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**Background:** COVID-19 has been associated with the development of AKI, and the incidence of AKI-D may be as high as 3-5% in patients hospitalized with COVID-19. We examined the initiation of outpatient (OP) dialysis for AKI-D following a diagnosis of COVID-19.
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 swabs. Prompted 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 these, 21 (61%) were hospitalised, 4 (11%) required intensive care and 9 (25%) died. Baseline characteristics are presented in Table 1. Less than a third had typical symptoms. Thresholds of 37.3°C and “basal temperature +0.5°C” had similar moderate sensitivity and high specificity in predicting COVID-19 (Table 2). Combining symptoms and either of these thresholds improved sensitivity to 85%.

Conclusions: Less than one third of HD patients have typical symptoms of COVID-19 or fever >38.0°C. Pre-dialysis temperature >37.3°C or 0.5°C above basal temperature markedly improves sensitivity for detection of COVID-19 in asymptomatic HD patients. A screening strategy combining symptom questionnaires and pre-dialysis temperature monitoring should be used in HD units in regions of high COVID-19 prevalence.

Table 1: Baseline characteristics in HD patients without and with COVID-19

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>COVID-19 positive (n=21)</th>
<th>COVID-19 negative (n=184)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male:0.06</td>
<td>67%</td>
<td>65%</td>
<td>0.77</td>
</tr>
<tr>
<td>Age (years)</td>
<td>60.8 (12.03)</td>
<td>67.8 (6.75)</td>
<td>0.03</td>
</tr>
<tr>
<td>Black race</td>
<td>29%</td>
<td>30%</td>
<td>0.02</td>
</tr>
<tr>
<td>Living in long-term care facilities</td>
<td>11%</td>
<td>32%</td>
<td>0.001</td>
</tr>
<tr>
<td>Primary kidney disease</td>
<td>12%</td>
<td>24%</td>
<td>0.67</td>
</tr>
<tr>
<td>Diabetes</td>
<td>20%</td>
<td>19%</td>
<td>0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>27%</td>
<td>24%</td>
<td>0.001</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>44%</td>
<td>47%</td>
<td>0.99</td>
</tr>
<tr>
<td>Diabetes</td>
<td>14%</td>
<td>14%</td>
<td>0.55</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>21%</td>
<td>32%</td>
<td>0.001</td>
</tr>
<tr>
<td>Heart failure</td>
<td>9%</td>
<td>24%</td>
<td>0.001</td>
</tr>
<tr>
<td>Temperature at screening (°C)</td>
<td>37.5 (0.70, 37.9)</td>
<td>37.5 (0.70, 37.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>Basal temperature (°C)</td>
<td>36.5 (36.3, 36.7)</td>
<td>36.6 (36.4, 36.9)</td>
<td>0.1</td>
</tr>
<tr>
<td>Change from basal (°C)</td>
<td>0.6 (0.03, 0.8)</td>
<td>0.6 (0.03, 0.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Above 37°C</td>
<td>28%</td>
<td>77%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Above 37.5°C</td>
<td>22%</td>
<td>82%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Above 38°C</td>
<td>22%</td>
<td>99%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Above 39°C</td>
<td>25%</td>
<td>75%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Protocool as present and moderate (25-75% percentile)</td>
<td>4%</td>
<td>0%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 2: Diagnostic performance of various thresholds

<table>
<thead>
<tr>
<th>Pre-dialysis temperature</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
<th>Positive likelihood ratio</th>
<th>Negative likelihood ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Above 37°C</td>
<td>71%</td>
<td>72%</td>
<td>35%</td>
<td>94%</td>
<td>2.7</td>
<td>0.33</td>
</tr>
<tr>
<td>Above 37.5°C</td>
<td>65%</td>
<td>11%</td>
<td>61%</td>
<td>39%</td>
<td>7.9</td>
<td>0.38</td>
</tr>
<tr>
<td>Above 38°C</td>
<td>59%</td>
<td>96%</td>
<td>74%</td>
<td>95%</td>
<td>0.67</td>
<td>0.04</td>
</tr>
<tr>
<td>Above 39°C</td>
<td>27%</td>
<td>100%</td>
<td>100%</td>
<td>87%</td>
<td>0.09</td>
<td>1.00</td>
</tr>
<tr>
<td>Basal 35-36°C</td>
<td>70%</td>
<td>93%</td>
<td>55%</td>
<td>99%</td>
<td>0.35</td>
<td>0.07</td>
</tr>
<tr>
<td>Basal 36°C</td>
<td>61%</td>
<td>91%</td>
<td>93%</td>
<td>91%</td>
<td>4.7</td>
<td>0.06</td>
</tr>
</tbody>
</table>

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 infection.

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.

PO0743

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 to twice weekly sessions. In patients without RKF, the evidence is limited. We studied 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 posdilutional 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 do not two groups according to thrice versus twice weekly schedule.

Results: 25 patients were evaluated, 16 (64%) were female, mean age was 42.04±18.02 years, 21 (84%) did not have RKF. The length session between thrice vs twice were 181.74±9.94 vs 196 ± 9.19 (p=0.001). When we analyzed the anuric patients we found a significant difference in post-session systolic and diastolic blood pressure when compared between groups (p = 0.014). We did not find difference in dry weight (p = 0.5). We found significant difference between total substitution volume between groups (24.43±10.91 vs 26.5± 12.48 L, p=0.042) and no difference in Kt/V (1.67 ± 0.25 vs 1.73 ± 0.34, p=0.35). We found significance difference between groups in serum creatinine (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.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO0745
Clotting of Hemodialysis 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 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
David Clark, Kenneth A. West, Karthik K. Tennankore. Dalhousie University Faculty of Medicine, Halifax, NS, Canada.

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. We examined the percentage COVID-19 tested renal failure patients with clotting of twice weekly hemodialysis patients for candidacy of twice weekly hemodialysis (N=473). Patients who fulfilled interdialytic fluid gain and serum potassium criteria were assessed by the primary nephrologist for eligibility using each of: III. good nutritional status, IV. no co-morbid conditions (cardiovascular and pulmonary).

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 the surge, between January 1 to February 29, 2020.

Figure 1. Stepwise approach and selection criteria to review all facility-based hemodialysis patients for candidacy of twice weekly hemodialysis (N=473).

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.

PO0747
Impact of the COVID-19 Pandemic on Virtual Care in Home Dialysis
Martin J. Schreiber, Adam J. Weinstein, Mahesh Krishnan, Brooke Bowblly, Mike Gonzales, Liz Mooney, Michelle Cassin. DaVita Inc, Denver, CO.

Background: While almost every provider and the majority of patients in the United States (US) possess the technology needed to conduct a telemedicine visit, prior to the current pandemic utilization in home dialysis was relatively low. The current study examined trends in telehealth utilization before and during the COVID-19 pandemic in US home dialysis patients treated by a large dialysis organization in the US.

Methods: Telehealth was delivered using a proprietary multiparty, video, secure messaging (HIPAA compliant), scheduling, and educational resource telehealth platform DaVita Care Connect™ (DCC™) application. IT systems data were utilized to develop ongoing reports depicting patient, facility, and physician adoption rates across 1750 home dialysis programs. Data were segmented by geographic areas (9) and by time of COVID-19 dissemination within localities.

Results: A meaningful increase in telehealth utilization was observed since the start of the pandemic (prior to March 2020). Among 28,500 home dialysis patients treated, the DCC™ application was installed on 18,300 patient cell phones (65.3%). Overall, 16,000 peritoneal dialysis (PD) patients and 2,200 home hemodialysis (HHD) patients participated in a telehealth visit. Fifteen thousand visits were performed in April 2020. There were 18,000 messages sent between the care team and patient and 6000 educational resources viewed by patients at home since the COVID-19 pandemic (mid-March). The numbers of social worker and dietician visits and interdisciplinary team rounds also increased over time. There was significant variation DCC™ app download and utilization across geographic regions.

Conclusions: The COVID-19 pandemic has dramatically increased the use of telehealth management for home dialysis patients in the US. Examining the impact of virtual visits on patient outcomes going forward will be critical in designing post-COVID care. Balancing the integration of telehealth visits and face-to-face visits to optimize care will necessitate advancing a new care model for patients with end-stage kidney disease.
COVID-19: Dialysis Patients

PO0748

Abstract Withdrawn

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 51±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 KDQOL 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

PO0751

Psychological Impact of COVID-19 and Implementability of Prevention and Control Measures in Hemodialysis Centers: A Provincial Questionnaire Survey in China

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Background: This study investigated the psychological status of patients and staff and implementability of prevention measures in hemodialysis centers in Guangdong Province of China during the Coronavirus disease 2019 (COVID-19) pandemic.

Methods: An electronic questionnaire survey was performed in an anonymous manner between March 28 and April 3, 2020. Two questionnaires were designed to investigate the psychological status for hemodialysis patients and general staff (doctors, nurses, technicians, and other staff), respectively. An additional questionnaire for administrators (directors or head nurses) of hemodialysis centers was designed to address the implementability of prevention measures, including strengthened patient triage management, restricting caregiver visits to patients during dialysis, strengthened prevention amongst staff, and improved patient education and protection. All the 516 hemodialysis centers registered in Guangdong Province were voluntarily invited to join the survey.

Results: Total 1,782 patients, 3,400 staff, and 420 administrators responded for this survey. Patients living in rural areas reported a higher incidence of severe anxiety compared to those living in other areas. Medical staff reported better mental health than non-medical staff. With respect to implementability of prevention measures, hemodialysis centers in general hospitals outperformed independent blood purification centers, and tertiary hospitals outperformed other level hospitals. However, restricting acceptance of non-resident patients was lower in tertiary hospitals than that in other hospitals. Under this condition, only one patient imported from Hubei Province was diagnosed with COVID-19.

Conclusions: The outbreak did not significantly affect the psychological status of most patients and medical staff. Due to the successful implementation of comprehensive prevention measures, the COVID-19 epidemic was controlled effectively. This provincial survey may provide experience for other countries and regions with similar epidemic.

PO0752

Persistent Viral Shedding and Antibody Response to the SARS-CoV-2 Virus in Chronic Hemodialysis Patients

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Background: The duration of SARS-CoV-2 viral RNA shedding and antibody response of chronic HD patients to the SARS-CoV-2 virus is currently unknown.

Methods: This is a retrospective case series of chronic HD patients who tested positive for severe acute respiratory syndrome corona virus 2 (SARS-CoV-2 RNA) on nasal or nasopharyngeal specimen between March 20 and May 28, 2020 at the James J. Peters VA Hospital. Patients were tested at varying intervals to document clearance of virus or for surveillance purposes. SARS-CoV-2 Virus IgG Antibody (Ab) testing was performed on all HD patients with COVID-19 (using the Abbott IgG nucleocapsid antibody test and i2000SR machine, Ref. range of the Ab titer: >1.39 positive).
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 positive 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.
Enhanced Sentinel Surveillance System for COVID-19 Outbreak Prediction in a European Dialysis Clinics Network

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Background: Accurate predictions of epidemic dynamics may enable timely organizational interventions in high risk regions. We exploited the interconnection of the EMEA Fresenius Medical Care (FMC) dialysis clinic network to establish a sentinel surveillance system where the occurrence of new cases in a clinic propagates distance-weighted risk estimates to proximal dialysis units. The surveillance system is embedded in an artificial intelligence model which predicts COVID-19 outbreak occurrence in HD clinics from trends in clinical practice patterns and regional COVID-19 epidemic metrics. The system stratifies clinics by their risk of new local outbreak.

Methods: The risk prediction model is computed considering a cohort of 640 clinics belonging to the FMC network. 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 EuChDi® 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 EuChDi® 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 1: 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°F over 10 days before COVID-19+ test and approached 99°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 40x10^9/L over 14 days before COVID-19+ test (Fig 1D).

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.
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, clinical 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 the NHS Research Ethics Committee 20/SW/0077 and Health 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 9 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.

PO0761
COVID-19 Infection in Kidney Transplant Recipients: A Single-Center Experience
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Introduction: The SARS-CoV-2 (COVID-19) pandemic presents significant challenges to kidney transplant recipients (KTRs) with risk for higher mortality yet sparse available data. We present our single center experience of COVID-19 infection in KTRs.

Case Description: Methods We reviewed the electronic health records of KTRs with confirmed COVID-19 infection using rt-PCR testing via nasopharyngeal swabs, at our transplant center. Results We identified four KTRs with diagnosed COVID-19 infection in our institution. Details of individual cases are summarized in Table 1. Patient A died of complications while patients B, C and D fully recovered. Patient A initially recovered from COVID-19 pneumonia but then was readmitted three weeks later and developed features closely resembling macrophage activation syndrome (MAS) and hemophagocytic lymphohistiocytosis (HLH) leading to death despite treatment with dexamethasone, IV immunoglobulin and anakinra. Patient C had minimal symptoms without cytokine storm possibly related to complement blockade from revulizumab, a C5 inhibitor, which was being used for treatment of aHUS.

Discussion: Our single center case series of COVID-19 infections in KTRs is small but highlights two important aspects: 1) development of MAS/HLH like features in patient A which to our knowledge has not been described in the setting of COVID-19 infection in KTRs, 2) development of minimal symptoms without cytokine storm in patient C likely related to use of C5 blocking agent revulizumab. Further studies are needed to shed light on these phenomenon.

Case series of varied clinical manifestation of COVID 19 infection at our center

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 incidence 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 (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 mechanical ventilation support 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.

Results: 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 CD3/CD4/CD8 counts and had higher inflammatory markers (ferritin, d-dimer, CRP, procalcitonin, interleukine-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 4.16, 1.09-18.87, p=0.046) and proBNP levels (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.
PO0765
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 only 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 at the onset of illness were fever and dyspnea (71%), followed by myalgia (54%) and diarrhea (33%). Management of anti-rejection therapy varied across centers: antihypertensives 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%).

PO0766
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 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.

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.

PO0768
Risk Factors for Mortality in Kidney Transplant Recipients with COVID-19

Background: There is limited information on the presentation and risk factors for poor outcome in kidney transplant recipients with COVID-19.

Methods: We reviewed data of admitted kidney transplant recipients at 12 system hospitals with COVID-19 between March 1, 2020, and April 30th, 2020. We analyzed risk factors for mortality.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
**Results:** 31 patients were identified, 30 were admitted. Median age was 58 (IQR 53–68) years, 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 antineutrophilic antibody (ANA) and 84% had anti-double-stranded DNA antibodies. 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 intubated (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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**Introduction:** AKI in patients with COVID-19 may be due to ATN from 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, dyspnea 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, dyspnea, 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 Kidney biopsy showed global and segmental capillary collapse with a variable degree of sclerosis and severe renal tubules injury. Electron microscopy showed structural changes in the podocytes, endothelial cells, and tubular epithelium similar to Coronavirus particles.

**Discussion:** Our experience above is part of a growing literature describing the direct visualization of SARS-CoV-2 in causing ATN and CSG. Pathogenic pathways remain to be elucidated.

**PO0769**

**Living Donor Kidney Transplant Practice in the COVID-19 Era: A Survey of U.S. 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 5/29/20 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, 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.
Results: Presenting symptoms and hospitalization rates were similar in waitlisted ESKD and kidney transplant patients with COVID-19. Azithromycin and dexamethasone 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 male, 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)
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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 experiences regarding kidney transplant (KT) management in the context of COVID-19 pandemic.

Methods: Descriptive analysis extracted from an online survey carried out among nephrologists, renal pathologists and other health workers treating kidney diseases at centers that perform KT in LA countries. 139 (49%) respondents routinely participate in the care of transplant patients and have been involved in the management of COVID-19 patients in their respective centers. Respondents were asked about the demographic data of centers as well as the practices and experiences they encounter in their routine practice and the management of COVID-19 patients.

Results: 430 responses were obtained of which 360 (84%) were considered for analysis. 139 (49%) respondents routinely participate in the care of transplant patients and have been involved in the management of COVID-19 patients in their respective centers. 43 centers reported that up to 50% of their patients experienced a mechanical ventilation or vasopressor/suppressors, 46% of their centers continued their transplant activity during the COVID-19 pandemic.

Conclusions: The results of the survey indicate that the majority of LA centers have not changed their clinical practices for the management of COVID-19 patients.

PO0774
ESKD Patients with COVID-19 vs. Kidney Transplant Recipients with COVID-19

Background: The Covid-19 pandemic has had significant impact on the ESKD population with reduction in kidney transplantation due to decreased organ availability and temporary cessation of transplant procedures. To better understand the impact on patients with ESKD, we compared the outcomes of Covid-19 positive patients on the waitlist with those with a functioning kidney transplant.

Methods: Our center developed a dashboard and active surveillance of Waitlisted and Kidney transplant recipients tested for SARS-CoV-2. From 3/13/20 to 5/20/20, we identified 55 Waitlisted patients who tested positive for SARS-CoV-2, and compared their clinical characteristics and outcomes with those who received a kidney transplant. Primary outcomes included hospitalization and mortality rates.

Results: A total of 51 patients tested positive (1.05% of the 1,195 CNI recipients, 21 tested positive (1.76%) of the 1,195 CNI recipients, 21 tested positive (1.76%) of the 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 rates of any coronavirus strain in those receiving CNIs to those not receiving CNIs.

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 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 (NCT04343508). Transplant nephrologists recommend continuing CNIs through the COVID-19 pandemic.

PO0775
What Do Data Tell Us About Patients Receiving Calcineurin Inhibitors (CNIs) and Contracting a Coronavirus
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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 (NCT04343508). 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 rates of any coronavirus strain in those receiving CNIs to those not receiving CNIs.

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
PO0774
A Machine Learning-Based Predictive Model for Outcome of COVID-19 in Kidney Transplant Recipients
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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 immunosuppression treatment with antiinflammatory agents. Predictions were made using a Data Envelopment Analysis(DEF)-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(47-63), 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≥30kg/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
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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 minory 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 co-infections 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 antimetabolites 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.
PO0777

**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 a scenario study of immediate-KT vs delay-until-after-pandemic for different patient risks, many centers have paused or reduced KT activity, yet data to inform such decisions are lacking.

**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 CFRRs 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

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**PO0778**

**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 people 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 patients with pre-dialysis CKD, 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)

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**PO0779**

**COVID-19 in CKD: Retrospective, Propensity Score-Matched Cohort Study**

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**Background:** The prognostic factors for COVID-19 in patients with chronic kidney disease (CKD) are uncertain. We conducted a propensity score-matched study to compare clinical and prognostic features between hospitalized COVID-19 patients with and without CKD.

**Methods:** Patients with estimated creatinine clearance below 60 ml/min/1.73 m² for more than three months, were included in the CKD group. Fifty-six patients and the propensity score-matched fifty-six control patients were followed-up at least 15 days or until death after diagnosis of COVID-19. All demographic data and diagnostic and therapeutic methods were evaluated. The endpoints were all-cause mortality and acute kidney injury (AKI).

**Results:** Patient and control groups were reviewed retrospectively over a median follow-up of 44 days (IQR, 36-52 days) after diagnosis of COVID-19. Patients in the CKD group had higher intensive care unit follow-up and mortality rates than the other group, but these results did not reach statistical significance (16 [28.6%] vs. 19 [33.9%]; p=0.54 and 11 [19.6%] vs. 16 [28.6%]; p=0.269, respectively). The frequency of AKI was significantly higher in pre-dialysis patients with CKD compared to the other group (8 [14.3%] vs. 5 [45.5%]; p<0.001), but there was no significant difference between the groups in terms of cytokine release syndrome and respiratory failure (13 [23.2%] vs. 8 [14.2%]; p=0.226, 25 [44.6%] vs. 22 [39.3%]; p=0.566, respectively). Multivariate logistic regression analysis revealed that respiratory failure (30.283 [95% CI 7.296 to 211.519; P<0.001) and AKI (10.961 [95% CI 1.688 to 71.186; P=0.012) were independent risk factors for the mortality.

**Conclusions:** The prognosis of COVID-19 in patients with CKD is worse than non-uremic patients. Also, AKI and respiratory failure are independent risk factors for mortality.

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

Underline represents presenting author.
Kidney and Clinical Outcomes of COVID-19 in the Mexican Population


Background: Coronavirus Disease 2019 (COVID-19) is a new disease of pandemic proportions. Currently, there are no reports about kidney involvement and the association with mortality in Mexico. Our aim was to describe the characteristics in our population, clinical course, and renal outcomes.

Methods: Prospective, descriptive, single-center study in patients diagnosed with COVID-19 (positive RT-PCR tests), admitted to our hospital from April 2020 to date.

Results: 48 patients (60.4% men) with an average age of 54.33 years were included. 23 (47.9%) had a previous diagnosis of hypertension, 11 (22.9%) had obesity (>30 kg/m²), 10 (20.8%) had neurological diseases, 4 (6.3%) had heart disease, 3 (6.3%) had malignancies and 1 (2.0%) had liver disease. 9.18% (5) patients had a history of smoking. At admission, the mean oxygen saturation was 85.76%. The main reason for consultation was dyspnea in 35 patients (72.9%). Regarding symptoms, 81.3% (39) had dyspnea, 87.5% (42) fever, 54.2% (26) headache, 72.9% (35) cough and, to a lesser extent, odynophagia, myalgia and malaise in 33.3% (16), 45.8% (22) and 41.7% (20) respectively. The mean creatinine, urea and bicarbonate was 1.34 mg/dl, 56.69 mg/dl and 18.49 mmol/l respectively. 25% of the patients required ICU admission and 27.1% mechanical ventilation. During the study period, 19 patients (39.6%) developed AKI, 20.8% classified as KDIGO stage 1 and 15.6% stage 2. 3 patients required RRT, with a total of 13 deaths (68.4%). There was a statistically significant difference in mortality between patients with AKI vs patients with normal kidney function (p=0.002), with a RR of 3.47.

Conclusion: This study showed a higher prevalence of AKI in the Mexican population compared to reports from other countries, with a significantly higher risk for death. Special attention should be paid to this outcome and as nephrologists, we must take an active role in the care of these patients.

Association Between Kidney Dysfunction at Admission and Outcomes in Hospitalized Patients with COVID-19

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Background: AKI is a major predictor of mortality in patients with coronavirus disease 2019 (COVID-19). Data regarding association of renal dysfunction (AKI, hematuria and proteinuria) at the time of admission with hospital outcomes is limited. We aim to assess if renal dysfunction on day one of hospital admission is associated with increased mortality risk of patients with severe COVID-19 infection.

Methods: In this retrospective single-center study, we analyzed electronic medical records data on 300 patients admitted with COVID-19 infection. AKI data collection included history of comorbidities, medications, vital signs, and admission and peak laboratory values. Outcomes included inflammatory burden (calculated using composite scores for multiple markers of inflammation), AKI during hospitalization, admission to the intensive care unit (ICU), need for invasive and non-invasive mechanical ventilation, mortality and length of stay. For multivariate analysis, a pre-specified genotype and clinical algorithm was used. The study cohort was divided into groups based on serum creatinine level on day one of hospital admission. Group 1 included patients with normal serum creatinine (SCr) < 1.10 mg/dl while group 2 included patients with high SCr > 1.10 mg/dl. The primary outcome was mortality. Secondary outcomes were the need for renal replacement therapy (RRT), duration of RRT, development of adult respiratory distress syndrome (ARDS) and need for mechanical ventilation. Comparisons between groups were done using Mann-Whitney U-tests for continuous variables and chi-square tests for categorical variables. Mortality was evaluated with a Kaplan-Meier Survival Analysis.

Results: A total of 77 in group 1 and 20 in group 2. Patients in group 2 compared to group 1 were older (67 vs. 56, p=0.04), more frequently African Americans (11% vs 45%, p=0.002), hypertensives (80% vs 52%, p=0.05) with chronic kidney disease (25% vs 0%, p=0.01), without significant differences sex, diabetes, smoking status, and exposure to renin angiotensin system blockers. In group 2 and 3 patients in group 1 died, with significant difference in cumulative survival (Figure 1). Need for RRT (55% vs 41%, p=0.33), duration of RRT (6 vs 3 days, p=0.08), development of ARDS (85% vs 81%, p=0.75) and need for mechanical ventilation (65% vs 61%, p=0.89) were not significantly different between groups 2 and 1.

Conclusions: The presence of renal dysfunction on the day of hospital admission is associated with increased hospital mortality in patients with severe COVID-19 infection.

Funding: Other NIH Support - No funding

COVID-19 in CKD Patients: Lessons from 553 CKD Patients with Biopsy-Proven Kidney Disease

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Background: COVID-19 is a novel coronavirus currently at the centre of a global pandemic, and patients with cardiovascular risk factors such as hypertension and diabetes are at risk of a serious complication such as hospitalization and death. Chronic kidney disease (CKD) increased cardiovascular risk and ~90% of CKD patients presented hospitalization. The prognosis and lethality of COVID-19 in patients with biopsy-proven kidney disease has not been previously studied.

Methods: Data included patients who underwent a kidney biopsy at the Vall d’Hebron Hospital between January 2013 and February 2020 with diagnostic confirmation and those with high clinical suspicion of SARS-CoV-2 infection during the period from March to May 2020.

Results: Of 553 patients, 39% were diagnosed with SARS-CoV2 infection. The mean age was 63+4±15 years. 48.7% were male, 31 hypertension, 19 diabetic, 12 obese and 19 African American. In-hospital mortality was 17.6% (99/553). Of these, 47.4% died with AKI, 41% had need for invasive ventilation, and 47.4% were treated with RRT. 59 patients were confirmed with COVID-19 infection at hospital admission [average hospital stay was 16 days±11], of which 4 in the ICU and 6 (15%) developed acute respiratory distress syndrome. 23 patients, 4 patients, 20 patients, 104 patients, 9 patients, 3 patients had blood transfusions, 9 patients, 10 patients, 9 patients, 28 patients, 29 patients, 12 patients, 8 patients, 9 patients, and 8 patients with hydroxychloroquine; 6 patients, tocilizumab; 9 patients, intravenous corticosteroids. 11 patients presented impaired renal function, of which 3 were transplanted and 8 with CKD. CKD patients under RAS blockade had less mortality than patients without RAS blockade treatment. The use of hydroxychloroquine was statistically associated with increased in-hospital mortality in patients with COVID-19 infection, suggesting that they should not be withdrawn.

Conclusion: COVID-19 was diagnosed in 7% of our CKD patients with kidney biopsy. The mortality was 15%, lower than the reported in hemodialysis patients. RAS blockade is not exerting a deleterious effect in our CKD patients with COVID-19 infection, suggesting that they should not be withdrawn.

COVID-19: CKD and Transplant Patients

PO0780

PO0781
Involvement and Outcome of COVID-19 Patients Admitted from a Federal Medical Facility

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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 56 ± 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. 13% 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 dialysis need (14% vs 12%, respectively). The overall mortality rates were higher in patients that required dialysis (80% vs. 6% for those who did not, P = 0.001). The need for acute dialysis was independently associated with mortality in multivariable models.

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.

Urinary 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. Sensitivity y and monoclonal chromatometric 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 = 11). 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 ≥ 2457 pg/ml (Specificity 76.9% and Sensitivity 90.0%, AUC 85.9%), L-FABP: Severe vs. Moderate: Mild ≥ 22.0 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 urinary 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.

Management of COVID-19 in kidney transplant recipients (KTR) should include treatment of infection and regulation of immunosuppression but there is no consensus on this issue yet. In this study, we aimed to describe our experience in KTR with COVID-19.

Results: Forty patients (20 female) were reviewed over a median follow-up of 32 days (IQR, 14-51 days) after COVID-19. 5 patients died during the follow-up. The frequency of graft dysfunction was similar between groups (n = 12 and n = 2; p = 0.615, respectively).

Conclusions: MicrExUrSed in CoV-AKI was comparable to that demonstrated in other forms of AKI.

Infection in Kidney Transplant Recipients: A Multicenter Experience in Istanbul

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Background: Management of COVID-19 in kidney transplant recipients (KTR) should include treatment of infection and regulation of immunosuppression but there is no consensus on this issue yet. In this study, we aimed to describe our experience in KTR with COVID-19.

Results: Among 161 cases of AKI, MicrExUrSed was performed in 20 (12.4%). Amnira and contact precautions were barriers to obtain specimens. GC were found in 17 (85%) of which 16 (80%) had "muddy" brown GC (MBGC). A median 5 MBGC per LPF (1-20) were found in a median 40% (10-95%) of LPFs. WC were found in 10 (50%) cases with a median 2 (1-5) per LPF, all of whom had MBGC also present. TCREC were found in 3 (15%) cases with a median 1 (1-4) per LPF. Altogether, ATI score was assigned to 17 (85%) patients, of which 12 (60%) had AKI either after a hemodynamic/ischemic insult (9) or after a toxic insult (3) (rhabdomyolysis, vancomycin, contrast) and 3 (15%) had biopsy-proven ATI along with collapsing glomerulopathy; for a total of 15 (75%) patients with either clinical or histological evidence on ATI matching the MicrExUrSed findings. Ten (50%) and 5 (25%) had WBCC and RBCs, respectively. Acanthocytes were found in 1 (5%) patient with presumptive proliferative endocapillary glomerulonephritis.

Conclusions: MicrExUrSed in most patients with CoV-AKI showed overt evidence of ATI with an abundance of MBGC and WC, including in cases of coexisting glomerulopathy. Pyuria was observed in half. The diagnostic utility of MicrExUrSed in CoV-AKI was comparable to that demonstrated in other forms of AKI.
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, treatments, 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 was 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 long 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.

Renal Artery Thrombosis with Infarction in a Patient with Mild COVID-19
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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 nonsegmental 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 aspirin.

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 thrombosis 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.

PO0788

PO0790

Thrombotic Microangiopathy (TMA) in a Patient with COVID-19
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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 afebrile, 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 antigen, elevated plasma C3b complement and plasma SC5b-9 complement levels suggesting an activation of the alternative complement pathway were found. Genetic testing 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) and platelet count have 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.

Renal Artery Thrombosis with Infarction in a Patient with Mild COVID-19
Ryan Mocerino, Neelja 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 nonsegmental 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 aspirin.

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 thrombosis 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.

PO0789

PO0791

A Case of Severe Thrombocytopenia in a Patient with COVID-19
Receiving Continuous Venovenous Hemodialysis
Hay Me, Zhou Zheng, Jennifer Griffthls, Anjani K. Dubey, Savneek S. Chugh. Westchester Medical Center Westchester Medical Center, Valhalla, NY.

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 hyperoxic 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.

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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%) of 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.

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 5 million infected and 330 thousand deaths worldwide. The incidence of acute kidney injury (AKI) is variable, from 0.5% to 29.8%. Rhabdomyolysis (Rb) is a life-threatening emergency, usually manifesting as myalgia, fatigue, pigmenturia, and AKI. One of its leading non-traumatic causes are viral infections. We report 5 cases of Rb associated with COVID-19.

Case Description: Of a total of 460 positive cases of COVID-19 infection (real-timePCR), at the NationalMedicalCenter20deNoviembre in MexicoCity,5were diagnosed with Rb and associated AKI(Cr< 0.5,000µI/uL and KIDIGO AKIcriteria). Characteristics of patients are presented in Fig.1. Age range was from 29 to 64 years, only one female, all with BMI<25 kg/m2, time from admission-diagnosis of Rb was on average one week. Most common symptoms were fever, cough, and dyspnea(5/3), as well as abdominal pain(4/3). Only(1/3) was oliguric at diagnosis. Average Cr at diagnosis was 7845 (18-165 µg/L) and all cases had high levels of interleukin-6. They were managed with aggressive hydration, 20% of them required renal replacement. At the time of this report, 2 had been discharged, 2 remained hospitalised(on one still on RRT), and one died.

Discussion: COVID-19 patients can develop AKI primarily due to low oral intake, sepsis, and anticoagulation. Patients with COVID-19 have multiple risk factors for Rb development: viral muscle cytotoxicity, continuous hyperthermia, and anticoagulation among others. This results in 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 managing patients as for AKI, 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.

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as any preexisting risk factors for calciphylaxis, must be kept in mind. Atypical presentations of COVID-19 due to a combination of procoagulant state, as COVID-19 caused a so-called "second hit" resulting in clinically apparent disease. Calciphylaxis given risk factors of secondary hyperparathyroidism and an additional insult of interventional care. We hypothesize that our patient had an underlying predisposition for evident. Management of calciphylaxis in PD patients is difficult under current intervention. 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. The patient is a 21-year-old man with VATER Syndrome who transitioned to intermittent hemodialysis and started on intravenous sodium thiosulfate and management challenges for nephrologists. We report an atypical manifestation of Retiform Purpura in a peritoneal dialysis patient. The Coronavirus disease (COVID-19) pandemic has posed diagnostic and management challenges for nephrologists. We report an atypical manifestation of COVID-19 presenting as a case of Calciphylaxis and COVID-19 Associated Thrombotic Retiform Purpura in a peritoneal dialysis patient. 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 lower legs (Figure 1). Laboratory findings are summarised in Table1. Her SARS-CoV-2-RT-PCR was positive. Imaging revealed no evidence of thrombosis. Skin biopsy showed severe ischemic dermopathy syndrome consistent with an overlap of COVID-associated thrombotic retiform purpura and calciphylaxis (Figure 2). The SARS-CoV-2 envelope protein was seen in endothelial cells within dermal blood vessels. The patient was transitioned to intermittent hemodialysis and started on intravenous sodium thiosulfate 25 grains 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.

### Table 1. Laboratory investigations

<table>
<thead>
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<th>Value</th>
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<tr>
<td>Proteinuria</td>
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</tr>
<tr>
<td>Creatinine</td>
<td>0.6-1.2 mg/dL</td>
</tr>
<tr>
<td>GFR (ml/min/1.73 m²)</td>
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</table>

### Case Description: Remote Peritoneal Dialysis Training in a COVID-19-Positive Patient

**Aditya V. Jain, Tina S. Samuel, Leslie A. Jansto, Erwin E. Morales, Cybele Ghossein. Northwestern University Feinberg School of Medicine, Chicago, IL.**

**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. Currently, he is fully trained and has initiated his full PD prescription.

**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.
Severe Hyponatremia as an Untintended 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 on patients with chronic diseases who avoid seeking 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 provided by daily living. She was antihypertensive but needed assistance with hygiene and meals. The family reported that over the past 7-10 days, she had become less interactive, remaining bedbound and resisting oral intake. There was an initial reluctance to bring her to the Medical Center due to the fear of contracting COVID-19 infection, given the patient's history. Despite the family being told to provide social distancing and 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 37.7% 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 hypoxia 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, respiratory 37, blood pressure 106/58 and O2 Sat 85% at room air, 95% with nasal canula at 4 L. PE was normal except for the chest which was clear. On lung auscultation her breath sounds were clear. Admission labs were remarkable for AKI and rhabdomyolysis. Serum creatinine was 3.61, BUN, and total 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 were negative. She initially received 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.

Bilateral Renal Artery Thrombosis in a COVID-19 Patient with Anuric AKI

Nitzy N. Munoz Casablanca, Osama El Shamy, Steven G. Coca, Jaime Uribarri, Shuchitra Sharma. Icahn School of Medicine at Mount Sinai, New York, NY.

Introduction: AKI is common in COVID-19. Hypercoagulability has been described. We present the case of a COVID-19 patient with anuric AKI who was found to have bilateral renal artery thrombosis (RAT) while on systemic anticoagulation.

Case Description: A 66-year-old woman with a past medical history of paroxysmal atrial fibrillation on apixaban (continued on admission), hypertension, and heart failure presented with 2 days of shortness of breath and a productive cough. She was found to be in hypoxic respiratory failure in the setting of COVID-19 pneumonia. Admission laboratory evaluation was significant for a white blood cell count of 36.8 x 10^3/μL, creatinine 6.04 mg/dL, and lactate dehydrogenase 2,600 U/L. The patient was intubated and mechanical ventilation was initiated. Her baseline serum sodium improved to 146 mEq/L, and serum creatinine improved to 0.7 mg/dL over a 10 day period. The patient was subsequently transferred to a rehabilitation unit.

Discussion: Despite the pivotal role of social distancing in preventing the spread of the novel Coronavirus, reluctance in seeking medical attention can lead to serious and even life threatening consequences.

A Case of Severe Hyponatremia in a Patient with COVID-19

Napur N. Upal, Bessy Suin Flores Chang, Hugo Andrade paz, Mala Sachdeva. Northwell Health, Manhasset, NY.

Introduction: Hyponatremia is a common electrolyte disturbance seen in association with conditions such as malignancy and infections. In the recent literature, hyponatremia has been linked to SARS-CoV-2 infection. To date, the most likely reported etiology of hyponatremia in setting of COVID-19 has been SIADH. We describe a severe case of hyponatremia, not due to SIADH, seen in a patient with COVID-19.

Case Description: 49-year-old male with history of hypertension, hyperlipidemia, positive novel coronavirus nasopharyngeal swab done as outpatient, presented to the emergency department with fever, cough and dyspnea for a week. On admission, he was afebrile with respiratory rate of 18 and oxygen saturation of 84% on ambient air. His BP was 166/105 and heart rate 105 beats per minute. Portable chest X-ray revealed rales bilaterally. Initial laboratory test showed serum sodium of 104 mEq/L and serum creatinine of 0.58 mg/dL. Additionally, C-reactive protein was elevated to 7.19, serum ferritin elevated at 1798 and D-Dimer was 158. CXR showed bilateral infiltrates. Serum lactate was low at 217, and urine studies showed elevated urine osmolality (328) and low urine sodium (< 35), suggestive for diagnosis of hypotonic hyponatremia from volume depletion. He received treatment with 3% hypertonic saline with a subsequent

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PO0804

Extracorporeal Cytokine Reduction Using Oxiris Blood Purification in COVID-19
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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 except for 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 hypoxia despite high FiO2. Oxygenation improved by HD10 (table 1) and he was successfully extubated on HD16.

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 flow of 250 ml/min and dialysate flow of 25 ml/kg/hour with either systemic heparin or regional citrate anticoagulation along with 1L/hr of pre-filter saline. For hemoperfusion we used the same parameters without dialyse. We observed rapid improvements in oxygenation (Figure 1). The findings are hypothesis generating though more data is needed to determine optimal timing and efficacy of this filter.

Table 1: Inflammatory and Respiratory Parameters.

PO0805

Rhabdomyolysis as a Late Complication of COVID-19 Infection
Benjamin Lindgard, 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 118U/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 on ITT. PCP was not performed. 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.

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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 hypoaalbuminemia. 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 cytopathic 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.

Table

<table>
<thead>
<tr>
<th>Patient</th>
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<th>Gender</th>
<th>Race</th>
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<td>Steroids</td>
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</tbody>
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a. AA: African American; b. UPCR: urine protein to creatinine ratio; c. Cr: Creatinine; d. CRP: C-reactive protein; e. HIV: Human immunodeficiency virus; f. LM: Light microscopy; g. IF: Immunofluorescence; h. EM: Electron microscopy.

PO0807

Attenuation of Circuit Longevity in COVID-19 Critical Illness with AKI on Continuous Venovenous Hemodiafiltration Despite the Use of Regional Citrate Anticoagulation (RCA) and Heparin-Bonded AN 69 (Oxiris®) Filter

Tung Lin Lee, Zhong Hong Liew, Manish Kaushik, Li Cho Michelle Ng, Jiunn Tung Lin, Hui-Lin Chuong, Han K. Tan. Singapore General Hospital, Singapore, Singapore.

Introduction: Critical illness in SARS-CoV-2 (COVID-19) infection can result in acute kidney injury (AKI). Continuous renal replacement therapy (CRRT) is part of the overall supportive ICU management.

Case Description: CRRT was delivered as Continuous Veno-venous Haemodiafiltration (CVVHDF) using the Prismaflex (Baxter Inc.) system with heparin-bonded filter (Oxiris®). The filters were electronically changed every 12 hours for first 5 days to augment cytokine adsorptive capacity. Regional citrate anticoagulation (RCA) was used to ensure filter longevity. Initial citrate dose was prescribed at 3.0 mmol/L. All 3 consecutive patients were male aged 66.7 ± 6.02 years. APACHE II score was 32.7 ± 6.51 and predicted mortality was 71%. Mean initial creatinine was 264.7 ± 60.7 μmol/L, and urine output was 6.7 mL/hour. All patients were on vasopressor support, broad spectrum antimicrobials and mechanical ventilation. 30 Oxiris filters were studied in the 3 patients. 6/30 (20%) filters clotted spontaneously before scheduled change. Mean filter lifespan (2430) was 689.6 ± 42.3 min before elective change. For the filters that clotted, mean circuit longevity was 515.7 ± 126.2 min. The observed difference was significant, p = 0.002. Importantly, filter clotting occurred despite adequate citrate dose of 3.0 mmol/L and mean post-filter ionized calcium of 0.34 ± 0.06 mmol/L. Vascular access issues were excluded by reviewing access site, return pressures. Citrate dose was increased to 3.2 mmol/L for all patients and this reduced the frequency of filter clotting subsequently. Two patients were extubated and had full renal recovery - mean duration of CRRT dependence was 9.5 days. However, the third patient remained CRRT dependent until demise on the 28th day of ICU stay.

Discussion: Attenuation of circuit lifespan was observed despite adequately dosed RCA and heparin bonded Oxiris filters. We theorise that this could be due to a pro-coagulant state induced by the SARS-CoV-2 infection. Possibly, higher citrate dose to target even lower post-filter ionized calcium may be required to optimise anticoagulation and filter lifespan, thereby ensuring optimal effluent dose and solute clearance, for critically ill COVID-19 patients.

PO0808

SARS-CoV-2 Infection in the Early Post-Transplant Period After a Living Donor Kidney Transplant


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 kidne y transplant (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. Patients 1 and 2 had minimal symptoms at diagnosis, whereas patient 3 had high grade fever, cough and shortness of breath. All 3 patients had lymphopenia at diagnosis and none required supplemental oxygen or intensive care unit monitoring. All 3 patients received hydroxychloroquine and hydroxychloroquine. Mycophenolate mofetil dose 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) which has not been described previously.

PO0809

COVID-19-Related Collapsing Focal Segmental Glomerulosclerosis and Apolipoprotein L1: A Report of Two Cases

Sandeeep Magoon, Varun Malhotra, Prasad B. Bichu. Eastern Virginia Medical School, Norfolk, VA; Nephrology Associates of Tidewater, Norfolk, VA.

Introduction: Acute kidney injury has been seen in approximately 15% of the patient with COVID-19 infection. Acute tubular injury was presumed to be the most common cause of AKI, but it did not explain significant proteinuria and hematuria. We present the case report of 2 patients with collapsing focal segmental glomerulopathy with COVID-19.
PO0811
Low-Sodium Disorders and the 2019 Novel Coronavirus Disease (COVID-19)
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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, very few reports or cases of hypomagnesemia 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 euovolemic. 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 mEq/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 14 mEq/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 improved 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 could be multifactorial as seen in the cases above. Clinical assessment of volume status and urine studies including osmolality and sodium with a thorough review of medications is the key to differentiating causes of hyponatremia and determining adequate management.

PO0812
COVID-19 Short-Term Outcomes of AKI and Chronic Hemodialysis
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Introduction: Acute kidney injury (AKI), albuminuria and hematuria are common and in patients with 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 few 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 (median time 39 days) with a creation(Cr) of 7.87mg/dL. Urinalysis revealed active sediments with 55 RBC/bhp, 65 WBC/bhp, and nephritic range proteinuria: 5 g/gm of creatinine. We 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. Cryoplasma(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). ATN is by far the most described glomerular lesion. Clinicians should be aware of AVF with GN as another potential pathology, and concurrent use of immunosuppression with treatment of infection, can lead to favorable clinical outcomes.
Case Description: 58-year-old African American male with past medical history of hypertension presented with cough, dyspnea and fever. On admission, he had a temperature of 104°F, BP of 149/90 mmHg, HR of 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 4.0 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 renal dysfunction. A clear viral cytopathic effect of SARS-CoV-2 on proximal tubular cells causing hypokalemia. In the case setting, 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.

Rhabdomyolysis in COVID-19 Patient Requiring RRT
Muhammad usama shah Hamdani, Jeremy Carlson, Hasan Zahid. University of Florida College of Medicine, Gainesville, FL.

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. The case setting 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.

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 these medications for the last seven days. She was not on statins. She was a healthcare worker at a nursing home that had a recent outbreak of the novel Coronavirus with 51 positive cases. In ER, she was febrile, tachypneic with WBCs of 11.8 thousands/mm3, Creatinine of 6.88 mg/dL, BUN 78mg/dL, and creatinine kinase (CK) of 167,770 U/L. Urinalysis showed large amount of blood with 17 RBCs. Chest X-ray significant for mild patchy airspace opacity in the Lingula. She also tested positive for COVID-19. She was adequately volume resuscitated and alkalinized. Due to her severe AKI, she did not meet criteria for Hydroxychloroquine and Azithromycin. Sarilumab was contraindicated due to transaminis. Patient was started on hemodialysis on day 3 of admission as her creatinine continued to rise. On the 10th day after admission, her transaminis improved and Sarilumab was administered. Repeat Covid-19 test before administering Sarilumab was positive. Her IL-6 levels checked before initiating the drug were <5 pg/mL. Her CK levels had started to trend down and were at 4880 U/L the day before starting Sarilumab. She remained oliguric and on hemodialysis with no signs of renal recovery at the time of discharge.

Discussion: Coronavirus has a huge range of presentation from asymptomatic to severe ARDS. Our goal is to highlight one of the complications of the novel corona virus leading to acute renal failure requiring hemodialysis.

Severe AKI from Thrombotic Microangiopathy and Acute Tubular Necrosis in a Patient with COVID-19 and Gemicitabine Chemotherapy Use

Introduction: Thrombotic microangiopathy (TMA) is a known but rare complication of gemcitabine therapy. However, gemcitabine-associated TMA has not been reported in a patient with concurrent COVID-19. Here, we present an interesting patient with COVID-19 who developed severe acute kidney injury (AKI) from acute TMA and acute tubular necrosis (ATN) following gemcitabine therapy.

Case Description: 45-year-old AA female with history of recurrent metastatic cervical cancer, peritoneal carcinomatosis, small bowel resection, coloso-valvulostomy, colostomy and bilateral nephrostomy tubes was hospitalized for severe symptomatic anemia, fever and AKI. A week prior to hospitalization, patient had received her third outpatient dose of gemcitabine. Four weeks prior to presentation, serum creatinine (Scr) was 0.77. On admission labs, Scr was elevated at 7.36 and hemoglobin was low at 4.8. Patient also tested positive for COVID-19 on admission labs. There was no evidence of hydrenephrosis on CT scan. Patient found to have clinical and labs findings of TMA (hypertension, thrombocytopenia, elevated lactate dehydrogenase and low haptoglobin) during hospital stay. Peripheral smear showed multiple schistocytes. Urinalysis was significant for microscopic hematuria and proteinuria. Spot urine total protein to creatinine ratio was 4.6. Complement C3 and C4 were not low. Patient was Coombs IgG positive and was initiated on high dose intravenous corticosteroids. Our patient also received one dose of rituximab therapy as per inpatient oncology team. Patient was initiated on hemodialysis for uremic symptoms. Kidney biopsy subsequently performed during hospital stay showed acute TMA and acute tubular injury with focal tubular necrosis.

Discussion: Our patient developed severe AKI in the setting of gemcitabine chemotherapy use and COVID-19. Kidney biopsy showed findings of both TMA and ATN. While the kidney biopsy findings are very interesting, it is unknown if either gemcitabine or COVID-19 or both were responsible for the severe AKI seen in our patient. Our patient remains oliguric and dialysis dependent.
First US Case Series: Continuous Renal Replacement Therapy with Adsorbent Oxiris Filter in the Setting of COVID-19 Infection

Introduction: Many COVID-19 hospitalized patients sustain acute kidney injury (AKI) requiring CRRT. Multisystem inflammatory response plays a large role in their infection leading to enhanced morbidity and filter clotting. Oxiris filters have been used in Europe in septic patients due to their properties of reducing cytokines and inflammatory mediators but have not been available in the United States until late April 2020. Use of these filters in COVID-19 patients has been very limited, and has not yet been reported. We report the first U.S. experience in 3 COVID-19 patients requiring mechanical ventilatory support and continuous venous to venous hemodiafiltration (CVVHDF) using oxiris dialyzers for their AKI.

Case Description: Case 1: A 73 year old male with laboratory tests revealing: creatinine 1.79mg/dl, C-Reactive Protein 1.01mg/dl, D-dimer 397, ferritin 13,000 ng/ml. He was started on CRRT on the ICU day of admission using CVVHDF with an oxiris filter and then switched to oxiris filter. He remained on oxiris CVVHDF for 9 days with no reported clotting events, a decline in ferritin by 90% to 1437ng/ml and a decline in IL-6 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 dialyzer was switched to oxiris. He had no clotting events while on CVVHDF for six days and his serum ferritin level decreased to 1759 ng/ml. Case 3: A 40 year old male on extracorporeal membrane oxygenation (ECMO). He was initiated on CVVHDF to the ECMO circuit using a M150 filter for 7 days and was switched to oxiris filter with no reported clotting events thereafter.

Discussion: The COVID-19 cytokine storm leads to activation of pro-inflammatory mediators leading to severe morbidity including coagulopathic events. Optimal treatment is still unknown. ECMO and CVVHDF with oxiris dialyzer in critical COVID-19 infection may play a role in decreasing inflammatory markers, which confers overall clinical improvement. Once switched to oxiris, our patients showed improvement in inflammatory markers and had no clotting of their dialyzers. In these patients, convective clearances (CVVHDF) may be more beneficial than diffusive therapies (CVVHD).

Pre-Filter Argatroban for Coronavirus Disease 2019
Pablo Villanueva-Meyer,1 Sandhya S. Thomas,2,3 Baylor College of Medicine, Houston, TX;1 Michael E DeBakey VA Medical Center, Houston, TX.

Introduction: Coronavirus disease – 2019 (Covid-19) has been implicated in a pro-thrombotic state. This has been well documented in numerous articles and has posed to be a clinical obstacle for those caring for Covid-19 positive patients. This has been particularly challenging for Nephrologists managing patients on continuous renal replacement therapies (CRRT). Amongst other things, filter clotting has been associated with an increased number of transfusions and interruptions in sustained therapy, as well as increased costs to the healthcare systems and patients.

Case Description: We present the case of a 73-year-old African American male with a past medical history of underlying chronic kidney disease, hypertension, diabetes mellitus, heart failure, and atrial fibrillation who was admitted from his nursing facility for respiratory failure and stage 3 AKI. Although MetHb is linked to severe illness including sepsis, little is known about its association with COVID-19 positive patients. Our report highlights the importance of considering alternative diagnoses of very high MetHb levels such as G6PD deficiency in COVID-19 patients. This is of particular relevance as Hydroxychloroquine has been used as experimental treatment for COVID-19 and in the current climate, G6PD deficiency could be an important issue in patients with AKI due to haemolytic anaemia and significantly elevated MetHb, particularly in those from regions of high prevalence and those treated with known triggers such as Hydroxychloroquine.

Pre-Filter Argatroban for Coronavirus Disease 2019
Viviam Tainaka, Aulio, Aromma Kapoor, St Helier Hospital, London, United Kingdom.

Introduction: Patients with COVID-19 can be asymptomatic or have severe illness. Oxidative stress may be a cause of increased severity and mortality in COVID-19 patients. Methaemoglobinemia (MetHb) and haemolysis can occur as a result of oxidative stress. MetHb is associated with sepsis, exposure to drugs and inborn errors of metabolism. Glucose-6-phosphate dehydrogenase (G6PD) deficiency may also manifest with MetHb and haemolysis.

Case Description: A 31-year-old man, originally from West Africa, with no comorbidities, presented with dyspnea, cough, anemia, and oligo-anuria. He had type 1 respiratory failure and stage 3 AKI, which led to critical care admission for ventilation and haemolysis. COVID-19 pneumonia was confirmed by nasopharyngeal swab and radiological imaging. He developed haemolytic anaemia. The MetHb was 3.5% (normal <1.5%). It rose to a peak of 10.7% with persisting anaemia and further investigations showed G6PD deficiency. He had no exposure to medications known to trigger haemolytic crises, such as Hydroxychloroquine. He was treated with supportive management including red cell transfusions and also with Ticlopidine for COVID-19. He was extubated after 15 days and recovered renal function. Data on 9 other patients admitted during this period to the ITU with COVID-19 and AKI showed 7 had normal MetHb levels and 2 had modest elevations (~3%).

Discussion: Triggers of G6PD deficiency include stress from infections, fava beans, or drugs e.g. Hydroxychloroquine. It typically presents as haemolytic anaemia, jaundice and AKI. Although MetHb is linked to severe illness including sepsis, little is known about its association with COVID-19 positive patients. Our report highlights the importance of considering alternative diagnoses of very high MetHb levels such as G6PD deficiency in COVID-19 patients. This is of particular relevance as Hydroxychloroquine has been used as experimental treatment for COVID-19 and in the current climate, G6PD deficiency could be an important issue in patients with AKI due to haemolytic anaemia and significantly elevated MetHb, particularly in those from regions of high prevalence and those treated with known triggers such as Hydroxychloroquine.

Rhabdomyolysis and Methaemoglobinemia
Nafees Naifee, Rouvick Gama, David Makanjuola, Virginia A. Quan.

Introduction: Covid-19-associated rhabdomyolysis has not been clearly established; therefore, clinicians might have low clinical suspicion for rhabdomyolysis.

Case Description: We are presenting five cases where Covid-19 patients became very catabolic and developed rhabdomyolysis, with AKI. One day later they were intubated for tachypnea and worsening oxygen saturation. They were admitted to the intensive care units and were treated with intravenous hydration. All the patients eventually required pressor support. AKI developed 10 days after onset of the symptoms and it was attributed to cytokine storm, ischemic acute tubular necrosis, and rhabdomyolysis. Intravenous furosemide was attempted with poor response. Renal replacement therapy (RRT) was needed approximately three days after development of AKI. Continues renal replacement therapy (CRRT) was the modality used. After 3 days of interrupted therapy due to clotting, there was no improvement and overall high mortality.

Discussion: Rhabdomyolysis has been associated with many infectious diseases, including viral infections. The direct viral invasion and circulating viral toxins may directly destroy muscle cell membranes leading to rhabdomyolysis. However the
Severe Hypertriglyceridemia Leading to CRRT Malfunction in a COVID-19 Patient

Richard 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 hypertriglyceridemia (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 T2DM presented to the hospital with shortness of breath and fevers found to have COVID-19. The patient was intubated on presentation due to hypoxic 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 on propofol for sedation may help to improve the vital prognosis of COVID-19.

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

PO0824

Severe Hypertriglyceridemia Leading to CRRT Malfunction in a COVID-19 Patient

Richard 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 hypertriglyceridemia (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.

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PO0825

COVAN, COVID-Associated Nephropathy: An Evolving Epidemic of Kidney Disease

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Introduction: We highlight COVID-19 related renal characteristics in 6 African American patients with positive nasopharyngeal RT-PCR for SARS-COV-2 infection, presenting without severe respiratory symptoms but with acute kidney injury and nephrotic range proteinuria.

Case Description: One of the patients was a transplant recipient. None required mechanical ventilation and no COVID-19 specific therapy was prescribed. All underwent a renal biopsy that showed varying combinations of collapsing glomerulopathy, podocyteopathy and protein overload tubulopathy (Fig 1A). Additionally, tubulo-vascular inclusions and virions (suspected to be SARS-COV-2 virions) were seen in electron micrographs (Fig 1B). APOL1 genotype was tested in 3 patients who were all found to carry high-risk genotypes, suggesting possible susceptibility of patients with high-risk APOL1 alleles to kidney involvement in SARS-Cov-2 (Fig 1C)

Discussion: There was discordance between the high risk G1/G1 genotype of the transplant recipient and the low risk G1/G0 donor kidney genotype, suggesting the important possibility of a systemic APOL1-related mechanism in kidney injury. In conclusion, these 6 cases draw attention to proteinuric kidney disease in 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.

Figure 1: 1A: Demographic and Clinical features of the Six Cases. 1B: Biopsy findings.

PO0826

AKI and Purpuric Rash in a COVID Patient

Zakir Shaik, Rui Song, Jared Hassler, Iris J. Lee, Dina Abdelwahab, Avrum Gillespie. Temple University, Philadelphia, PA.

Introduction: AKI in COVID-19 patients are reported in several studies with an incidence of 23%. We report a case of COVID-19 pneumonia with AKI and purpuric rash.

Case Description: A 54 y/o female with hypertension, CKD stage 3, with a COVID+ swab, presented with CT chest findings consistent with COVID-19 pneumonia, purpura of the lower limbs concerning for leukocytoclastic vasculitis and non-oliguric AKI. Creatinine on admission was 8.5mg/dL (baseline of 1.6mg/dL), CBC showed a wbc 26.9, Hb 6.9, platelets 196 and eosinophilia. Serologies were notable for elevated direct coomb, low haptoglobin, low C3/C4, and rheumatoid factor of 26. UA had no hematuria, UPUR 0.75 mg/mg. Home medication, naproxen was stopped one month ago. Renal biopsy showed severe acute tubular injury (ATI), coarse vacuolization of tubular epithelial cells, severe leukocytic infiltration of lymphocytes, neutrophils, eosinophils, severe vascular hyalinosis, global glomerular sclerosis (11 out of 30 glomeruli), severe (60%) interstitial fibrosis & tubular atrophy. Per institutional protocol, Immunofluorescence could not be performed in COVID+ patients. Renal function improved significantly after a 5 day course with IV steroids alone and patient remained stable with a creatinine of 3.4 mg/dl.

Discussion: This case features multiple potential mechanisms for AKI in a COVID-19 patient. Viral effects include, acute interstitial nephritis (AIN), severe ATI, and endothelial inflammation leading to vasculitis and purpuric rash. Recently, vasculitis similar to Kawasaki disease has been described in COVID-19 patients. Our case suggests that immune deregulation from COVID infection may result in autoimmune findings such as elevated RF and hemolytic anemia. AKI improved in our patient after steroids, suggesting that a biopsy with features of AIN should be treated and could change the course of the disease.
PO0827


Kevin S. Ha, Rasha Alawieh, 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.

PO0828

Does Cyclophosphamide Exposure in Patients with Vasculitides Lead to Better COVID-19 Outcomes?

Sayed mohammed fazzan M. Zabiullah,1,2 Arie Gunarsa,1 Ashok P. Chandhari.1 Metropolitan Hospital Center, New York, NY; 2New York Medical College, Valhalla, NY.

Introduction: COVID 19 is a pandemic disease caused by novel coronavirus called SARS-CoV-2. End Stage Renal Disease patients are at high risk for developing severe manifestations of the disease often associated with high morbidity and mortality. Excessive and uncontrolled immune response is thought to be one of the important underlying mechanism for severity of the disease. We present 3 ESRD patients with underlying vasculitides who were admitted with respiratory distress due to COVID 19.

Case Description: 3 patients with COVID 19 infection were treated. A 37-year-old male with ANCA-PR3 related vasculitides resulting in ESRD, on hemodialysis. He had been treated with Cyclophosphamide and prednisone induction. The third patient is a 43-year-old female with SLE; ESRD secondary to lupus nephritis. She had been treated with cyclophosphamide and prednisone induction. The patient 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

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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 reverse transcriptase polymerase chain reaction (PCR) via nasopharyngeal swab. 3 patients were suspected, but PCR-negative. Common comorbidities include hypertension, hyperlipidemia, and obesity. Patients had AKI with creatinine range 1.2 to 13.48 mg/dL. Kidney ultrasound showed enlargement and increased echogenicity. Biopsies were performed 9 to 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 paraffin-embedded 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 2/3 AKI. Biopsies were examined using light and electron microscopy. Immunohistochemistry 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 immunohistochemistry or in situ hybridization.

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.
Methods: Liposomal nanoparticles displaying the SARS-CoV-2 spike protein trimer (S1 and S2) on their surface (virosmes) were generated. We evaluated spike protein and virosmes 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 discovered specific KIM-1 spike inhibitor, JB-1 was tested in its ability to block virosmes 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 virosmes 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 virosmes uptake, despite no change in ACE2 expression. This KIM-1 specific uptake was inhibited by JB-1. Human kidney tubuloids also endocytosed virosmes, and tubuloids with enhanced KIM-1 expression secondary to infection of KIM-1-adenovirus had increased uptake of virosmes. 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±0.310 nM respectively.

Conclusions: KIM-1 is a receptor for SARS-CoV-2. KIM-1 specific uptake of the SARS-CoV-2 virosmes suggests that KIM-1 confers efficient SARS-CoV-2 binding in kidney epithelial cells when these cells are expressing KIM-1. The KIM-1 dependent virosmes uptake by 3D tubuloids indicates that 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 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

PO0833

Morphological Evidence Suggests That Kidney Injury Molecule 1 May Serve as a Proximal Tubule Receptor for SARS-CoV-2

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Background: Kidney injury molecule-1 (KIM-1), a type-1 transmembrane glycoprotein, has been well studied as a 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 investigate 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 AKG7 antibody) and scored from 0 to 3+. Electron microscopy was used for examining uptake of virosomes. The results were analyzed using the Wilcoxon rank-sum test.

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 to 7.0 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 1+ to 3+ granular staining in the PT cytoplasm as well. The KIM-1 staining in COVID19+ kidneys was significantly lower than in the control kidneys, 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 studies validated the observed differences. Our study is one of the first to show KIM-1 expression in COVID+ kidneys revealed spotty granular staining in the cytoplasm and diffuse 1+ to 3+ granular staining in the PT cytoplasm as well. The KIM-1 staining in COVID19+ kidneys was significantly lower than in the control kidneys, indicating active regulation in response to injury.

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PO0832

Kidney Injury Molecule 1 Is a Receptor for SARS-CoV-2

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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, and KIM-1 is a scavenger receptor in kidney epithelial cells. We hypothesized that KIM-1 is a receptor for SARS-CoV-2 and may play an important role in COVID-19-associated AKI.

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

Underline represents presenting author.
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 our protocol (Arazi 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. 25,994 single cell profiles passed QC with a median of 433 cells per sample [IQR 271 to 718]). Cellular clusters were annotated to immune (9780 cells, Fig: cluster 3-7), renal epithelial (4364, cluster 1) and bladder cells (4151, cluster 2). The SARS-CoV-2 receptor ACE2 was found in epithelial cells and co-expressed with CPEB3. The COVID-19 therapeutic target IL-6 was robustly detected in both myeloid and epithelial cells with co-expression networks linking IL-6 expression in proximal tubular epithelial cells to HMG1, VEGF and HIF signaling and to viral response networks in myeloid cells.

**Conclusions:** Urine single cells contain a spectrum of epithelial and immune cells expressing viral receptors of SARS-CoV-2 and therapeutic targets of emerging COVID-19 therapies offering a window to monitor renal cellular responses in COVID-19 trials.

**Funding:** NIDDK Support

PO0836

**Stimulus and Cell-Specific Responses to Volume Depletion, Ischemia, and COVID-19**

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**Background:** A stimulus-response map of the injured kidney might reflect a common response of the injured kidney (Rossa-Donati et al. J Am Soc Nephrol 31: 2020). Emerging COVID-19 therapies offering a window to monitor renal cellular responses in immune cells expressing viral receptors of SARS-CoV-2 and therapeutic targets of SARS-CoV-2 infection. Therefore, we investigated the gene expression profile of a broad range of immune cells using single-cell RNA sequencing (scRNAseq).

**Methods:** We developed a novel protocol (Arazi et al. Nat Immunol) allowing for immediate isolation of urine cells by lysis into a cell pellet followed by a 10X Chromium-based scRNAseq. We generated 25,994 single cell profiles 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. 25,994 single cell profiles passed QC with a median of 433 cells per sample [IQR 271 to 718]). Cellular clusters were annotated to immune (9780 cells, Fig: cluster 3-7), renal epithelial (4364, cluster 1) and bladder cells (4151, cluster 2). The SARS-CoV-2 receptor ACE2 was found in epithelial cells and co-expressed with CPEB3. The COVID-19 therapeutic target IL-6 was robustly detected in both myeloid and epithelial cells with co-expression networks linking IL-6 expression in proximal tubular epithelial cells to HMG1, VEGF and HIF signaling and to viral response networks in myeloid cells.

**Conclusions:** Urine single cells contain a spectrum of epithelial and immune cells expressing viral receptors of SARS-CoV-2 and therapeutic targets of emerging COVID-19 therapies offering a window to monitor renal cellular responses in COVID-19 trials.

**Funding:** NIDDK Support

PO0837

**AKI and Collapsing Glomerulopathy Associated with COVID-19 and APOL1 High-Risk Genotype**

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**Background:** Acute kidney injury (AKI), with or without proteinuria, has been described in patients with Coronavirus disease 2019 (COVID-19). Kidney involvement in COVID-19 has been reported to be of greater severity in African Americans (AA). Here, we report genetic, histopathological and molecular findings in 6 AA patients with COVID-19 presenting with AKI and de novo nephrotic-range proteinuria.

**Methods:** Percutaneous kidney biopsies were performed in 6 patients with COVID-19 with respiratory manifestations and proteinuric AKI. Peripheral blood was obtained for apolipoprotein L1 (APOL1) risk allele assessment. Kidney tissue was also examined by situ hybridization (ISH) for viral detection and by NanoString for COVID-19 associated genes and genes related to tubular injury.

**Results:** Six AA patients with COVID-19 (4 men, 2 women), mean age 55 years (37-65) were included in the series. At biopsy day, the mean serum creatinine was 6.5 mg/dL (2.9 – 11.4) and the mean urine protein-to-creatinine ratio was 11.5 g (3.6 – 25.0). Five patients were African American, three patients were Hispanic, and two were Caucasian. Nine patients had varying degree of proteinuria. Eight patients had severe COVID-19: Clinical and Basic Science Characteristics

**PO0838**


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**Background:** Acute kidney injury (AKI) has been recognized as a common complication of severe COVID-19 in hospitalized patients. Proteinuria and microscopic hematuria have also been observed. While a recent autopsy series of patients who died with severe COVID-19 in China found acute tubular necrosis (ATN) in the kidney, few case reports of collapsing glomerulopathy in COVID-19 have also been reported.

**Methods:** To better understand the clinical and histopathologic findings, we looked at 10 kidney biopsy cases in patients with COVID-19 along with clinical features of AKI with or without proteinuria or hematuria in our institution. We described their clinical features, pathologic findings and outcomes.

**Results:** The mean age of the patients who underwent kidney biopsy was 65 years. Four patients were African American, three patients were Hispanic, and two were Caucasian. Nine patients had varying degree of proteinuria. Eight patients had severe...
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 patients 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
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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 demonstrating abnormalities in renal function. 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/m², of which 6 (67%) had hypertension and 4 (44%) had diabetes. AKI was present in 7 of 9 (78%), 4 (44%) 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 0.96 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 out of 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
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Background: While acute kidney injury (AKI) is a common and serious complication of patients with COVID-19, the mechanisms are unclear. Histopathological 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, or with severe autolysis were 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 out of 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 Podoocyte Injury and Collapsing Glomerulopathy in Kidney Biopsies
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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 multiorgan failure including acute kidney injury (AKI), some cases also manifesting nephritic 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 clinco-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 (3) or diffuse (2) active tubulointerstitial inflammation around arterioles (10-40%), diffuse interstitial inflammatory infiltrate, moderate ascites (4).
diabetic kidney disease in 2. No immune deposits were localized by IS. By EM, variated glomerular capillary loop 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-interstitial inclusions in 2. Viral particles are identified within cells of glomeruli and tubulo-interstitial area, scattered or in clusters in the cytoplasm and endoplasmic reticulum vesicles, confirmed by IS.

Conclusions: The constellation of typical glomerular collapsing features with tubulointerstitial findings and localization of virus by EM, suggests a distinct viral associated nephropathy, reminiscent of HS associated nephropathy. A role for viral cytopathic effect, cytokines and antibody mediated APLD gene variants could be considered.

PO0842
COVID-19 Renal Pathology Protocols and Pathology Practice in Latin America: Analysis from GlomCon Latin America Working Group (LGlomCon)
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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 75 questions in 6 sections, directed to pathologists, nephrologists and other specialists from 16 Spanish speaking LA countries treating COVID-19 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 corresponded to pathologists that respond renal biopsies derived from 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 immunohistochemistry (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 cases. Autopsy and biopsies showed 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. Practical changes 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 has not been 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
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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 Toxicoid (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 catalase 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.

PO0844
Renal Pathology of 34 Consecutive COVID-19 Autopsies: A Single-Institution Experience
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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 nasal swab for SARS-CoV-2 except 3 (presumed false negative). All had on average 3.4 comorbidities (range: 0-7; hypertension (HTN), diabetes (DM), obesity, COPD, asthma, stroke, dementia, cancer), frequently HTN (29) and DM (25). 31 required intubation and 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%), to >50% (17%), and moderate (40%) or severe (40%) chronic vascular scarring. Other findings: obesity related renal disease (2), atherosclerosis (2), arteriovenous malformations (1), 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 tubulointerstitial capillaries. C6b-9 staining was positive in 2strong, 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 autopsies kidney from 30 patients with COVID display glomerular disease with co-morbidities present that are related to AKI with AKI or ESRD (59%). Despite varied tissue autolysis and the absence of significant proteinuria, the majority of AKI is presumed 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.

PO0845
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, reported mortality and research work that assessed the association of ACEi/ARBs on the severity of illness.

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-infection (1) ACE/ARB analysis (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 tubulointerstitial capillaries. C6b-9 staining was positive in 2strong, 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: Based on the results of this meta-analysis, ACEi/ARB are not associated with increased mortality or severity in COVID-19 subjects.
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 initiated on ACEI/ARBs during hospitalization, group 2 (n=58 patients; 19%) 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 (P= 0.001, 95% CI of 1.78-9.59) 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= 0.002, 95% CI of 1.2-11.2). Their mortality rate is increased 2.9 times (P=0.026, 95% CI of 1.23-7.44). 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

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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 FIO2 ≥ 0.25 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 SaO2/FiO2 ratio, SaO2/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.

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

Underline represents presenting author.

Table 1. Clinical characteristics of patients (N16)

PO0848

Renin-Angiotensin-Aldosterone System Blocking Drugs in Patients with SARS-CoV-2: Systematic Review and Meta-Analysis

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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 blocking agents 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). Pooled 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).

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.

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

Underline represents presenting author.
PO0849

Association of Prehospital RAAS Inhibitor Use with AKI and Death in a Cohort of Hospitalized COVID-19-Infected Patients
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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 3 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. The described RAASi use were older (71.9 vs 63.6 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 1.3299% CI 1.04-1.68)) and a higher OR for death (OR 1.53 (95% CI 1.18-1.98). Multivariable adjustment for age, demographics, and clinical comorbidity 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 0.68-1.24)). 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
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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% (48/80) 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 not on multivariable 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 multivariable analysis, continuation of these agents during hospitalization predicted lower ICU admissions (OR=0.25, 0.08-0.81, p=0.02), peak CRP (-6.9 ± 3.1 mg/dl, p=0.03) and peak inflammatory score (-2.3 ± 1.1, p=0.001) 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)
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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 43 (4%) and physicians in training 11 (3%). 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 70.8% 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
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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 diseases. 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 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 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
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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. Test for COVID-19 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: CKD, CKD4, and post kidney transplant. Since April 8, 2020, average 0.038% of dialysis patients were tested positive for COVID-19 and average 0.015% were diagnosed with COVID-19.

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
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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 commerical 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 is noted that when adjusting for per diseased 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
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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

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conditions was conducted. The feedback to the program and the psychological assessment repeated after one month.

Results: Totally, 181 patients showed active responses to the program, with 289 people-time medical consultations occurred during the study. The virtual care program provided a rapid triage, with 17% patients provided a timely referral to in-patient medical care. The median time from request to response was 75 minutes (IQR 30-120). The program was helpful for 180 patients (94%). One patient (0.5%) believed the program was helpful. The outcome of symptoms (OR 1.309, 95%CI 1.113-1.541; P=0.001) and being enrolled during pandemic (OR 3.939, 95% CI 1.174-13.221; P=0.026) were associated with high stress. After the follow-up, the high-stress CKD group at baseline showed a significant decrease in average CKD stage (9±1.4 vs. 8±1.9, P=0.015).

Conclusions: The delivery of patient care, which has remained largely unchanged for decades and relied primarily upon direct, in-person care, has had to evolve to meet the demands of a world in pandemic. As a result, significant changes have occurred with staffing structure and variations in the way they interact with the pharmaceutical industry.

PO0856

Background: 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 specialties as they unfolded and to understand how the model of patient care delivery will change moving forward.

Methods: Survey data was collected weekly or bi-weekly between March 20th and May 19th. Participants were asked questions about their telemedicine program. Approximately 50 nephrologists participated in each wave, along with 200 neurologists, dermatologists, rheumatologists and gastroenterologists.

Results: The impact of the COVID-19 outbreak on physician practices was swift and monumental. As of early April office visits were down more than 70% across specialties. As noted by 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 somewhat buffered from overall declines due to their dialysis patient responsibilities. Not only did these significant drops in patient office visits impact patient access to medical care, patient financial practices also suffered drastic financial impacts. More than half of the specialists reported a “substantial” impact on the financial health of their practice by early May. Practices responded swiftly with telemedicine adoption, and by early April more than 90% of most specialties had adopted some telemedicine capabilities. By the final wave, 78% reported that the COVID-19 experience will have a lasting impact on how their practice operates from the way physicians interact and see patients to long-term staffing structure and variations in the way they interact with the pharmaceutical industry.

Conclusions: The delivery of patient care, which has remained largely unchanged for decades and relied primarily upon direct, in-person care, has had to evolve to meet the demands of a world in pandemic. As a result, significant changes have occurred with the adoption of telemedicine, and given physicians and patients a new way to interact. Additionally, as practices try to rebuild from significant lost revenues, staffing structures and typical in-office activities, such as meeting with pharmaceutical representatives, along with conference attendance, will likely never return to their pre-pandemic levels. 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
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Background: The COVID-19 pandemic has necessitated increased use of telemedicine for outpatient care. Accessing a large group of patients impacted access to 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 northeast Pennsylvania. We also examined the association between patient characteristics (age, sex, patient portal status, Charlson Comorbidity Index [CCI]) and use of telemedicine visits.

Results: From 3/15/20-5/29/20, nephrology was the top adult specialty using telemedicine at Geisinger in terms of proportion of office visits using telemedicine (televideo 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 a95% each week from (3/22/20-5/29/20). 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 telemedicine used televideo was 42% overall with large differences by CCI score, and patient portal status (Figure). For example, the proportion of telemedicine visits using televideo 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 older patients and many comorbidities who are particularly susceptible to ill effects from COVID-19. Patient portal users were much more likely to use televideo 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.
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 take 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 area reduction 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 (up to 8h), and generally achieved UF goals. Later HD nurses cunnulated 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

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 haemodialfiltration (CVVHDF)). With the onset of the COVID-19 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 CVVHF/HDF consumables & new machines to deliver this requirement; all critical drivers to seek local solutions for RRT provision beyond usual capacity

Methods: A kidney unit neighbour described their successful experience trialing SC+ in COVID19 patients. Translation of SC+ from home use to safe HD 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+ & 2 supporting RO machines were critical determinants in making 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 35.5, 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: At 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

COVID-19: Clinical and Basic Science Characteristics
P00863
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 anti-viral 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 ventricular 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 first patient is expected to be enrolled in June 2020.

Funding: Commercial Support - Renibus Therapeutics

P00864
The COVID-19 Infodemic
Tejas Desai,1 Arvind Conjevaram.1 NOD Analytics, Harrisburg, NC, ‘The Banglore Hospital, Banglore, India.

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” as “the volume of coronavirus related 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, Pathophysiology). We programmed 1) an application programming interface to download tweets and their metadata in JavaScript Object Notation beginning 11 March 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 pandemia events. Finally, TD created a free repository of the dataset in the #NephTwitter Archives (https://bit.ly/2M6HJIG) 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 the WHO. 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 category. 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 the WHO. 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 category.

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.

P00865
The Impact of the COVID-19 Pandemic on the Mental Health of Health Workers Treating Patients with Kidney Diseases in Latin America (LA):
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Poster

Background: The 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 and 340 were complete. 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. Preventing symptoms were anxiety, insomnia, and depression, with 75.2%, 42.5%, and 18.2%, respectively. Physical or verbal violence from the community was reported by 18% (5%) of the participants because they were seen as a source of viral transmission. 179 (55%) considered personal protective equipment (PPE) was sufficiently provided and 212 (62%) had to invest up to 20% of their income to obtain PPE. In addition, 144 (44%) of the respondents reported a shortage of COVID-19 tests and only 99 (30%) felt their hospital was well equipped to care for COVID-19 patients. 126 (39%) of the health workers responded that they received adequate training, while 105 (32%) endorsed they did not prepare in the management of patients with COVID-19.

Conclusions: This survey reveals the considerable impact that the COVID-19 pandemic is generating among physicians treating patients with kidney diseases in LA. Possible aggravating factors also found in our survey included lack of testing, PPE availability, and overall hospital preparedness.

Funding: Private Foundation Support

P00866
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 hospital stay, there is a high vulnerability of these patients to COVID-19.

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 concerted 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.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
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PO0867
SARS CoV-2 Continuous Quality Improvement Program: Initiation of a Standardized Protocol for AKI Prevention
Adam Dossaji, Asad H. Khan, Spencer Hodgings, Daniel L. Landry, Daniel Engelman, Jonathan Slater, Bill Mcgee, Michael J. Germain. Baystate Medical Center, Springfield, MA.

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 4/15-5/15/2020 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 consults & utilization of a renal-protective strategy including monitoring volume status, scrutinizing nephrotoxic medications & urine studies. 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 CoV2 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, 58% of 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 getting 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 CoV2 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.

PO0868
Renal Critical Care Project Management of COVID-19 Pandemic Surge
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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 resources as critical care areas expanded 2-3 fold. In addition to well chronicled ventilator management resources over multiple hospital sites planning 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 identified likely shortfalls in the quantity of Baxter Prisma machines for Long Island Jewish and NorthShore University Hospital. Of 4579 patients, 51.8% were male. Median age was 65 years, IQR (52-76). 3313 (72.3%) were positive for the COVID-19. Hypernatremia, hyponatremia, hyperkalemia, hyperglycemia, hypocalcemia, and hypoalbuminemia were significantly more common in hospitalized patients with COVID-19 (p<0.0001).

Conclusions: Dysnatremias, hyperkalemia, and hyperglycemia were more common in patients with COVID-19. Hypocalcemia was more common in patients with COVID-19 but this may be due to a higher prevalence of hypocalcemia. Further studies are needed to adjusted models to describe the association between electrolyte abnormalities and clinical outcomes.

Funding: NIDDK Support

PO0869
Electrolyte Abnormalities in Hospitalized Patients with COVID-19
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Background: Electrolyte abnormalities have been observed in hospitalized patients with COVID-19. Whether the prevalence of electrolyte disturbances differ between hospitalized patients with and without COVID-19 is unknown.

Methods: We performed a retrospective observational study of adult patients hospitalized in a large tertiary healthcare system in the Bronx between March 11-April 26, 2020. We compared the prevalence of the disturbances in sodium, potassium, calcium and magnesium between patients with and without COVID-19 using Chi-square. Electrolyte disturbances were defined as the following: hypernatremia (>145 mEq/L), hyponatremia (<135 mEq/L), hyperkalemia (>5.5 mEq/L), hyperglycemia (<3.5 mEq/L), hypermagnesemia (>2.5 mEq/L), hypomagnesemia (<1.5 mEq/L), hypocalcemia (<8.5 mg/dL) and hypoalbuminemia (<3.5 g/dL).

Results: Of 4579 patients, 51.8% were male. Median age was 65 years, IQR (52-76). 3313 (72.3%) were positive for the COVID-19. Hypernatremia, hyponatremia, hyperkalemia, hyperglycemia, hypocalcemia, and hypoalbuminemia were significantly more common in hospitalized patients with COVID-19.

Conclusions: Dysnatremias, hyperkalemia, and hyperglycemia were more common in patients with COVID-19. Hypocalcemia was more common in patients with COVID-19 but this may be due to a higher prevalence of hypocalcemia. Further studies are needed to adjusted models to describe the association between electrolyte abnormalities and clinical outcomes.

Funding: NIDDK Support

PO0870
Quality Improvement Project: Examining Urine Sediment and Microscopic Findings in COVID-19 AKI Patients
Abdulhadi T. Gelagain, Ajai S. Rajabalan, Janice P. Lea, Jose E. Navarrete, Jason Cobb. Emory University School of Medicine, Atlanta, GA.

Background: The examination of the urine microscopy manually is common in the work-up of AKI. SARS-CoV-2 has been detected in urine samples of infected patients. There have been safety concerns about the handling of urine samples in patient under investigation and COVID-19 confirmed cases. Limitations in personal protective equipment have provided challenges. There have been limited reports of urine microscopic findings during the COVID-19 pandemic. We developed a QI project examining the urine sediment of COVID-19 AKI patients from digital pictures provided by the IRIS IQ200 Microscopy System.

Methods: This QI project took place at Emory University Hospital Midtown. We retrospectively evaluated baseline characteristics, labs, and urine volume. The urinalysis and urine sediment were evaluated for each patient by digital images produced by the IRIS IQ200 Microscopy System.

Results: A total of 17 African American patients with a mean age of 71±12.5 years (range, 35 to 98); 64.7 % were female. Comorbidities included hypertension (94.1%), diabetes (58.8%), CAD (11.9%) and CKD (52.9%). Average serum creatinine was 3.1 mg/dL. 8 patients (47%) were oliguric; 4 patients had FE Na < 1%. 8 patients (47%) had 2+ proteinuria. 9 patients (52.9%) had a positive leukocyte esterase and all were nitrate negative. 8 patients (47%) had ATN with visible muddy brown casts; 6 patients (35%) had a 5 wbc/hpf and 11 patients (65%) had a 5 rbc/hpf. 8 patients (47%) had shock requiring vasopressor support; 8 patients (47%) required dialysis and 13 patients (76.5%) required mechanical ventilation.

Conclusions: Urinalysis and urine microscopy are important in evaluation of AKI, and there is a paucity of data about findings in COVID-19 AKI patients. Without conclusive evidence of the infective potential of urine samples, it is much needed value of this time to device a safe alternative to manual urine microscopic examination. Almost half of our patients had ATN and we were able to arrive at the diagnosis using digital images from this automated urine microscopy system. Use of such technology will help nephrologists safely examine urine sediments and minimize exposure to COVID-19.

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Underline represents presenting author.
PO0871 Clinical Relevance of AKI Trial Data for Severe COVID-19 Patients
Rita N. Barcis, Brian O’Rourke, Sunny H. Nguyen, Arno W. Tilles, Payal Garg, Christopher V. Gemmini, Brian Miller. Sentien Biotechnologies Sentien Biotechnologies, Lexington, MA.

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 systemic 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/I 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.

PO0873 Constitutive Activation of Hedgehog Signaling Disrupts Nephrionic and Stromal Differentiation
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Background: Nephron progenitors (NPs) and stromal cells differentiate from a common Osr1+ progenitor. While maldevelopment of nephronic and stromal tissue is caused by a deficiency 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-Deloui et al., 2018). Here, we investigated mechanisms that function 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-/-) as well as 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+ nephronic 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 mediatory stromal markers Tgfα (2.60 fold-change [FC], p=0.01) and Pdgfrβ (1.60 FC, p=0.01), and decreased expression of nephron markers Nephl (0.23 FC, p<0.01), Slc3a1 (0.32 FC, p<0.01), and Slc2a1 (0.08 FC, p=0.01). 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 mediatory 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 nephroblastoma.

Funding: Government Support - Non-U.S.

PO0874 Caspase Inhibition in a Mouse Model of Prenatal Ureteropelvic Obstruction Rescues Normal Ureteral 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 knockdown of Exoc5, 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 Exoc5lox/lox-Ksp-Cre ureters, we performed IP injections of caspase inhibitors into pregnant mice at gestational day 16.5. Also, diaphragma toxin (A TA) mice crossed with KspCre-lox/lox mice were used to investigate the effect of inducing urethral cell death with tamoxifen administration at E16.5.

Results: Morphologically, dying Exoc5-KO urethral cells appeared more necrotic than apoptotic, and they were negative for cleaved PARP and active caspase-3. However, a single injection of pan-caspase inhibitor z-VAD-FMK at E16.5 rescued ureteral development in all Exoc5lox/lox-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 Exoc5lox/lox-Ksp-Cre mice survived to adulthood. Interestingly, caspase-1 inhibitor Ac-YVAD-cmk did induce UPJO at an earlier stage of 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 ureters 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 inflammation-associated caspase-1 may play a role in activating cell death in urethral cells with disrupted exocyst trafficking.

Funding: NIDDK Support

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Underline represents presenting author.
PO0875

Exocyt Inactivation in Urothelial Cells Disrupts Autophagy and Upregulates the Fibroblast Growth Factor-Inducible 14 (Fn14) Receptor

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Background: Despite their prevalence, the etiology of congenital ureter obstructions in infants is poorly understood, with little evidence identifying genetic or environmental causes. We previously reported a unique mouse model of in vitro ureteropelvic junction obstruction (UPJO) in which ureteral urothelial cells with deleted Exoc5 gene failed to differentiate into a striated epithelium and underwent cell death. This resulted in bilateral UPJO, hydroureter, and neonatal lethality. Here, we investigated the urothelial cells prior to cell death to identify the disrupted cell processes necessary for urothelial differentiation and ureter development.

Methods: Gene expression profiling was performed on E16.5 ureters of Exoc5fl/fl; Ksp-Cre mice and control littermates, with validation using real time qPCR and immunohistochemistry. Follow up investigations utilized an evivo ureter explant organ culture model, where mouse embryonic ureters were isolated at E15.5 and maintained in culture for 72 hours. Additionally, we used primary human urothelial cells (pHUCs) and immortalized SV-HU/C1 cells for advanced studies on exocytosis regulation of autophagy, which was measured through immunoblotting and immunostaining of pel, LC3II/III, and autophagy-related genes (ATGs).

Results: Analysis of gene profiling data from E16.5 Exoc5fl/fl;Ksp-Cre ureters revealed that metabolic pathways were significantly downregulated and NF-κB signaling was significantly upregulated, indicating cell stress. The highest upregulated gene was Fn14 (30-fold), a member of the TNF receptor subfamily that binds the ligand TWEAK. Fn14 is upregulated in damaged tissues and can activate non-canonical NF-κB signaling and cell death via multiple pathways. Using ureter explants and cell line models, we found exocytosis is critical for autophagosome, when disrupted, to lead to a high Fn14 increase and cell death.

Conclusions: From our data, we propose that autophagy is necessary for urothelial differentiation during ureter development, and irregular autophagy may trigger urothelial cell death through Fn14 signaling. This disruption of autophagy during a critical stage in ureter development may contribute to UPJOs in humans.

Funding: NIDDK Support

PO0876

Transcription Factor 21 Regulates Nephrin Progenitor Cells Self- Renewal/Induction and Podocyte Development

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Background: Most forms of CAFUT arise from mutations in genes of kidney development. We previously showed that Transcription Factor 21 (Tcf21) regulates branching morphogenesis by downregulating GDNF. We now aim to study Tcf21 in nephrin progenitor cells (NPC). During nephrogenesis, WNT9b signals to NPC through the canonical Wnt/β-catenin pathway, which promotes both self-renewal at a state of low β-catenin level, and induce NPC differentiating at state of high β-catenin. Following induction, NPC can either promote cell death for MET to progress. Additional, optimal intensity of β-catenin is essential for NPC differentiation to podocytes. Hence, discrete levels of β-catenin promote disparate cell fates. It remains unclear however what drives this change and direct NPC to exit self-maintenance/survival.

Methods: Kidney organoids were generated from human embryonic stem cells (hESC). Transplantation of Six2CreTcf21fl/fl mice were used for qPCR and immunohistochemistry. MK3 cells were used to study Tcf21 signaling. Recombinant Tcf21 was used for over-expression.

Results: Six2CreTcf21fl/fl kidneys show marked decrease in Cited1 expression from E12.5 through P0 compared to control, while still expressing normal levels of Six2, indicating decreased self-renewing NPC population. Six2CreTcf21fl/fl kidneys also demonstrated low Lef1 expression suggesting decreased NPC epithelization. However, Wnt4, a marker of the prethuber aggregate, was persistently elevated in the developing nephrons of Six2CreTcf21fl/fl. This state of Cited1Wnt4Lef1 is in the mutants suggests arrested MET and persistently elevated β-catenin levels in the differentiating progenitors. In uninduced mesenchymal cell culture (MK3), over-expression of wild-type Tcf21 led to enhancement of genes that mark renewing NPC. Cited1, Talaf, and Plac2β, while over-expression of mutated-Tcf21 abrogated that enhancement, again supporting Tcf21 involvement in NPC dynamics. As to podocyte differentiation, lineage tracing of Tcf21Cre showed its expression in a subset of NPC in the cap-mesenchyme and then in developing and mature podocytes. At P0, Six2CreTcf21fl/fl kidneys showed very low podocyte expression. This suggests that Tcf21 is required for NPC differentiation to podocytes.

Conclusions: Together, these data suggest that Tcf21 modulates Wnt/β-catenin signal intensity spatially and temporally to direct NPC toward self-renewal or differentiation.

Funding: NIDDK Support, Private Foundation Support

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 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 LT1-pattering 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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Underline represents presenting author.
Kidney Organoids Derived from a Pediatric Patient with Type 1 Diabetes and Steroid-Dependent 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 (iPSCs) 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, CDH1, GATA3, PODXL, NPHS1, NPHS2, and CD31. Organoids were also stained for gremlin, SGLT2, and KIM-1 to investigate the 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.

Funding: NIDDK Support, Other NIH Support - NCATS, T32
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 renovascular units. These consisted of both well-developed renal tubules, epithelial tube of different neuron 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 Kidney Development
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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 were upregulated with development; however, structural changes during maturation are unclear.

Methods: Mice were decellularized, stained for 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 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 corticomedullary 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.

Funding: Other NIH Support - National Institutes of Health [DP2 AT009833 to S.C.]

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 μmFigure 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 using ultracentrifugation. 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 EVs 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 confirmed the in vitro reality detectability of labeled-EVs. Importantly, as expected MRI studies showed that EV homing to the kidney injected intracardiacally 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.

Funding: Private Foundation Support
Obesity Blunts the Reparative Function of Human Adipose Tissue-Derived Mesenchymal Stem Cells in Ischemic Murine Kidneys

Nattawat Klomjit,1 James Krier,1 Sabena Conley,1 Xiang yang Zhu,1 Christopher M. Ferguson,1 Kyra L. Jordan,1 Hui Tang,1 Amir Lerman,2 Lilach O. Lerman,3 Division of Nephrology and Hypertension, Department of Medicine, Mayo Clinic, Rochester, MN;2 Department of Cardiovascular Medicine, Mayo Clinic, Rochester, MN.

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 (5x10⁶-200 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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Funding: NIDDK Support
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 unprecedented 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 cells 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 developed a detectable epithelial outgrowth that expressed markers of UB markers PAX2, 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 epithelia into CD principal cells, identified by expression of AQP2 and SCN1A/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 hPSCs, 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 morphologic development of the collecting system.

Funding: NIDDK Support, Other NIH Support - NCATS

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-phenylbutanoyl 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 dose leading to a reproducible increase in fibrotic, and oxidative stress response. CytochromeC-GFP biosensor iPSC 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 morphological changes of the mitochondria. Hemin injured organoids treated with nephrotoxin or hemin exhibit cytoplasmic GFP signal in the injured cells and reproducible increase in fibrotic, and oxidative stress response. CytochromeC-GFP iPSC lines were generated using AA VS1 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-phenylbutanoyl acid (PTBA) analogs for 10 days and analyzed to determine changes in fibrotic, and oxidative stress markers.

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.

Funding: Other NIH Support - R01 DK069403, Private Foundation Support

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 organoids 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/directionality, 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, toxicity assays and bioengineering of functional replacement cells or tissues.

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

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 GEnGlx 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 GEnGlx changes in human disease and investigate whether MR inhibition could preserve the GEnGlx 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 GEnGlx 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 GEnGlx and limit the development of DN. Our glomerular permeability assay was used to directly measure the albumin permeability (Ps’alb), 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, GEnGlx depth was reduced compared to patients with TBMD (p=0.013). Diabetic rats developed albuminuria and the Ps’alb increased 1.6-fold (p=0.001). Again, GEnGlx 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 GEnGlx, restored Ps’alb to control values and prevented albuminuria progression. Reduced urinary active MMP2 (p=0.012) were seen following MR blockade in DN. GEnGlx enzymatic degradation, with hyaluronidase, reversed the effect of MR blockade in DN confirming the importance of GEnGlx preservation in this model.

Conclusions: MR blockade in DN preserves the GEnGlx, reduces Ps’alb and retards the development of albuminuria. Alternate approaches to block MR and preserve GEnGlx 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 TGF-β Activation
Elena Liarte Marín,1 Liuhua Liang,1 Asha Seth,1 Stephanie C. Heasman,2 Vinkesh Selvarajah,3 Iain MacPhee,4 Xiaoaohe Wang,1 Judith Hartleb-Geschwindner,5 Carol P. Moreno Quimi,6 David J. Baker,7 Denis Feliers.1
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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 serious 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 sequester latent TGFβ through the binding of latency-associated peptide (LAP) 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 αvβ3 and works allosterically reducing its affinity for the LAP domain, thereby 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. Intraperitoneal injection of MED8367 reduces 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 β3/β8 or an anti integrin β6 antibody at 12 weeks of age for 3 weeks. Blocking integrin β3 did not affect albuminuria in these mice while blocking integrins β3/β8 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 multi-omic analysis of 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 Bir-CHiP.

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 PCK1, ALDOB, FBP1, and G6PC and the sodium bicarbonate exchanger, SLC44A1 (Figure 1; green=upregulated, red-downregulated). Increased expression of G6S and GLUD1 implied glutamine 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 ammogenesis 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-3993673), a PPARγ 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 2ks 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 transcriptions, 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), and revealed new insights: DMP4, a fibrotic marker in MD, was strongly expressed in podocytes. Integrative analysis of cell type enrichment and differentially expressed genes across all clusters. These expression changes included 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) probably reflecting compensation. Sglt1 expression was strongly downregulated in db/db reninAAV MD, and Sglt2 inhibition partially restored this expression. MD Sglt1 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 therapies in a mouse model. Drug specific and overlapping gene expression patterns were identified and should help elucidate cell-specific mechanisms of therapeutic benefit.

Funding: Commercial Support - Janssen Research & Development

The β3-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 β3-adrenergic receptor (AR) agonist 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
Underline represents presenting author.
Methods: RTCPT from rabbits were isolated using the iron oxide perfusion method and cultured for 14 days in a 90% glucose or 17 mM mannitol as an osmotic control for 96 hr. ATP, uncoupled oxygen consumption rate (OCR) and mitochondrial dynamics and energetics proteins were measured. D/h dB and non diabetic/dB/m control mice were treated with either vehicle or formoterol (1mg/kg, i.p.) daily for three weeks beginning at 10 weeks of age. At 12 weeks, kidneys were harvested and changes in mitochondrial proteins were measured.

Results: RTCPT treated with glucose for 96 hr exhibited a decrease in ATP, uncoupled OCR and the mitochondrial fusion protein Mfn1. In contrast, the fusion protein Pdpl and ETC complexes I-V increased. Treatment with formoterol (30mM) restored ATP, Mfn1, Pdpl and ETC complex proteins to control levels. Similarly, vehicle treated dB/db mice exhibited increases in ETC proteins complexes I, II, III and V, and Pdpl in renal cortex. Diabetic mice showed a decrease in Mfn1 in renal cortex. Loss of Mfn1 and complexes I, II, III and V, Pdpl 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 fusion/descrease fusion) and decreases ATP in spite of increased ETC proteins. Formoterol reverses these glucose-induced effects and may be used as a potential therapy to prevent early disease progression of DKD.

Funding: NIDDK Support, Veterans Affairs Support

PO0988
UCP2 Activates Autophagy to Protect Against Albuminuria and Podocyte Injury in Diabetest Qianqian Gao, Xiaobo Li, Junwei Buadi. Second Affiliate Hospital of Nanjing Medical University, Nanjing, China.

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 generated a novel model of podocyte injury and autophagy 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, LC3, 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 glomerular 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.

Funding: Government Support - Non-U.S.

PO0899
Darunavir Protects Mice with Type 1 Diabetes Against Kidney Injury Xiao Bao, Guandi K. Tandoh, Heidi Karttunen, Michael J. Ross. Albert Einstein College of Medicine, Bronx, NY.

Background: Despite the success of antiretroviral therapy (ART) in improving the prognosis of HIV-positive patients, the disease still has 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), and specific individual risk factors, particularly obesity predispose diabetic patients to more rapid progression of CKD, we studied the efficacy of DRV in a non-HIV animal model of DKD.

Methods: eNOS−/−9 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. Albumin-to-creatinine ratio (ACR) assay, immunocytochemical, western blotting and real-time PCR were performed with routine protocols. Mouse blood pressure (BP) was measured before and after DRV treatment. 14 weeks after STZ induction, mice were treated with DRV or control. We found DRV and formoterol treatment decreased renal injury and prevented loss of synaptopodin expression in podocytes. Since the renin-angiotensin system (RAS) is an important contributor to DKD pathogenesis, we studied whether DRV affects expression of RAS components. Unexpectedly, DRV decreased renin expression and may be used as a potential therapy to prevent early disease progression of DKD.

Conclusions: These data demonstrate that DRV protects mice against type I 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.

Funding: NIDDK Support

PO0900
Prostate Mediated NF-E2 Degradation Occurs Upstream of JNK Activation-Mediated CTGF Expression in Renal Tubules and Diabetic Kidneys Madhavi J. Ranc, Ji Li, Shunying Jin, Michelle T. Barati. University of Louisville, Louisville, KY.

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) decrease 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 h. 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 vs OVE26 mice already displayed significant albuminuria were immunoblotted with appropriate antibodies. MG132 were injected 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.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
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 mice and streptozotocin-induced diabetic mice for analysis. In vitro, mouse 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, western blotting, nanoliter tracking assays (NTA), and flow cytometry. 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 Rab27b functions 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 consequent secretion of exosomes.

Funding: NIDDK Support

PO0904

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/l-D-glucose), but not CSE or MCT. CBS protein expression was correlated negatively with glucose concentration (0.5,10,15,20,25,mM) (p<0.01). The significant decrease of CBS by glucose occurred at 1, 2, 24 and 48 hrs. Uptake/secretion of CBS was increased remarkably (588.7±140, p<0.01) within 5 hr before 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 LAMP2, a lysosome marker, reached the maximum at 30 min. The decrease of CBS mRNA expression was also found at post-Glucose (12hr High glucose treatment).The decrease of CBS mRNA expression was also found at post-Glucose (12hr High glucose treatment). The expression of CBS and NT was increased by inhibition of CBS protein with its siRNA but was reversed 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 unaltered L66a.6±6.6 vs 117.e6.6 ug/dl, p<0.01) mesangial matrix proliferation and glomerular basement membrane thickening were ameliorated by exogenous supplementation GYY4137 at 20ng/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.

Funding: Government Support - Non-U.S.

PO0905

Lysosphospholipids Predict Fast Decliners with Diabetic Kidney Disease Kentoaro Yoshikai,1,2 Yusuke Hirakawa,1 Kensuke Kojima,1 Masaomi Nangaku,1 Reiko Inagi,3,4 Kyowa Kirabushiki Kaisha Kenkyu Kairitsu, Chiyoda-ku, Japan; 1University 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 cytoplasms by visceral fat and regarded as one of the most important risk factors for renal dysfunction. 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) were 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 5 years (called “fast decliners”; about 10% in total) were statistically extracted. We also validated the metabolomic candidates with animal DKD model of SDT-fat 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 lysosphospholipids (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-fat rats, while we did not see those damages in normal SDT rats. In vitro experiments: the exposure of LPLsX to HK-2 cells showed a significant downregulation of NT gene expression within 24 h and upregulated pro-apoptotic gene expression. More physiological changes were investigated in reference to transcriptomic analysis, and we could find that LPLsX also damaged the lipid metabolism, estimated by intracellular lipid droplet accumulation, and increased the level of mitochondrial reactive oxygen species. Conclusions: 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.

Funding: Commercial Support - Kyowa Kirin Co., Ltd.
Podocyte-Specific Induction of KLF6 Attenuates Diabetic Kidney Disease in Mice

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Background: Krippe-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-KLF6 to generate Klf6flox/flox mice. TRE-KLF6 transgene were generated using the (TetO7/CMV) regulatory element driving the full-length human KLF6 coding sequence (UCDS 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-UNX) was utilized to induce DKD in mice. First, DOX diet was administered at 8 weeks of age in all mice. UNX 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-UNX treated NPHS2-rtTA, DOX-VEH-Sham treated NPHS2-rtTA and KLF6flox/flox 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-UNX treated KLF6flox/flox mice exhibited significantly lower albuminuria, focal and global glomerulosclerosis, mesangial expansion, and improved mice survival as compared to age and gender-matched DOX-STZ-UNX untreated NPHS2-rtTA mice. DOX-STZ-UNX treated KLF6flox/flox mice also exhibited less tubulointerstitial fibrosis and inflammation (pathology scoring) as compared to age- and gender-matched DOX-STZ-UNX treated NPHS2-rtTA mice.

Conclusions: These data suggest that podocyte-specific induction of human KLF6 attenuates podocyte injury and DKD, and improves overall survival in mice.

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

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 Axioscan Z1 scanner (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. Algorithms for automatic segmentation of kidney compartments (e.g. glomeruli, tubules) in the PAS layer were then developed using deep convolution neural network DeepLabV3+. We achieved a DICE coefficient of 0.95 for glomeruli and 0.89 for tubules. Quantification of renal markers was performed using machine learning classification methods. In accordance with published studies, our quantitation demonstrated loss of podocyte marker WT1, endothelial marker CD31, and tubular marker Lotus tetragonolobus lectin correlating with the progression of DKD, concomitantly with increased tubular atrophy and expression of fibrotic markers.

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 rPOD pancreas cohort, all histological stages of disease can be detected in affected kidneys, providing a pseudo-time-line of the evolution of DKD and supporting the potential to identify novel therapeutic targets.

Funding: Commercial Support - Novo Nordisk, Inc.

PO0908
Nerve Growth Factor Protects Podocyte Apoptosis by Regulating Sirt1 Expression

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Background: Podocyte injury contributes to the progression of diabetic kidney disease (DKD). In the previous studies, we demonstrate that expression of Cdk5/p35 play an important role in the diabetic kidney and associated with the progression of DKD in human. As know, podocyte can secret NGF and Sirt1 is one substrate of CDK5, so 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.

Methods: The immortalized mouse podocyte was cultured in vitro, then were transfected with control siRNA or siNGF vector to detect protein level of Sirt1 and apoptosis associated protein Cleaved caspase3 through western blot. In addition, podocytes were also given different concentration of NGF to detect the expression of Sirt1 and Cleaved caspase 3 in order to find the relationship of NGF and Sirt1, and the role of NGF on podocytes.

Results: To understand the role of NGF on podocyte, we stimulated immortalized mouse podocytes with NGF in different concentration, the protein level of Sirt1 was positive associated with NGF expression. 2. Podocytes were transfected with control siRNA or siNGF vector by using ViaFect™ Kit, the effect of siNGF was verified by western blot. knockdown of NGF decreased the expression of Sirt1 and Cleaved caspase 3. 3. When gave NGF stimulation, the protein level of Cleaved caspase3 was decreased.

Conclusions: NGF plays a key role in protection podocyte by regulating the expression of Sirt1, NGF/SIRT1 axis may be a new biological target for preventing podocyte injury.

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PO0909
Integrin αvβ8/TGF-β Activation in Kidney Is Associated with Renal Function Deterioration and Can Be Monitored in Urine

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Funding: AstraZeneca, Gaithersburg, MD; 1University of Colorado, Aurora, CO; 2Astrazeneca, South San Francisco, CA; 3AstraZeneca UK Ltd, Cambridge, United Kingdom; 4AstraZeneca, Gothenburg, Sweden.

Background: Integrin αvβ8/TGF-β activation plays a central role in fibrosis. The specificity of TGFβ 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 TGFβ activation and fibrotic initiation in the kidney and the potential for non-invasive monitoring of renal TGFβ activation.

Methods: Kidney biopsies were obtained from CKD cohorts of diverse aetiologies and living donor (LD) controls. Gene profiling data (Microarray) were obtained from glomeruli and tubulointerstitial. Renal fibrosis was evaluated and the correlation with TGFβ activation as well as cGFR was assessed.

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<1.094e-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
stage 3 and 4, ITGB8 was higher in tubular tissues in kidney biopsies from DN patients and co-localized with areas of fibrosis. Moreover, TGFβ activation signature of 30 genes was significantly correlated with ITGB8 expression (R=0.58, p=2.39e-16, N=169) and inversely correlated with sGFR (p<0.02). Active TGFβ was detectable in urine by a Simon immunosassay. The active TGFβ/creatinine ratio was increased by 4.4 fold (p=0.0003) in CKD subjects (median: 7.5 ug/g, N=20) compared to non-CKD controls (1.4 ug/g, N=20). The level of active TGFβ in urine can potentially identify patients at risk for fibrosis and progression of DKD.

Conclusions: In conclusion, fibrosis is associated with CKD severity, most prominent in DN. Integrin b8 is enriched in DN and correlates with TGFβ activation. The fibrosis status may be monitored via measuring active TGFβ in urine.

Funding: Commercial Support - AstraZeneca

PO0910 Omentin 1 and Histone H1 Variants as Remote Candidate Prognostic Biomarkers of CKD Among People with Type 1 Diabetes Mellitus (T1DM)

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Background: It has been difficult to identify biomarkers that antedate the development of CKD. In a previous study we identified omentin-1 and histone H1 (HISTH1) variants as candidate surrogate prognostic biomarkers associated with future CKD development in T1DM Diabetes Control and Complications Trial (DCCT) study participants. We present here the results of this follow-up study from the Epidemiology of Diabetes Interventions and Complications (EDIC) study.

Methods: Pair-designed serum samples from 23 controls (defined as participants with stable renal function) and 23 cases (defined as participants who went on to develop CKD stage 3 (GFR<60ml/min/1.73m2) were examined prior to and following the development of CKD. HISTH1 variant proteins were quantified using a parallel reaction monitoring (PRM) LCM method to quantitively HISTH1 variant specific peptides unique to H1.1, H1.2, H1.3, and H1.4. Omentin-1 was quantified using a commercial ELISA kit for omentin-1 (BioVendor; Asheville, NC). Protein abundance data were analyzed using Kruskal-Wallis rank sum tests with an unadjusted p-value 0.05 considered significant.

Results: HISTH1 peptide levels did not differentiate (p > 0.05) DCCT cases and controls. Omentin-1 levels were significantly increased in EDIC cases over controls. A multivariate logistic regression analysis of histone peptide quantified omentin-1 as the best classifier to differentiate controls from EDIC cases. Omentin-1 quantification confirmed discovery findings (DCC control < case, fold-change 1.2, p <0.05). Additionally, in cases, omentin-1 increased significantly (p = 0.0001) from the DCCT to the EDIC (1.4) whereas it did not (p = 0.06) in controls (fold-change 1.1).

Conclusions: Plasma HISTH1 variants levels did not predict future CKD3 status but did predict DCCT versus EDIC cohorts. Increased plasma omentin-1 levels in EDIC compared to DCC controls were associated with advanced CKD stage 3. These data suggest a role for omentin-1 or pathways regulating omentin-1 expression are associated with progression of kidney function loss in T1DM.

Funding: NIDDK Support, Veterans Affairs Support

PO0911 Investigations on Urinary Exosomal miRNA Biomarkers That Reflect Pathologic Features of Patients with Diabetic Kidney Diseases

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Background: Diabetic kidney disease (DKD) is a leading cause of end-stage renal disease worldwide. Although histological severity of DKD is a well-established predictor of adverse renal outcomes, investigations on the identification of non-invasive biomarkers that can reflect intrarenal status are scarce. The aim of this study was to discover urinary exosomal miRNA biomarkers of DKD and to examine their associations with the degree of advanced pathologic injuries.

Methods: We collected and analyzed urinary samples obtained from 95 patients with biopsy-proven DKD and 32 healthy controls. The candidate microRNAs of DKD were selected based on the analysis of GEO dataset (GPL22895 and GPL24120) and public microRNA databases (miRBase, TargetScan, microRNA). Urinary exosomes were extracted by column-based isolation kit, and the levels of selected candidate microRNAs were measured by quantitative real-time polymerase chain reaction.

Results: Mean estimated glomerular filtration rate and urinary protein-to-creatinine ratio were not significantly different between patients with DKD compared to controls. Plasma creatinine (median 0.9 mg/dl, range 0.5-1.7 mg/dl) and 6.8 g/kg creatinine, respectively. Upon the analysis of public dataset, we identified 9 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-335-5p levels showed positive correlation with the degree of interstitial inflammation and arterial hyalization, 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.

PO0913 Renoprotective Effect of a GLP-1 Receptor Agonist, Liraglutide, in an Early Phase of Diabetic Kidney Disease in Spontaneously Diabetic Tori Fatty Rats

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Background: Early intervention is extremely needed for preventing the progression of diabetic kidney disease (DKD) to end-stage renal disease. The aim of this study is to investigate the renoprotective effect of GLP-1 receptor agonist, liraglutide, in early phase of DKD and to determine the mechanisms underlying its effects using an animal model of type 2 diabetes with various metabolic disorders.

Methods: Male spontaneously diabetic torii (SDT) fatty rats (n = 30) at 8 weeks of age were randomly assigned to three groups; the liraglutide group (n = 11) was subcutaneously injected liraglutide. Another treatment group (n = 6) was subcutaneously administered insulin against hyperglycemia and was given hydralazine against hypertension for 12 weeks. The control group (n = 13) was injected only a vehicle. Urinary tubular marker, L-type fatty acid-binding protein (L-FABP), was measured to evaluate the effect of liraglutide against tubulointerstitial damage.

Results: Control group of SDT fatty rats exhibited hyperglycemia, obesity, hypertension, glomerular sclerosis and tubulointerstitial injury with high levels of urinary albumin and L-FABP, whereas treatment with liraglutide reduced body weight, food intake, both blood glucose and blood pressure levels, as well as, amelioration of renal pathologic findings with lower levels of both urinary albumin and L-FABP. Liraglutide increased in expressions of both phosphorylated (p)-ENO1 and p-AMPK in glomeruli. It also down-regulated renal expression of p-ITOR, and up-regulated renal expressions of LC-3 II, suggesting activation of autophagy. However, these effects were not brought
by the treatments of both insulin and hyaluronic, despite comparable levels of both hypoglycemia and hypotension. These findings imply that the effects of insulin on the glomerular endothelial dysfunction and cellular loss differ from those of hyaluronic.

Conclusions: Lispro may exert a renoprotective effect via prevention of glomerular endothelial dysfunction and cellular loss in the early phase of DKD, independently of both blood glucose and blood pressure levels. Furthermore, urinary 1-FABP may be a useful marker reflecting the therapeutic efficacy of lispro.

PO0914
PLVAP 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 plasma membrane vesicle associated protein (PLVAP) has been found to be necessary for the formation of endothelial diaphragms in fenestrates. Previous studies reported glomerular expression of PLVAP in transplant glomerulopathy, in mesangio proliferative glomerulonephritis model and in mice developing renal thrombocytopenia microangiopathy as a consequence of defective GpIa/AMP signaling in renal cells. Therefore, we investigated whether PLVAP expression in glomerular capillaries is induced in different models of DN.

Methods: To induce a model of type I 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 brachyuric (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 PLVAP. 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, 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 PLVAP. We co-stained the Intercellular Adhesion Molecule 2 (ICAM2) as a marker for endothelial cells.

Conclusions: PLVAP expression in glomerular capillaries is induced in different models of DN.

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 kidney disease (DKD). However, the role and mechanisms for regulating alternative complement pathway activation in podocyte dysfunction and DKD are not understood.

Methods: STZ-induced DKD mice, db/db mice, Podocyte-specific TSC1 deletion 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. Knocking down 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, CFB induction, and alternative complement pathway activation in the glomeruli. In cultured podocytes, high glucose culture could activate mTORC1 signaling, stimulate STAT1 phosphorylation and upregulate CFB expression. Blockade of mTORC1 or STAT1 signaling could significantly reduce proteinuria, thereby downregulated CFB expression in podocytes.

Conclusions: This study uncovers that mTORC1/STAT1 activation in podocytes may promote DKD progression through activating complement alternative pathway.

Funding: Government Support - Non-U.S.

PO0916
Loss of Nr2 Exacerbates Diabetic Kidney Disease in Akita Mice
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Background: Diabetic kidney disease (DKD) is a devastating microvascular complication with considerable mortality in patients with diabetes mellitus. Excessive 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) plays essential role in protection against oxidative/taxotoxic 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 knockout mice and Akita mice (Nr2f2) by crossing Tspo2/2 (Akita) mice (C57BL/6J) with Nr2f2 knockout (Nr2f2/2) 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:Nr2f2 mice displayed more pronounced hyperglycemia and hyperlipidemia than Akita mice did. While expression of Nr2-targeted genes Nqo1 and Hmox1 was induced in Akita mouse kidneys; the expression was significantly reduced in kidneys of Akita:Nr2f2 mice. Histologically, Akita mice showed modest mesangial expansion, but Akita:Nr2f2 mouse glomeruli showed marked distended glomerular basement membranes, with significant expansion of the mesangial matrix. ICAM2 was significantly decreased compared to control mice (p<0.05). Expression of CFB and IL-17 and claudin-1, which are targets of TTP and HuR, as evidenced by RNA

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
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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/Chr-Lebr-fa/af, 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 (μgCR/g (mmol) 0.9±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 μl/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 in diabetic and diabetic and hypertensive 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 (RBPs) that play pivotal roles in the diabetic and hypertensive rat model and may become an effective treatment option for diabetic and chronic kidney disease patients.

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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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immunoprecipitation. In cultured podocytes, exposure to high ambient glucose amplified HIF-1α expression. Increased HIF-1α expression was associated with diabetic microvascular complications. Other probes expressed gene upregulated IL-17 and class 1-m, and promoted podocyte injury. Thus, TTP hypoxic- and HIF hyperactivity is sufficient and essential to diabetic podopathy. Moreover, in silico analysis revealed that several kinases govern phosphorylation and activation of TTP and HIF, and glycogen synthase kinase (GSK)-3β activated both TTP and HIF, which harbor putative GSK-3β consensus phosphorylation motifs.

**Conclusions:** TTP and HIF are dysregulated in DKD via a GSK3β-mediated mechanism and play crucial roles in podocyte injury via posttranscriptional regulation of diverse molecules implicated in inflammation and podopathy. Our findings provide novel insights into the mechanism of and identify therapeutic targets for diabetic kidney disease.

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

**PO0919**

**Nogo-B and Soluble Nogo-B Modulate VEGFA/VEGFR2 Signalling in Glomerular Endothelial Cells**

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**Background:** Nogo-B is an endoplasmic reticulum protein present either as a full-length or circulating soluble isoform (sNogo-B) corresponding to the first ~200aa of the N-terminus. Nogo-B is expressed in the vascular and in glomerular endothelial cells (GECs) and downregulated in diabetic glomeruli. Overexpression of Nogo-B ameliorates diabetic glomerulosclerosis, but the biological mechanisms are unknown. We hypothesise that, in GECs, Nogo-B and/or sNogo-B modulate VEGFA/VEGFR2 signalling and vascular remodelling.

**Methods:** Nogo-B deficient human GECs were generated with CRISPR/CAS9 technology. VEGFA signalling was studied in differentiated, serum starved (5 h, FBS 2%) GECs exposed to VEGFA (50 ng/ml) for 5, 10 and 15 min. VEGFR2 phosphorylation (Tyrosine 1175) was assessed in western immunoblots. Proliferation experiments were conducted in GECs transfected with adenoviral vector expressing sNogo-B or control vector. To investigate the role of Nogo-B on GEC survival, Caspase-3/7 activity was utilised as marker of apoptosis in WT and Nogo-B deficient GECs after 5 h incubation in 2% FBS. In vivo Matrigel-angiogenesis assay in wild-type (WT) and Nogo-B/A deficient mice were conducted in parallel.

**Results:** When compared to WT GECs, Nogo-B deficient cells appeared more elongated with a peripheral distribution of F-actin but maintained expression of endothelial markers (E-selectin, CD31). Phosphorylated VEGFR2 total VEGF:ratio was similar in baseline condition in WT and Nogo-B deficient GECs. VEGFA-mediated VEGFR2 phosphorylation (15 min) was observed in WT GECs but not in Nogo-B deficient GECs (p<0.01). In the presence of sNogo-B, there was significant reduction in VEGFA-mediated VEGFR2 phosphorylation in WT GECs (p<0.05). There was no significant effect of sNogo-B on VEGFR2 phosphorylation in Nogo-B deficient GECs. Apoptosis was higher in Nogo-B deficient GECs when compared to WT ones (p=0.04). Preliminary work in in vivo Matrigel angiogenesis showed that Nogo-B deficient ECs were unable to form vascular structure when compared to wild-type cells (p<0.05). Presence of sNogo-B blunted the angiogenesis in WT mice.

**Conclusions:** Nogo-B is required for VEGFA-mediated VEGFR2 phosphorylation and for vascular remodelling (angiogenesis). Overexpression of Nogo-B blunts VEGFA-mediated VEGFR2 phosphorylation. sNogo-B could represent a tool to modulate VEGFA signalling in diseases.

**PO0920**

**Cytosine Methylation Changes in Early Diabetic Kidney Disease (DKD) in a Pima Indian Cohort**

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**Background:** Pima Indians of Arizona have an extremely high prevalence of type 2 diabetes and DKD. Genetically related Pima Indians living in Mexico, whose lifestyle remains traditional, have a much lower prevalence of these morbidities. In Pima Indians, the role of environmental factors play an important role in disease origins and suggest involvement of epigenetic programming. We analysed cytosine methylation (5mC) changes in Pima Indians from Arizona.

**Methods:** 327 Pima Indians (205 women, 122 men) were selected from a longitudinal cohort, all had an eGFR greater than 60ml/min and ACR <3000mg/g at baseline. DNA methylation from peripheral blood leukocytes was analyzed on an Illumina Infinium HumanMethylation 450 Beadchip. Preprocessing and Quality Control were performed using Minfi Package, normalization was performed using BMIQ. Methylation changes were assessed in biological replicates (N=4), in case of age, sex, duration of diabetes, mean blood pressure, HA1c, genotype, batch, cell count and correction efficiency. P-values were corrected for multiple comparisons.

**Results:** Mean age was 42.4±11.9 years, diabetes duration 7.8±7.5 years, HA1c 8.8±2.4%, GFR 107±16 ml/min and median albuminuria was 20.2±48.2mg/g. Subjects were followed for a median of 10 years (range 3-17 years) and had a mean GFR decline of 2.0±2.8 ml/min/year. Ranked regression, adjusted for key variables, identified 20 probes that passed the corrected significance threshold for kidney function decline. Most significantly enriched on genomic regions associated with metabolism and enhancers. The top identified probe was cg05171186 around the Maternally expressed gene 3 (MEG3)on chromosome 14, (p=2.66E-10). MEG3 is a non-coding gene that is specifically deleted in Wilms tumor and linked to susceptibility to sporadic renal cell cancer. Another probe identified was cg13366628 (p=1.02E-5) in Platelet Derived Growth Factor Alpha (PDGFA) on chromosome 7, a known type 2 diabetes risk gene, as well as cg06392169 (p=3.1E-5) in Interferon Related Factor 4 (IRF4) on chromosome 6 and cg12577105 (p=4.1E-5) in Craniofacial 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.
TSPAN-9 correlated with extent of interstitial fibrosis, proteinuria and serum creatinine. It was significantly upregulated by mannitol and high glucose in vitro, TSPAN9 in HMC. This study aimed to identify compounds that reduce LD accumulation and mitochondrial function by regulating mitochondrial dynamics by targeting OPA1. Overexpression of Loxl4 prevents high glucose-induced decrease of oxygen consumption rate.

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 lysine 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 deacetylation hystox oxidase like 4 (Loxl4) interacts with OPA1 in mitochondria. Overexpression of Loxl4 prevents high glucose-induced acetylation, preserved mitochondrial network 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. Loxl4 promotes mitochondrial function by regulating mitochondrial dynamics by targeting OPA1.

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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 (BTBR db/db). Thus, compounds that reduce LD accumulation may protect podocytes from injury and prevent the progression of DKD. The goal of this study is to identify compounds that reduce LD accumulation in vivo and lead to the identification of therapeutic candidates for 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. The assay is highly suitable for screening with a Z factor consistently > 0.5.

Results: We performed a pilot screen using 100 compound mixtures, each containing thousands of compounds, obtained from the Torrey Pines Institute for Molecular Studies (TPIMS). We identified one compound mixture (2275) that consistently reduces LD accumulation in a dose-dependent manner. 2275 significantly reduces LD accumulation induced by TNF, a pro-inflammatory cytokine associated with DKD, and induced by sera from patients with DKD. The TPIMS hit deconvolution method will be used to identify the active compound(s) within the 2275 mixture.

Conclusions: We identified compounds that significantly reduce LD accumulation in cultured human podocytes in response to stress stimuli, including sera from DKD patients. Further studies to deconvolve and validate those compounds, and test them in an animal model of DKD, are underway.

Funding: Government Support - Non-U.S.
safety and efficacy of the ASK1 inhibitor Selonsertib (SEL), higher serum sTNFR1 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 effects of SEL 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 allow 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 (MSDA). Data shown as fold-of-change or mean ± standard error of the mean (s.e.m.)

**Results:** TNFα significantly increased expression of both TNFRSF1A and1B in the RPTEC channel (1.4 and 2.6-fold, respectively vs. control), and SEL decreased TNFRSF1A expression by 108% (p=0.0058) and lowered TNFRSF1B expression by 64% (p=0.1549). SEL decreased TNFα-induced expression of IP-10 (6.4 vs. 37.3-fold, p=0.0083) and IL-18 expression (0.67-fold vs 1.6-fold, p<0.0001) in proximal tubules. Osteoactivin and Clusterin, biomarkers used to assess proximal tubule 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 by 33.7 and 33.7% ± 7.82 ± 0.44 pg/ml (p<0.0001) and clusterin (28.9 ± 44.24 pg/ml, p<0.0001) but downregulated by Empa (0.3-fold and 0.2-fold, p<0.0001 each) as early as 1h and at least for 24h after ligand stimulation in HK-2 and RPTEC cells, respectively. Coadministration of Empa and SEL significantly reduced TNFRSF1A mRNA expression by 1.7-fold (p<0.001) and sTNFR1 protein expression.

**Conclusions:** By demonstrating an inhibitory effect of Empa on basal and IL-1β-mediated CCL2 and endothelin1 expression in two independent HPTCs, we present novel evidence for early non-hemodynamic, nephrro-protective effects of SGLT2.

**PO0930**

**Comparison of the Effect of Calorie-Matched High Saturated Fat and High Unsaturated Fat Diets on Lysosomal Renal Injury in Non-Obese, Strepト佐チン-Injected 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 diabetic models, there are few studies that equalized calorie intake and body weight. We reported that a high-fat diet induced renal injury with impaired lysosome-mediated autophagic degradation in streptozotocin (STZ) injected mice (AS Nen Kidney Week 2019). However, the effect of fat type, saturated- or unsaturated-fat, was not determined. In the current study, an AIN93DM 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 C57Bl/6J mice were randomly divided into three pair-fed groups with 380 kilocalorie/100g energy from 7 to 20 weeks of age. CONT group: AIN93DM 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 immunohistochemical 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.

**PO0931**

**Overexpression of ACE in Macrophages Accelerates Diabetic Kidney Disease**

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**Background:** SGLT2 inhibitors (SGLT2i) slow the progression of type II diabetic kidney disease (DKD). Although ACE in macrophages has been shown to be important in controlling inflammation, the expression and function of ACE in macrophages in DKD are still unknown.

**Methods:** Diabetes was induced by five consecutive daily intraperitoneal injections of streptozotocin (55 mg/kg) using C57Bl/6J male mice. Primary peritoneal macrophages

**Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only**
were harvested after intraperitoneal injection with 2 mL of 4% thio-glucose solution into mice. Mouse ACE 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 hyperglycemia 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 (LK4400-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 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 result was in 2.1-fold increased expression of active PKCα, 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 prosclerotic 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, Col-I protein, and PAS-positive extracellular matrix similar to diabetic GS with increased MGF. Further studies of glomerular MGF inhibition in diabetic mice may help define the potential value of this maneuver in blocking GS.

**Funding:** Private Foundation Support

**PO0933**

**Severe Diabetic Glomerulosclerosis as Chronic Hypoxic Housing of db/db Mice: The Role of Mesangiolysis and Podocyte Injury**

Naoki Takahashi,¹ Haruyoshi Yoshida,² Hideki Kimura,¹ Kazuko Kamiyama,¹ Seiji Yokoi,¹ Kenji Kasuno,¹ Hiroyuki Kurosawa,¹ Yoshiaki Hirayama,¹ Masanori Hara,¹ Masayuki Iwano,² Fuku Daigaku Igarakubo, Shizuoka, Japan; ¹Sugita Genpaku Kinen Koritsu Ohama Byoin, Ohama, Japan; Denka Sekken Kabushiki Kaisha Niigata Kyo, Gosen, Japan; Iwamura Health Promotion Center, Niigata, 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 shed PCX-positive microparticles into the urine. After 16 weeks of hypoxia, the mice also had higher hematuria with lower serum glucose and various degrees of mesangioytic glomerulosclerosis with microaneurysms and the infrequent occurrence of nodular lesions. Immunohistologically, hypoxic mice showed significantly decreased podocyte densities early during hypoxia and decreased podocyte densities later. In both hypoxic and normoxic mice, glomerular macrophage 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 chemottractant 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.

Summary of the glomerular changes in db/db mice exposed to chronic hypoxia.

**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 (bardoxolone 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 mechanisms 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+/−/Nrf2290°C-Tg mice by cross-breeding Akita Nrf2 knockout mice (Akita Nrf2−/−) with Nrf2 transgenic mice (Nrf2290°C-Tg) overexpressing Nrf2 in RPTCs, studying them until age 20 weeks. Immortalized human RPTC (H2K) stably transfected with plasmid containing SGLT2 gene promoter were also used.

**Results:** Akita Nrf2+/−/Nrf2290°C-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 oligotraz (a Nrf2 activator) or transfection of Nrf2 cDNA increased SGLT2 mRNA expression and promoter activity in H2K. These effects were blocked by small interference (si) RNA of NFR2. Deletion of NFR2-responsive elements (NFR2-REs) in the SGLT2 promoter abolished the stimulatory effect of oligotraz on SGLT2 promoter activity. NFR2 bound to NFR2-REs of SGLT2 promoter was seen on gel mobility shift and chromatin immunoprecipitation assays.

**Conclusions:** Our results identify a novel mechanism by which NFR2 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-Istots, 3D Organoids of Pancreatic Islet and Mesenchymal Stem Cells, Effectively Reduces Diabetic Nephropathy in Immune-Component Non-Obese Diabetic Mice

Chi Hong, Korea

Background: We demonstrated that the i.p. administration of allogeneic “Neo-Istots” (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 I 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 Th5, 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 C57BL6 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 (Tirchome staining). The vehicle treated NOD mice (Group 2) had higher levels of proteinuria, albuminuria and creatinine, lost weight, had systolic hypertension and showed extensive interstitial fibrosis, glomerulosclerosis, proteinuria, hypertension and elevated SCr and BUN levels, while NI treated, euglycemic NOD mice (Group 3) showed significantly lower degrees of glomerulosclerosis, interstitial fibrosis, proteinuria, hypertension and better preserved renal function. All tested variables remained normal in non-diabetic Group 1 control mice.

Conclusions: The presented data demonstrate that NI 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

Poster

IL-17A Deficiency Attenuates Autophagosome Formation in Streptozoto- cin-Induced Rat Diabetic Nephropathy
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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 inflammatory responses during DN. In this study, we examined whether IL-17A deficiency affects the autophagy process in streptozotocin (STZ)-induced DN in kidney.

Methods: The autophagic response for IL-17A in the nephrotoxicity of STZ administration induced phenotypes of hyperglycemia and diabetic renal fibrosis. Futhermore, NQO1 deficiency reduced the autophagy down-regulating hVps34 and ATG4L of PI3-complex and increased pro-fibrotic genes including TGF-β1, Snail3, and MMP9, in vitro and in vivo. The fluorescence intensity of both hVps34 and ATG4L was reduced in NQO1 KO mice. However, NQO1 deficiency aggravated the expression of hVps34 and ATG4L but, reduced the expression of TGF-β1, Snail3, and MMP9.

Conclusions: NQO1 deficiency aggravated renal fibrosis mediating autophagy induction and phagophore formation. This results suggested that NQO1 may have a potential role for DN amelioration.

Funding: Government Support - Non-U.S.

Poster

Cell Sex and Sex Hormones Modulate Glucose and Glutamine Kidney Metabolism: Implication for Diabetic Kidney Disease
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Background: Male sex predisposes to diabetic kidney disease (DKD). We uncovered androgen-induced perturbations in kidney metabolic proteins that may drive faster DKD progression in men. Our goal is to characterize cell sex- and hormone-specific alterations in the kidney cell metabolism.

Methods: Human primary proximal tubule epithelial cells (PTEC) from 3 male and 3 female donors were stimulated with control, dihydrotestosterone (DHT), or estradiol (EST). We assessed glycolysis (extracellular acidification rate, ECAR) and oxygen consumption rate (OCR) in a Seahorse analyzer. We also studied sex differences in 16-week-old diabetic Akita mice.

Results: Male PTEC showed significantly higher ECAR, OCR, oxygen levels, and urinary output was monitored over the course of treatment.

Conclusions: Male PTEC showed significantly higher ECAR, OCR, oxygen levels, and urinary output was monitored over the course of treatment.

Funding: National Institute of Diabetes and Digestive and Kidney Diseases, National Cancer Institute, National Heart, Lung, and Blood Institute, Department of Veterans Affairs.

Poster

Effects of Dagadiluzin-Induced Glucosuria on Urinary Tract Infection Susceptibility
Kristin Bender, Laura Schwartz, John D. Spencer. Nationwide Children's Hospital, Columbus, OH.

Background: Individuals with diabetes mellitus (DM) have a higher risk for urinary tract infection (UTI). The infection is more likely to cause acute kidney injury leading to an increased risk for chronic and end stage kidney disease. Dagadiluzin is one of the proposed mechanisms by which people with DM have increased UTI risk, but this association is understudied and uncertain. In order to study the relationship between glucosuria and UTI susceptibility in vivo, mice were treated with an SGLT-2 inhibitor Dagadiluzin (Dapa) and subjected to experimental UTI.

Methods: Non-diabetic C57BL6/6 female mice were treated via oral gavage with vehicle or Dapa at 0.1, 1, or 10 mg/kg/dose. One group received a 2-dose regimen: 6 hours before and 3 hours post infection. Another group was treated daily for 7 days. Mice were challenged with Escherichia coli (E.coli) UTI 24 hours post infection (hpi). Bacterial burden was enumerated in the urine and bladder. Serum glucose, urine glucose, and urinary output was monitored over the course of treatment.

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Results: Compared to controls, Dopa-treated mice developed glucosuria while maintaining normoglycemia and comparable weights. After UTI with the 2-dose regimen, control and Dopa-treated mice had comparable bladder and urine UPEC titers. Mice treated over a longer time course had no significant differences in CFUs in the bladder and urine at 24 hpi – suggesting that glucosuria may not be a primary UTI risk factor. Urea nitrogen was increased in mice treated with Dopa which could impact infection susceptibility.

Conclusions: These data suggest that there is no direct relationship between glucosuria, SGLT2 inhibitors, and UTI susceptibility. Also, glucosuria alone doesn’t explain the increase in ICU-associated UTI risk. More studies are needed to understand the mechanisms that increase UTI susceptibility in individuals with DM.

Funding: NIDDK Support

PO0940

Systemic Therapies Targeted to Ischemia in a Model of Diabetic AKI

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Background: In acute kidney injury (AKI) and chronic kidney disease (CKD), ischemia in the kidney results in inflammation and tissue damage. The initial response to injury is the infiltration of reactive macrophages into the kidney with subsequent pro-inflammatory cytokine expression. Upon systemic administration, hydroxyl dendrimers selectively target reactive macrophages in the ischemic kidney with renal clearance maximizing kidney exposure.

Methods: Diabetes was induced in Wistar rats by administration of streptozotocin (70 mg/kg) as a single intraperitoneal (IP) injection. Rats with a blood glucose of ≥167 mM were allocated to 4 groups (G1-4; n=3/group). After 6 weeks, ischemia-reperfusion injury (IRI) was conducted with 60 min ischemia (H) 60 min reperfusion (R) (G2), or 45 min I/24 h R (G3 & G4). A sham surgery was performed as a control (G1). Hydroxyl dendrimers labeled with Cy5 (D-Cy5) were administered IP 1 hr after IRI in G1, G2 and G3 and 12 hr after IRI in G4. Renal function was assessed by clinical chemistry, glomerular filtration rate (GFR), and kidney injury biomarkers. Rats were euthanized (G2 or G4) 24 h post surgery. Kidneys were evaluated for tubular damage and tubular epithelial necrosis and stained by DAPI and anti-CD68 antibody (macrophage).

Results: Glucose levels increased to ~330 mM prior to IRI. GFR was significantly reduced from 1.8 mL/min (sham) to 0.8 mL/min in IRI rats. Serum creatinine and blood urea nitrogen were significantly elevated in IRI groups (G4>G3>G2). The degree of kidney injury was not significantly different when the longer reperfusion period was prior to sacrifice (P<0.05; G1, G2 and G3 > G2). In all IRI groups, renal tubular necrosis was moderate to severe and proximal tubule damage was severe. Maximal uptake of the D-Cy5 was observed in renal tubules in reactive macrophages in G2.

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 provide a model and treatment strategy to evaluate targeted therapies with hydroxyl dendrimer drug conjugates to treat AKI and CKD.

Funding: Commercial Support - Ashvathaa Therapeutics, Inc.

PO0941

Novel Analysis Approach for Intravital Single Nephron GFR Measurement in Mice

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Background: Intravital microscopy in animals is an emerging technique with advanced applications in kidney research. Particularly, the measurement of single nephron (SN) GFR in mice comprises a method to assess a key parameter of kidney disease. Filtration in single glomeruli is measured by two-photon microscopy in a time series after intravenous injection of a freely filtered fluorescent dye. From the intraglomerular capillaries to the connected proximal tubules (PT) the glomerular filtration is observed and the intratubular dye intensity shift is measured. However, existing methods for the analysis of the image data in rats (Kang et al. 2006) had limited robustness in mice, due to smaller size, higher tubular curvature and therefore smaller acquisition distances.

Methods: By continuous, rather than punctual measurement of signal intensity across the PT over time against the exact tubular volume, the filtered volume per second is calculated by linear regression.

Results: With the method published by Kang the results were highly variable in our hands. After repeated analysis of image material (10 glomeruli in 5 animals, analyzed 5 times each), the GFR varied by a mean relative SD of 41%. By reducing overall user interaction with our method, this SD could be decreased to 14%. When applying the analysis to image data acquired in healthy and diabetic C57BL/6j mice, we detected a 4-fold increase in SN GFR in diabetic mice. Administration of the ACE inhibitor enalapril for three days ameliorated this effect in diabetic mice by 50%.

Conclusions: To increase the reliability of SN GFR measurements by intravital microscopy in mice, we extended an existing workflow by continuous measurement, 3D-modelling and sophisticated data analysis while reducing manual interaction. User interaction with microscopy data acquired in diabetic and healthy mice prove the general applicability and high reliability of this novel analysis approach. The clinical relevance is apparent in the context of monitoring disease progression as well as effects of medical intervention.

PO0942

A Hyaluronan Synthesis Inhibitor Delays the Progression of Diabetic Kidney Disease in a Mouse Experimental Model

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Background: There is a paucity of options to treat Diabetic Kidney Disease (DKD) in the clinical practice. Hyaluronan is an important morphological feature of DKD. However, the role of hyaluronan (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.

Aim: In this study, we assessed the effects of hyaluronan synthesis inhibitor 4-Methylumbelliferyl-4-MU (MU) on the development of DKD. As a model, we used the diabetic and moderately hypertensive endothelial nitric oxide synthase/leptin receptor deficient (eNOS C57BL/6J×C57BL/6J) double mutant mice.

Methods: In the diabetic model mice were separated into two similar groups regarding sex, body weight, non-fasting plasma glucose concentrations, and consanguinity; then, experimental animals were fed ad libitum identical artificial diets formulated by Enviro-Teklad, containing or not 5% of 4-MU sodium salt for 9 weeks. Our measures of daily food consumption show that treated animals had a dose of 270±50mg per day of 4-MU (about 6.2g/kg body weight/day). At the end of the experimental period, we found that 4-MU-treated diabetic animals: 1) kept their average GFR, while a significant reduction of GFR was observed in diabetic controls (P<0.042; n=9/8 per group) compared to the average urine ACR and plasma cytokine-c values significantly lower than controls (P=0.049 (n=12 per group) and P=0.043 (n=11/10 per group) respectively); 3) had lower average kidney weight (P=0.041, n=6), and 36% less hyaluronans in kidneys (P=0.095; Effect size=1.32, n=5); and 4) MU-treated animals kept their body weight/stature/maximum weight relationship (P<0.001) (n=5/4) better than diabetic controls (P=0.002, n=16/15 per group) as well as their median survival was 6.4 weeks longer (P=0.048, n=6/5 per group). Moreover, after the treatment, an independent histopathology study showed a significant lower glomerular injury score in kidneys of 4-MU-fed animals (P=0.039, n=5/7 per group).

Conclusions: These results showed that the hyaluronan synthesis inhibitor 4-MU effectively slowed the progression of DKD. 4-MU provides a potential new therapeutic approach to treat DKD.

Funding: Private Foundation Support

PO0943

Therapeutic Benefit of CCR2 Antagonism in a Model of Diabetic Nephropathy Suggests a Mechanism of Action Distinct from Nrf2 Activation


Background: Diabetic nephropathy (DN) affects nearly half of the patients with type 2 diabetes and is characterized by albuminuria and/or a relentless decline in renal function that may lead to ESRD. We have recently shown that a CCR2 antagonist improved renal structure and reduced proteinuria in the db/db murine model of DN, as well as in the Adiraycin and 5/6 nephrectomy models of CKD. To understand the mechanism we compared CXX872, a small molecule antagonist of CCR2, with Bardoxolone methyl, an investigational drug targeting Nrf2 pathway in the db/db murine model of DN.

Methods: The [K51] CCR2 specific inhibitor CXX872 and Nrf2 activator Bardoxolone methyl were formulated in 1% HPMC and dosed for 2 weeks. Proteinuria (urinary albumin excretion rate- UAER) and glomerular filtration rate (GFR) were assessed by measuring urinary albumin ELISA and FITC-insulin, respectively. The kidneys were disrupted non-enzymatically, and preparations enriched in glomerular cells were obtained by filtration. Activated parietal epithelial cells (PECs) were analyzed in these preparations by flow cytometry.

Results: UAER was rapidly and significantly reduced after treatment with CXX872: 59% (p=0.004) and 76% (p<0.0001), versus vehicle by week 1 and 2 respectively. In contrast, Bardoxolone did not improve UAER. The db/db mice had kidney hyperfiltration, which measured 943±36 μl/min at 8 weeks. Bardoxolone reduced hyperfiltration in db/ db mice by 36% versus vehicle at week 2, while CXX872 had no effect on GFR. UAER in CXX872 significantly reduced the number of CD44 positive activated PECs in the glomerular cell preparations(=0.04), while Bardoxolone had no effect on the number of these cells.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only; Underline represents presenting author.
Can Nrf2 Inducers Cause Renal Proximal Tubule Epithelial Cell De-Differentiation?

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Background: Nrf2 is a transcription factor serving as a master regulator of cytoprotective responses. Nrf2 and its inducers have been shown to mitigate renal injury in animal models of kidney disease. However, use of these agents in the clinical setting is limited and defining/comparing mechanisms of action of different agents remains to be defined. Previous lab studies showed two Nrf2 inducers (Protandim [nutritional supplement] and DMF [Dimethyl fumarate]) caused differing effects on renal protection by different mechanisms in the db/db model of DN.

Methods: Human proximal tubule cells (HK-11 cells) were cultured in high glucose (HG; 25mM) or normal glucose concentrations (NG; 5mM) for 24h, followed by additional treatment with 1 or 10μM DMF for another 24h. To test markers of EMT and cytoskeleton, cells were immuno-stained for vimentin and fibronectin, and actin filaments stained with FITC-phalloidin. Cell extracts were immunoblotted for E-cadherin and vimentin.

Results: Protandim and DMF increased vimentin filament expression by image analysis of immunoblotted cells, and HG+DMF conditions led to a further increase. Treatment with Protandim following culture in both HG and NG caused collapse of actin filaments (as previously observed) and vimentin encasulated and co-localized with the collapsed actin. The cell-cell junction protein E-cadherin was downregulated by DMF and culture in HG prior to DMF was not additive to this effect. Protandim did not alter E-Cadherin expression. Extracellularly deposited fibronectin increased with HG and this effect was augmented by additional treatment with DMF.

Conclusions: Protandim and DMF distinctively regulate the cell cytoskeleton. Increased vimentin filament formation with Protandim may be a compensatory mechanism due to collapse of actin filaments. DMF decreases E-Cadherin and increases vimentin and ECM deposition, suggestive of tubule cell de-differentiation. The disparate effects of these two Nrf2 inducers may lead to varying outcomes if used for treatment of diabetic or other types of kidney disease.

Funding: NIDDK Support

Beneficial Effect of Chloroquine and Amodiaquine on Diabetic Tubulopathy by Attenuating Mitochondrial Nox4 and Endoplasmic Reticulum Stress

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Background: Oxidative stress induced by chronic hyperglycemia is recognized as a significant mechanistic contributor to the development of diabetic kidney disease (DKD). Nonphagocytic nicotinamide adenine dinucleotide phosphate oxide 4 (Nox4) is a major source of reactive oxygen species (ROS) in many cell types and in the kidney tissue of diabetic animals. We designed this study to explore the therapeautic potential of chloroquine and amodiaquine for inhibiting mitochondrial Nox4 and diabetic tubular injury.

Methods: Human renal proximal tubular epithelial cells (hRPTCs) were cultured in high-glucose media (30 mM D-glucose), and diabetes was induced with streptozotocin (STZ, 50 mg/kg i.p. for 5 days) in male C57BL/6J mice. Chloroquine and amodiaquine were administered to the mice via intraperitoneal injection for 14 weeks.

Results: Chloroquine and amodiaquine inhibited mitochondrial Nox4 and increased mitochondrial mass in hRPTCs under high-glucose conditions. Reduced mitochondrial ROS production after treatment with the drugs resulted in decreased endoplasmic reticulum (ER) stress, suppressed inflammatory protein expression and reduced cell apoptosis in hRPTCs under high-glucose conditions. Notably, chloroquine and amodiaquine treatment diminished Nox4 activation and ER stress in the kidneys of STZ-induced diabetic mice.

In vitro, we observed attenuated inflammatory and albuminuria in STZ-induced diabetic mice after chloroquine and amodiaquine treatment.

Conclusions: We substantiated the protective actions of chloroquine and amodiaquine in diabetic tubulopathy associated with reduced mitochondrial Nox4 activation and ER stress alleviation. Further studies exploring the roles of mitochondrial Nox4 in the pathogenesis of DKD are required for new therapeutic targets for patients with DKD.

Funding: Government Support - Non-U.S.

In Vivo Evaluation of [18F]Canagliflozin, a Potential PET Tracer for Imaging Tissue Distribution of the SGLT2 Inhibitor Canagliflozin in Type 2 Diabetics Patients In Vivo

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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 2.6% ± 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.

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 biological expression of target genes. Using STRING database to build protein-protein interaction network. Enpreseq 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 mRNA profile, Mir-1237-3p-SH2B3, Mir-1238-5p-ZNF652 and Mir-766-3p-TGFB1I axis may be involved in diabetic nephropathy. C3 is located at the center of PPI network. Correlation analysis with GFR showed STX, CXCL1, LYN, VWF, ANXA1, C3, HLA-E, RHOA, SERPING1, EGF and KNG1 may be related to diabetic nephropathy.

Conclusions: C3 may serve as a therapeutic target for diabetic nephropathy.
PO0948
Apolipoprotein C3 Inhibition Reduces Diabetic Kidney Disease and Atherosclerosis in a Mouse Model
Cheng-Chieh Hsu,1 Farah Kramer,1 Charles E. Alpers,1 Rosanne M. Crooke,2 Jenny E. Kanter,1 1University of Washington School of Medicine, Seattle, WA; 2Ionis Pharmaceuticals Inc, Carlsbad, CA.

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 in insulin-insufficiency and regulates plasma triglyceride levels.

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-associated atherosclerosis in the brachiocephalic artery and the aorta (aortic lesion was 9.3 ± 1.5 mm² lesion 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 and APOC3-accumulation, which was attenuated by APOC3 ASO-treatment. Diabetes led to a doubling of glomerular volume (45126 ± 1908 μm³/gglomerular 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 ± 2240 μm² glomerular volume in OB mice and 230 podocytes/106 μm² 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 36331 ± 2240 μm², p<0.05; PAS area 1761 ± 131 μm², p<0.01; and podocyte density 114 ± 9 podocytes/106 μm² 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-associated atherosclerosis and DKD.

Funding: NIDDK Support

PO0949
Shen-Qi-Yan-Shen Formula Attenuates Diabetic Renal Lipid Deposition by Down-Regulating Proteoglycan Expression
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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-R 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 bioinformatics analyses, we found that the candidate miRNAs targeted proteins of 6 pathways (the Ras signaling pathway, Signaling pathways regulating pluripotency 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.

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Longitudinal Changes in Plasma Biomarkers and Diabetic Kidney Disease Progression in VA NEPHRON-D

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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 (sTNFR1, sTNFR2) 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], monocyte chemoattractant 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 <80, respectively, or ESRD), adjusting for biomarker, sex, race, treatment arm, BMI, HgbA1c, eGFR, UACR at baseline and age, 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 sTNFR1, sTNFR2, 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

A Polysubiquitinated Form of PTEN Predicts Declining Kidney Function and ESKD in Type 2 Diabetes

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Background: Fibrosis is a major driver of chronic kidney disease and epithelial-mesenchymal transformation (EMT) may contribute to its development. A polysubiquitinated form of phosphatase and tensin homolog (PTEN K27polyUb) promotes EMT in vitro and may be a useful biomarker of progressive kidney fibrosis.

Methods: PTEN K27polyUb was measured in 234 serum samples from American Indians (80 men, 154 women) with early diabetic kidney disease (DKD). Quartiles of serum PTEN K27polyUb were assessed as risk factors for DKD progression (≥40% loss of GFR) or onset of end-stage kidney disease (ESKD) using Cox proportional hazards models adjusted for age, sex, diabetes duration, HbA1c, blood pressure, measured GFR and albuminuria.

Results: Baseline, mean age was 42.8 years (SD 10.5), diabetes duration 11.5 years (7.1), mean arterial pressure 90.5 mmHg (9.5), HbA1c 9.3% (2.4), GFR 151 ml/min (45) and median albumin:creatinine ratio 38 mg/g (interquartile range 14-217). 168 subjects had a ≥40% loss of GFR and 74 (64 with prior ≥40% GFR loss) developed ESKD during median follow-up of 6.3 and 15.8 years, respectively. In univariate analysis, serum PTEN K27polyUb was associated with risk of ≥40% GFR decline and of ESKD (Figure). After adjustment for clinical covariates higher PTEN K27polyUb was associated with greater risk of ≥40% GFR decline [Hazard ratio (HR) for the 4th vs. 1st quartile = 3.67, 95% CI 1.98-6.78, p<0.001] and with ESKD [HR quartile 4 vs. 1 = 5.00, 95% CI 1.77-14.11, p<0.002]. Adding serum PTEN K27polyUb increased the model c-statistics from 0.696 to 0.725 for DKD progression and from 0.738 to 0.766 for ESKD.

Conclusions: Higher serum PTEN K27polyUb is associated with increased risk for GFR decline and ESKD in type 2 diabetes and improves prediction over standard clinical measures.

Funding: NIDDK Support

Survival plots for kidney outcomes by quartile of serum PTEN K27polyUb.
PO0953

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 ≤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

PO0954

Lower Cardiorenal Risk with SGLT2 Inhibitor vs. DPP4i 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 CVD-free.

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 (age: 60.5±13.0 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/linagliptin (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 [0.80-1.11]).

Conclusions: In this large multinational observational study of CVD-free 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

PO0955

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 (2^nd 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 were excluded for lack of renal bx. 4,205 Pts were analyzed (age range: 8 - >89 years; males 53.5%). Bx indication: acute kidney injury (AKI), acute nephritic syndrome (ANS), rapidly progressive renal failure (RPFR), hematuria (Heme), suspect a non-DN renal disease (Non-DN), sudden increase in
proteinuria (Prot) or chronic kidney disease (CKD). We recorded a specific rule out (r/o) diagnosis if one was given. BX DN Grade: 1 EM changes; II Mesangial increase; III Nodular sclerosis; IV > 50% Global sclerosis.

Results: A 2nd DX was found in 1750 (38%) cases. Overall, there were 40 2nd DXs: AT 41%, acute interstitial nephritis 14%, infection-related glomerulopathy (GN) 7%, etc. There were multiple unexpected 2nd DXs: fibrillary GN, amyloid, dense deposit disease among others. The highest odds ratio (OR) of a 2nd DX was in Ps with AKI at 3.25 whereas CKD had an OR of 0.03 (Table). Age correlated with a 2nd DX (p < 0.001) with the Bx incidence ranging from 29% in Pts < 30 to 56% for those ≥ 80. In 1,589 cases, a specific DX was to be ruled out. A 2nd DX was found in 48% of Bx’s with a r/o DX versus 33% when no r/o DX was given (OR=1.83, CI (1.62, 2.08), p < 0.001). Lesser grades of DN significantly correlated with a 2nd DX; I - 75%, II - 64%, III - 38%, IV - 20% (p < 0.001).

Conclusions: In Bx proven DN, a significant 2nd DX was found in 38%, with AKI and ANS most likely to yield a 2nd DX. Age and a r/o DX can further differentiate patient groups most likely to have a 2nd DX. Given the worldwide toll of diabetes, the finding of a potentially treatable 2nd DX in diabetics already at high-risk of end stage kidney disease should provide significant savings in morbidity, mortality and health care expense.

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 and tubular lesion (IFTA) with incidence of end-stage kidney disease (ESKD) was examined using a 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 multi-center 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 eight EM 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% 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 to 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.
PO0959

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 this 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 forty (74.5%) achieved RRT in the follow-up, 36 in DKD group, 10 in the N DKD group and 58 in the group with both DKD and N DKD. Patients with highest degree of fibrosis (grade 2 and 3 vs 1) (n = 93) had a higher risk of starting RRT (RR 9.53, CI 95% 1.77- 51.3, p=0.009). Kidney survival was poorer in the DKD and N DKD group (p = 0.002) (Figure 1).

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.

PO0960

The Aging Kidney: Renal Parenchymal Volumes from MRI, a Comparison Between Type 2 Diabetes and Non-Type 2 Diabetes in 37,450 UK Biobank Participants

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Background: It is well known that Type 2 Diabetes (T2D) early on is associated with increased kidney volumes but also can cause Diabetic Nephropathy. UK Biobank (UKB) is a large-scale cross-sectional study aiming to examine 100,000 subjects aged 44 to 82 years using Magnetic Resonance Imaging (MRI). Resulting images allow measurements of Kidney Parenchyma Volume (KPV). The purpose of this study was therefore to quantify KPV and investigate the association with age in T2D and non-T2D subjects.

Methods: An automated deep learning-based method for direct KPV segmentations and measurements was developed and validated and applied to UKB MRI in 37,450 subjects. KPV was analyzed as a function of diagnosed T2D (defined as diagnosis of diabetes after 40 yo), sex and age. Furthermore, correction for lean tissue volumes assessed by MRI was performed in all subjects.

Results: KPVs from 37,450 subjects (47.6% males) as a function of T2D, sex and age are shown in Fig1. In non-T2D a steady decline in KPV is seen in both males and females. KPV is significantly larger in T2D subjects (1126 males, 530 females), over 50 years of age as compared to non-T2D. This is followed by a faster KPV decline in T2D compared to non-T2D subjects. Adjusting for lean tissue volumes from MRI did not change the difference in decline rates between T2D and non-T2D subjects.

Conclusions: T2D subjects have a larger KPV than non-T2D in middle aged subjects but show a faster KPV decline, independent of lean tissue volume differences. The faster decline in T2D can potentially be explained by increased hyperfiltration and oxidative stress in T2D.

Funding: Private Foundation Support, Government Support - Non-U.S.

Table 1. Predictors of kidney failure in diabetic nephropathy

<table>
<thead>
<tr>
<th>Variable</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Kidney failure (n=20)</td>
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<tr>
<td>Serum creatinine</td>
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<td>Glomerular volume</td>
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<tr>
<td>GFR</td>
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<tr>
<td>Proteinuria</td>
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<tr>
<td>Hemoglobin A1C</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Total KPV as a function of T2D, sex and age. Mean values and 95% confidence intervals are shown from a sliding window of 7 years.

PO0961

Assessment of Histopathological Prognosticators in Diabetic Nephropathy: Single-Center Experience

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Background: Diabetic nephropathy (DN) is the leading cause of end stage kidney disease worldwide. Identification of clinical, laboratory and histopathological predictors of kidney failure in DN may improve outcomes.

Methods: We identified 45 kidney biopsies between 2017 to 2018 that were diagnosed with DN. Clinical, laboratory and histopathological variables were analyzed to prognosticate 1-year kidney failure.

Results: Sixteen of 45 patients with DN had kidney failure within 12 months of kidney biopsy while 29 patients did not. All patients who developed kidney failure had diabetic retinopathy as shown in table 1. Laboratory findings such a serum creatinine (597μmol/L vs. 205μmol/L, P<0.0001) and presence of hematuria (88% vs. 45%, P<0.01) prognosticated kidney outcome, while neither proteinuria or Hemoglobin A1C did. IFTA score (2.4 vs. 1.8, P=0.02) and global glomerular sclerosis (52% vs. 32%, P=0.002) were the only histological findings that prognosticate kidney failure. Patients who have a second kidney diagnosis in addition to DN such as IgA, FSGS and MN had favorable outcomes compared to DN and AIN or DN only [figure 1].

Conclusions: We identified serum creatinine, hematuria, IFTA and glomerular sclerosis as prognosticators of kidney failure at 1-year following DN diagnosis. Identification of patients at risk of kidney failure help individualize therapy and hence improve kidney outcomes.
PO0962
Phosphorylated Akt (pAkt) and Myostatin: The Yin and Yang of the Control of Muscle Protein Metabolism in Patients with Diabetic Kidney Disease

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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. We studied intracellular pAkt (a downward 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).

Methods: Rectus abdominis muscle biopsies were obtained during the insertion of peritoneal dialysis catheters and during elective surgery for abdominal wall hernias (C). Protein expression (pAkt, MSTN, p38MAPK) was evaluated by immunohistochemistry and western blot, mRNA expression (MSTN, Murf, Atrogin) by q-PCR.

Results: The expression of pAkt was significantly more downregulated in DKD 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 DKDCKD and in NDCKD with respectively a 21- and a 18- fold increase compared to controls. Atrogin and MURF mRNA were both upregulated in DKD and in NDCKD; in DKDCKD MURf mRNA presented a 18- and atrogin mRNA a 16- fold increase compared to controls while in NDCKD we found respectively a 12- and a 9- fold increase.

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 conjuction with myostatin overexpression are likely to orchestrate the wasting syndrome.

PO0963
Incident CKD in Diabetes, Hypertension, and Prediabetes

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Background: Hypertension (HTN), diabetes mellitus (DM), and prediabetes (PDM) are major risk factors for chronic kidney disease (CKD), yet community-level longitudinal studies of CKD incidence are lacking. The study aim was to determine CKD incidence rates in these at-risk groups by practice- and guideline-based definitions.

Methods: The Center for Kidney Disease Research, Education, and Hope (CURE-CKD) registry is curated from electronic health records with clinical and administrative data from two large non-profit healthcare systems. CKD incidence (95% CI) in adults was calculated over 4, two-year time periods during 2010-2017 adjusted for age, sex, and race/ethnicity. CKD was identified by 2 definitions: 1. Practice-based, CURE-CKD: At least 2 laboratory measures for CKD ≥90 days apart (estimated glomerular filtration rate - eGFR <60 ml/min/1.73m², urine albumin/creatinine ratio - UACR ≥30 mg/g, or urine protein/creatinine ratio - UPCR ≥30 mg/g) or CKD administrative code. 2. Guideline-based, Kidney Disease Improving Global Outcomes (KDIGO): At least 2 eGFRs <60 ml/min/1.73m² or 2 UACRs/UPCRs ≥30 mg/g≥50 mg/g ≥90 days apart.

Results: Overall adjusted CKD incidence rates declined over 2010-2017 by both definitions with lower rates by KDIGO (Table). By CURE-CKD, CKD incidence increased in the HTN group.

Conclusions: The practice-based CURE-CKD definition produced higher estimates of CKD incidence than the stricter guideline-based KDIGO definition. CKD incidence declined in all groups, except for HTN by the CURE-CKD definition, and was highest in patients with DM/HTN. Targeting these at-risk conditions for control may mitigate new onset CKD in these groups.

Funding: Other U.S. Government Support

PO0964
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 the 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

AUCROC, area under the ROC curve; NPV, negative predictive value; PPV, positive predictive value; SVM, support vector machine; RF, random forest

Analysis flow for the development and evaluation of the model
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 the 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.

Conclusion: Our model provided reliable estimates of disease progression among T2D patients with CKD. The 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

PO0965

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 that 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 hazard model for time to a composite endpoint (all-cause death or ESRD). The processes were correlated using a hazard model for time to a composite endpoint (all-cause death or ESRD). This model undertook calibration and validation against the CRIC patients with T2D and CKD over a 7-year follow-up period.

Conclusion: 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

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 serum 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/m^2 and 12% had uncontrolled diabetes (A1C>10%). 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 eGFR60 mL/min/m^2 experienced hyperkalemia when compared to 21% of patients with eGFR<60 mL/min/m^2 (p=0.01). Hyponatremia (<135 mEq/L) was seen in 12% of patients, with values <130 mEq/L seen in 2%. Hypomagnesemia (<1.5 mg/dL) was present in 3% and hypocalcemia (albumin-corrected calcium<7 mg/dL) was seen in 0.1%.

Conclusion: Patients with eGFR60 mL/min/m^2 are particularly at high risk of developing hyperkalemia post-SGLT2 initiation. Effective monitoring and treatment strategies are needed to mitigate risks associated with hyperkalemia.

Funding: Commercial Support - Relypsia Fellowship grant

Incidence of electrolyte abnormalities (%)

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 linked 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 before 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 diagnosis of DM 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 for DM + CKD + MACE and 89 for DM + CKD + MACE. ACM incidence increased in line with increasing comorbidity burden, to 146.73 per 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 (797.27/635.26 per 1,000 PYs with/without MACE, respectively) and lower in patients without CKD (384.13/246.83 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 MACE was associated with higher levels of RAAS prescription (61.91% vs 74.86%–76.28%).

Conclusions: DM patients with CKD and/or MACE are at increased risk of HK and ACM. Routine monitoring of SK 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 hyperglycemia 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 creat measurements from 1/2008 to 12/2010. Index date was defined as the date of first outpatient serum creat measurement. Duration of T2D was calculated by the first occurrence of ICD-9 codes for T2D, Hba1C > 6.5% or use of anti-diabetic med 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 outpatient serum creat measurements from 1/2008 to 12/2010. A propensity score matched cohort was generated using propensity scores of baseline variables including demographics, duration of T2D, Hba1C, retinopathy, BMI, other anti-diabetic med and comorbidities was used to develop propensity scores of baseline insulin use (22% were on insulin at baseline). A propensity score matched cohort (N = 324,064) 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 cGFR 71±24. There were 16,648 of hypoglycemic episodes over 1,529, 224 years of follow up. There was a gradual 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 cGFR ≥90 with no insulin use (Fig), the risk of serious hypoglycemic episodes was highest in the stage 4 CKD group on insulin (HR 4.79, 95% CI 4.31 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.

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

PO0972
The Effect of Microalbuminuria on 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.

Results: 1Bland-Altman analysis results demonstrated that consistency of eGFR-Cys2 equation and Ruijin with sGFR were better than other equation, but all the equation were above the limite professional point. The slopes of EPI-Cys2 equation were closer to the identical line. (2)Bias of EPI-Cys2 equation was smaller than other equations. EPI-Cys2 equation underestimated actual GFR and other equations overestimated GFR. 30% and 6% accuracy rate of Ruijin equation and EPI-Cys2 equation were higher than other equations. (3)As to diagnosis CKD in DM patients, EPI-Cys2 equation was more sensitive and accurate, and the cut-point of EPI-Cys2 equation and Ruijin equation was closer to 60ml/min.

Conclusions: All six equations show bias in estimating actual GFR. Compared with the equations induced by plasma creatine, EPI-Cys2 equation was more accurate and efficient, and followed by Ruijin equation. All equations should be amended when applying to Chinese DM patients.

Funding: Government Support - Non-U.S.

PO0969
Cumulative Average and Variability of Blood Glucose, Blood Pressure, and Lipids Are Associated with Incidence of Albuminuria, but Not Reduced Kidney Function, Among Patients with Type 2 Diabetes
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Background: We evaluated the effect of cumulative average and variability of fasting blood glucose, blood pressure and lipids on the incidence of albuminuria and reduced estimated glomerular filtration rate (eGFR) among a population with diabetes.

Methods: The study was based on the Kailuan cohort in Tangshan of China. The study baseline was the 2014-2015 circle of health examination. Totally, 1569 patients with type 2 diabetes identified in the 2008-2009 circle, with participation of at least 3 circles of health examination (3-5 times) between 2008 and 2015, and with negative finding in dipstick test and a normal cGFR at baseline were included. The occurrence of albuminuria (urine albumin to creatinine ratio ≥30mg/g) and eGFR<60ml/min/1.73m2 (with an absolute decline of ≥10%) was ascertained during 2016-2017. cGFR was determined with the CKD- EPI creatinine equation in the 2014-2015 circle and corresponding cystatin-C equation in the 2016-2017 circle. Cumulative average and intravariandial standard deviation (SD) of fasting blood glucose (FBG), systolic blood pressure (SBP), triglycerides and low-density lipoprotein cholesterol (LDL-C) were calculated. Multivariable logistic regression was used to estimate the association of the average and SD values of each variable with the events.

Results: The mean age of the population was 61.8±8.6 years, with a male dominance (77.6%). In the 2016-2017 circle, there were 499 events of albuminuria and 184 of reduced estimated GFR. Both average and SD of SBP were associated with both albuminuria amounts focusing on elderly diabetes.
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 (≥65 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 [95% CI, 1.29-6.70] for microalbuminuria, 11.16 [6.47-19.24] for macroalbuminuria). The HR of all-cause death 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.

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. 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 [95% CI, 1.29-6.70] for microalbuminuria, 11.16 [6.47-19.24] for macroalbuminuria). The HR of all-cause death 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

Cardiovascular Disease and Medication Use by CKD Risk Groups in People with Type 2 Diabetes: A Post Hoc Analysis from CAPTURE
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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 (<60, 60-89, 30-399, ≥300 mg/dl) was 35%, 44%, 18% and 3%, respectively, and by UACR (<30, 30-399, >300 mg/dl) 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
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 to 6.3] years. At baseline, mean ± SD age was 60 ± 10 years, median kidney function 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 of type 2 diabetes: -1.0 [95%CI: -1.4 to -0.5] ml/min/1.73m²/year (p=0.001) and controls: -0.95 [95%CI: -1.4 to -0.5] 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 assessed by heart rate variability was associated with steeper decline in kidney function during 6 years of follow up. Cardiovascular autonomic dysfunction may be a predictor of 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 ⁸²Rb PET/CT scan. In 2019, survivors (n=82) were invited for a repeated cardiac ⁸²Rb PET/CT scan 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 was similar between both groups (p=0.62) and did not differ between visits within the groups (C:p=0.51, T2D:p=0.001). CACS was higher in persons with T2D compared to C at both visits. CACS increased between visits within both groups (C:p=0.015, T2D:p<0.001), and the change was higher in T2D (p=0.002). In the total cohort, lower eGFR at baseline was associated with higher decline in MFR (p=0.027), 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.
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 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 were 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.

Association Between the Urinary Proteome and Diabetic Retinopathy in the DIRECT-Protect 1 and 2 Trials

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Background: Diabetic retinopathy (DR) is a complication of paramount importance in type 1 and type 2 diabetes. Given the association of DR and diabetic kidney disease (DKD), we investigated the association between the urinary proteome and the presence of DR in patients with type 1 and type 2 diabetes, and the identified peptide fragments were not conclusively associated to development of diabetic retinopathy.

Methods: Baseline proteomic analysis was performed in both the DIRECT-Protect 1 and 2 studies in a random selection of 800 and 821 subjects respectively. The 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. Thereafter, identified peptide fragments were investigated for association to baseline DR score in the validation cohort and for development of endpoints in both cohorts, adjusted for sex, age, diabetes duration, smoking, total cholesterol, HbA1c, systolic blood pressure, urinary albumin excretion rate, serum creatinine, and randomization group at baseline.

Results: Follow-up ranged from 4.0-4.7 years. Eleven out of 427 peptide fragments were inversely associated to baseline DR in the discovery cohort after adjustment. In multivariate Cox regression analyses lower alpha-1 type I collagen (COL1A1) (seq. ApGΔD–), GKN2C, and LGD1– was significantly (p<0.05) associated to the development of RET2 and lower COL1A1 (seq. LGD2–) and COL1A1 (seq. EDGΔK–) 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 COL1A1 fragment (seq. AFGΔS–) 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.
Background: Diabetes (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 kd size 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, cubulin, monocyte chemotactic factor [MCP-1], NGAL, and VDBG 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, 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.

**PO0984**

The Importance of Addressing Multiple Risk Markers in Type 2 Diabetes: Results from the LEADER Trial

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Background: The benefit of multifactorial intervention in type 2 diabetes (T2D) was demonstrated in the small Steno-2 study in microalbuminuric T2D. Larger studies in more diverse cohorts are limited. We investigated the importance of multiple risk-marker change for micro- and macrovascular outcomes in the LEADER trial.

Methods: LEADER (N=9340, ClinicalTrials.gov number NCT01179048) randomized patients with T2D to lixisenatide or placebo (S11) in addition to standard of care. We categorized patients according to number of risk markers with a clinically relevant change at year 1 of treatment and investigated subsequent risk of an expanded cardiovascular outcome (MACE-6) or nephropathy. We defined clinically relevant change in MACE-6 as: body weight loss ≥5%, HbA1c reduction ≥1%, systolic blood pressure reduction ≥5 mmHg, LDL reduction ≥0.5 mmol/L, eGFR reduction ≥0.1 ml/min/1.73m² and urinary albumin-to-creatinine ratio reduction ≥30% of baseline value. Numbers of risk markers with change were classified as: none (group G0), 1 (G1), 2 (G2), 3 (G3) and 4 (G4). Cox regression analysis risk of the outcomes adjusted for continuous baseline levels of the risk markers.

Results: Compared to patients with no risk-marker change, risk of cardiovascular disease was lowest for patients with 2 (HR [95% CI] 0.81 [0.66–0.98]) or 3 (0.80 [0.65–0.92]) risk-marker changes, and risk of nephropathy was lower for those with 3 (0.50 [0.35–0.72]) or ≥4 (0.45 [0.31–0.73]) risk-marker changes (Table). Test for trend of number of improved risk markers as a continuous variable: p=0.004 and p<0.001, respectively.

Conclusions: Improvement in multiple risk markers within 1 year translates into reduced risk of micro- and macrovascular outcomes in T2D, underscoring the benefit of pleiotropic antidiabetic treatments.
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 a hematuria group (N = 189), 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 the 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 group, 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 and founding 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.
PO0990
Virtual Patient Simulation in Diabetic Kidney Disease: Successful Strategy for Improving Recognition and Management
Amy Larkin, Medscape LLC, New York, NY.

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: 1) Patient: Diagnosis DKD 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) Oral patient education: 15% improvement (52% pre-CG vs 67% post-CG; P<.01) 2) Patient: Diagnosis DKD 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) Oral 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.

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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 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±3-fold increase in GFR vs. non-MCD) with long-term 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.

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

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 this analysis were to describe the prevalence of glycated-hemoglobin (HbA1c) measurement, distribution of HbA1c and association 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 chart 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 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 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 Wu1, Ping Wang,2 Li Luo,3 Min Zhang,4 Bingqing Xia,5 Lizhe Fu,6 Fang Tang,7 Xinlong Zhang,8 Xusheng Liu,9 Fuhua Lu,1 Renal Division, 1The Second Affiliated Hospital of Guangzhou University of Chinese Medicine (Guangdong Provincial Hospital of Chinese Medicine), Guangzhou, China; 2Department of Internal Medicine, Yufa 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 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 other DOPPS regions. Further investigation related to frequency of measurement and control of HbA1c via treatment is warranted.

Funding: Commercial Support - This abstract was sponsored specifically by Amgen Middle East FZ LLC. Global support for the ongoing DOPPS Programs is provided without restriction on publications by a variety of funders. For details see https://www.dopps.org/AboutUs/Support.aspx.

Background: Few specifics were proved effective to delay DKD progression while accumulating evidence supported potential merits of self-management on it. This study aimed to evaluate the association between self-management and progression of non-diabetic CKD3-5 DKD patients.

Methods: Data including demographics, procedure notes, laboratory findings, and medication of the included cohort were analyzed. The cohort was divided into self-management group and control group based on previous self-management exposure. The between-group comparison of renal function at 2 years and survival analysis were conducted.

Results: Total 92 patients were included(47 in self-management group and 45 in control group). Declined serum creatinine level and preserved eGFR were detected in self-management group after 2 years both with no significant difference(ΔeGFR=-0.69, P=0.56), while significantly higher serum creatinine level(ΔP=0.01) and decreased eGFR with no evident significance(ΔeGFR=-0.059) after 2 years were found in control group. We defined eGFR<50ml/1.73 m2, initiation of renal replacement therapy and death as composite endpoints, and calculated time-to-event point in self-management group(mean survival time 221.3±12.97 weeks) and 17 in control group(mean survival time 168.3±15.03 weeks) were recorded, with significant difference between group(p=0.012). Further Cox proportional hazards regression with three adjustment models showed that self-management engagement was an independent factor associated with reduced risk of incident endpoints.

Conclusions: The findings documented predisposing preserved renal function of patients with self-management at 2 years and self-management engagement as an independent factor for decreased risk of endpoints, indicating its potential benefits on delaying DKD progression.
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 healthcare 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±1.98 vs 50.4±2.4 yrs, p<0.0001) but age did not correlate with any finding. Mean creat was 1.8±1.5 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 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±0.14 vs 3.93±0.23, p=0.039). DIAB pts ate fewer carbohydrates (137.4±11.6 vs 211.8±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 1.96±0.6, p=0.015) and less refined grains (3.01±0.43 vs 4.61±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 towards the healthcare environment while encouraging an eating plan that includes fruits and vegetables. 4. The test for glycated hemoglobin, HbA1C, is the basic blood test used for diabetes control measures. This finding was particularly true of White pts to White providers and with Black pts to Black providers.

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 diabetes. There is limited exploration of the relationship between adherence to HbA1c testing, diabetes control, and congruent provider/patient race and ethnicity. This study examines 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 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 an 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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Background: Chronic kidney disease (CKD) is associated with increased risk for new-onset diabetes. Decreased circulating iron, as expressed by low transferrin saturation (Tsat), is associated with diabetes in the general population, but it has not been investigated if Tsat 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 Tsat and ferritin was developed using cubic regression splines.

Results: Of the 1,159,371 Veterans with CKD, 54,990 met the inclusion criteria. The means ± SD for age and eGFR were 73.8 ± 11.8 years and 43.8 ± 10.4 mL/min/1.73 m2, respectively. The median (IQR) Tsat and ferritin values were 23.0 (16.9, 29.7)% and 112.1 (50.6, 210.0) ng/mL. Over the mean follow-up period of 4 years, the risk of diabetes was inversely associated with Tsat, while it was positively correlated with serum ferritin. The surface contour map suggests that lower Tsat range (<20%) has a stronger relationship with incident diabetes than other.

Conclusions: In Veterans with pre-dialysis CKD, decreased Tsat is closely associated with incident diabetes risk, while increased ferritin exacerbates the risk.

Funding: Veterans Affairs Support

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
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 glyemic control reduces GH. Since elevated serum uric acid (SA) 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 SA among diabetics.

Methods: We examined the National Health and Nutrition 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 glycose-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 SA 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 SA, and those with no diabetes treatment. In the multivariable model, female sex was the strongest predictor followed by Hispanic ethnicity, higher SA, and younger age (Table).

Conclusions: GH is more common in the first 10 years of diabetes and associated with higher SA. It is more common among females, Hispanic race, and younger diabetes patients. Further studies should examine the potential role of sex, ethnicity, age, and SA 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 (per 10y)</td>
<td>0.91 (0.89, 0.92)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gender (Female vs. Male)</td>
<td>16.44 (10.54, 25.54)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ethnicity (Hispanic vs. White)</td>
<td>3.04 (1.76, 5.09)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HbA1c (per 1%)</td>
<td>1.49 (1.09, 1.40)</td>
<td>0.06</td>
</tr>
<tr>
<td>Uric Acid (per 10 mg/dL)</td>
<td>2.28 (1.13, 4.62)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

PO0998
Continuous Glucose Monitoring in a Diabetic Hemodialysis Patient
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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 glubride 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 measurements to monitor his glycemic status. During this time he had wide fluctuations in his glucose levels with asymptomatic hypo- and hyperglycemia, and his HbA1c levels were typically 10-12%. Due to poor glucose control, his endocrinologist advised him to use CGM (Dexcom G5, later transitioned to Dexcom G6, San Diego, CA). Since transitioning to CGM, the patient reports 1) greater adherence to glycemic monitoring, 2) improved hypoglycemia detection, 3) minimal lifestyle interruption, and 4) improved quality of life. In addition, he has less glycemic variability, increased time-in-target glucose range, and improved HbA1c levels to 6.8%.

Discussion: This case demonstrates CGM is a practical method for glucose assessment with the potential to improve glycemic control in diabetic ESRD patients. Further studies are needed to determine the comparative effectiveness of CGM vs. SMBG in diabetic HD patients.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
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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 urinary 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<0.0001). 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 95% CI 0.85–1.05).

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

PO1001

Acute Declines in eGFR During Treatment with Canagliflozin (CANA) and Its Implications for Clinical Practice: Insights from CREDENCE

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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; between 0 and 10% decline; and no decline. Baseline characteristics associated with acute eGFR drop >10% were evaluated using logistic regression. Long-term eGFR decline and safety outcomes were estimated in each eGFR decline category by linear mixed effects models and Cox regression with adjustment 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
The SGLT2 Inhibitor Canagliflozin Reduces the Plasma Markers TNFR-1, TNFR-2, and KIM-1 in the CANVAS Trial

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Background: Tumor Necrosis Factor Receptor (TNFR)-1, TNFR-2 and Kidney Injury Molecule 1 (KIM-1) are biomarkers known to predict kidney outcomes in patients with type 2 diabetes (T2D). We assessed the effect of the SGLT2 inhibitor canagliflozin (CANA) on TNFR-1, TNFR-2 and KIM-1 in CANVAS study participants to determine whether changes were consistent with subsequent kidney outcomes.

Methods: The CANVAS trial randomized participants with T2D at high cardiovascular risk to CANA or placebo (PBO). TNFR-1, TNFR-2 and KIM-1 were measured with immunoassays (proprietary multiplex assay performed by RenalytixAI, NY, USA) at baseline and years 1 and 3, and were reported as unadjusted levels.

Results: Among 3827/4330 (67%) CANVAS participants with available plasma samples at baseline and follow-up, median baseline TNFR-1, TNFR-2 and KIM-1 were 25.59, 96.12, and 108 pg/mL. Difference between CANA and PBO in TNFR-1, TNFR-2, and KIM-1 during follow-up were 2.8% (95%CI −3.5, −0.2; P = 0.028) and −26.7% (−30.7, −22.7; P < 0.001). Increases in TNFR-1 and TNFR-2, but not KIM-1, at year 1 were independently associated with a higher risk of the kidney outcome (Table).

Conclusions: CANA reduces TNFR-1, TNFR-2 and KIM-1 in patients with T2D at high cardiovascular risk. Early increases in TNFR-1 and TNFR-2 were independently associated with higher risk of kidney disease progression and have the potential to be pharmacodynamic markers of non-response to CANA.

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

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PO1005
Canagliflozin and Risk of Skin and Soft Tissue Infections in People with Diabetes Mellitus and Kidney Disease in the CREDENCE 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 CREDENCE trial and determine whether canagliflozin affects the risk of SSTI.

Methods: We performed a post-hoc analysis of the CREDENCE trial that randomised people with type 2 diabetes and albuminuric stage 2 and 3 chronic kidney disease to either canagliflozin 100mg daily or placebo. Adverse events were assessed by two blinded authors 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-first 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 CREDENCE trial participants with type 2 diabetes mellitus and albuminuric chronic kidney disease.

Funding: Commercial Support - Janssen sponsored the CREDENCE trial but did not sponsor this post-hoc analysis.

PO1006
Early Change in Albuminuria with Canagliflozin (CANA) Predicts Kidney and Cardiovascular (CV) Outcomes
Megumi Oshima,1,2 Brenda L. Neuen,1 Jingwei Li,1 Vladko Perkovic,1 David M. Charytan,1 Dick de Zeeuw,1 Robert Edwards,1 Tom Greene,2 Adeera Levin,1 Kenneth W. Mahaffey,1 Luca De Nicola,3 Carol A. Pollock,4 Norm Rosenthal,1 David C. Wheeler,5 Meg J. Jardine,2 Hiddo L. Heerspink,1 The George Institute for Global Health, UNSW Sydney, Sydney, NSW, Australia; 2Department of Nephrology and Laboratory Medicine, Kanazawa University, Kanazawa, Japan; 3Nephrology Division, NYU School of Medicine and NYU Langone Medical Center, New York, NY, USA; 4Department of Clinical Pharmacy and Pharmacology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands; 5Janssen Research & Development, LLC, Raritan, NJ, USA; 6Division of Biostatistics, Department of Population Health Sciences, University of Utah, Salt Lake City, UT; 7Division of Nephrology, University of British Columbia, Vancouver, BC, Canada; 8Stanford Center for Clinical Research, Department of Medicine, Stanford University School of Medicine, Stanford, CA; 9Department of Advanced Medical and Surgical Sciences, Nephrology and Dialysis Unit, University Vanvici, Naples, Italy; 10Kolling Institute of Medical Research, Sydney Medical School, University of Sydney, Royal North Shore Hospital, St Leonards, NSW, Australia; 11Department of Renal Medicine, UCL Medical School, London, United Kingdom; 12Cordis Repatriation General Hospital, Sydney, NSW, Australia; 13Department of Clinical Pharmacy and Pharmacology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands.

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 association is comparable regardless of diabetes duration, number of therapies or HbA1C at baseline.

Methods: In this post-hoc analysis of the CREDENCE 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 (HHF) 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 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.

Funding: Commercial Support - Janssen
PO1008

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: MeansDSD baseline estimated glomerular filtration rate (eGFR in mL/min/1.73 m2) in EASE-2/EASE-3 was 97.3±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<0.0001) and -3.56 (p<0.0001), respectively. Mean placebo-corrected eGFR changes with empagliflozin 10mg and 25mg were −2.05 (p=0.02; n=226) and −2.60 (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<300mg/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 ≥30 mg/g, UACR decreased by 16% (p=0.27) and 30% (p=0.02) 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.

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 Diabetics Alliance

PO1009

Empagliflozin 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 cardiovascular 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 5 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.

Conclusions: In patients with T1D, SGLT2 inhibition increased plasma TCA cycle metabolite levels, suggesting an impact on mitochondrial function. Lipid metabolite levels were also increased after SGLT2 inhibition, suggesting a possible increase in beta oxidation. Further work is needed to determine if these changes contribute to cardiorenal protection with SGLT2 inhibitors.

PO1010

Effect of Dapagliflozin on Risk for Fast Decline in eGFR: Analysis from DECLARE-TIMI 58 Trial

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Background: SGLT2 inhibitors may lead to short term decrease in eGFR with later stabilization and long-term reduction in risk for end stage kidney disease. Fast decline (FD) in eGFR can be defined as reduction of ≥3 mL/min/1.73m2/year and is associated with poor long-term renal prognosis. In this post hoc analysis we studied the effect of dapagliflozin (dapa) on risk of FD in the DECLARE-TIMI 58 trial.

Methods: In DECLARE-TIMI 58, 17,160 patients with T2D and established or increased risk for CVD, with mean baseline eGFR of 85.2 mL/min/1.73m2, were randomized to dapa vs. placebo and followed for median of 4.2 years. The risk for FD was compared between treatments.

Results: In the time frame of 0.5 years (after stabilization) to 4 years, the proportion of patients with FD was reduced with dapa vs. placebo (26.8% vs. 37.1%, respectively, p<0.0001) and in all subgroups assessed (Figure). The mean (SD) reduction in eGFR per year was 6.3 (3.7) vs. 0.0 (2.5) mL/min/1.73m2/year in FD (N=4,788) vs. non-FD (N=10,224) patients. In patients that had FD, mean (SD) reduction in eGFR was −5.9 (3.2) vs. −6.6 (4.1) mL/min/1.73m2/year in dapa vs. placebo arm, while in patients that did not have fast decline it was 0.2 (2.5) vs. −0.2(2.5) mL/min/1.73m2/year, respectively. The proportion of patients with FD during entire study period (i.e. 0-4 years) was also reduced with dapa vs. placebo (33.6% vs. 37.0%, respectively, p<0.0001).

Conclusions: Dapa reduced the risk for FD in eGFR in a broad population of patients with T2D and relatively preserved renal function, irrespective of patients’ baseline characteristics.

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)

Eun Sil Koh,1 Kyungdo Han,1 Hyewon Lee,1 You-Seon Nam,1 Eric T. Wittbrodt,4 Peter Fencik,1 Mikhail Kostobrod,1 Hildo J. L. Heerspink,2 Soon-Jib Yoo,2 Hyuk-Sang Kwon.1 The Catholic University of Korea Yonsei Saint Mary's Hospital, Yeongdeungpo-gu, Seoul, Republic of Korea; 2AstraZeneca Korea Co Ltd, Seoul, Republic of Korea; 3Soongsil University Department of Statistics and Actuarial Science, Dongjak-gu, Seoul, Republic of Korea; 4AstraZeneca, Gaithersburg, MD; 5AstraZeneca, Cambridge, United Kingdom; 6Saint Luke's Mid America Heart Institute, Kansas City, MO; 7University Medical Center Groningen, Groningen, Netherlands; 8The Catholic University of Korea Bucheon Saint Mary's Hospital, Bucheon, Gyeonggi-do, Republic of Korea.

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 Type 2 DM and CKD. 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 for 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) 89.2±27.4 ml/min/1.73m²; 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/1.73m² 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: Commercial Support - AstraZeneca

PO1013

Cardiovascular Outcomes with SGLT-2 Inhibitors vs. GLP-1 Receptor Agonists in Patients with Type 2 Diabetes and CKD: A Systematic Review and Network Meta-Analysis

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Background: Type 2 diabetes mellitus (DM) and chronic kidney disease (CKD) increase the risk of cardiovascular disease. Sodium-glucose cotransporter-2 (SGLT-2) inhibitors and glucagon-like peptide-1 receptor agonists (GLP-1 RA) are known to reduce cardiovascular disease. However, no study compared the effect of SGLT-2 inhibitors on cardiovascular diseases with that of GLP-1 RA in CKD patients.

Methods: We performed a systematic literature search up to March 2020. We selected randomized control trials. First, we performed meta-analysis to compare SGLT-2 inhibitors vs placebo and GLP-1 RA vs placebo. Next, we performed a network meta-analysis to compare SGLT-2 inhibitors with GLP-1 RA indirectly. Risk ratios (RRs) with corresponding 95% confidence interval (CI) were synthesized.

Results: Total thirteen studies were selected. SGLT-2 inhibitors led to a risk reduction in MACE (RR [95% CI]; 0.80 [0.72-0.89], p = 0.0001). On the other hand, GLP-1 RA did not show significant difference with high heterogeneity (0.88 [0.74-1.04], p = 0.15, I²=58%) (Figure 1). The network meta-analysis did not show significant difference between SGLT-2 inhibitors and GLP-1 RA (0.90 [0.77-1.08]) (Figure 2).

Conclusions: In patients with type 2 DM and CKD, SGLT-2 inhibitors were associated with decreased risk of MACE, but GLP-1 RA did not. Network meta-analysis did not reveal significant difference between SGLT-2 inhibitors and GLP-1 RA.

Funding: Veterans Affairs Support

PO1011

Comparative 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 did not reveal significant difference between SGLT-2 inhibitors and GLP-1 RA.

In patients with type 2 DM and CKD, SGLT-2 inhibitors were associated with lower risk of all-cause death associated with SGLT-2i vs 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: Commercial Support - AstraZeneca
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 Ipagliflozin. 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; \(eGFR\geq60\)) 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±6.0% in HR vs +5.0±7.6% in LR). In DF, ACR was also decreased (median: -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) and %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 damage.

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 less annual reduction in BMI, 0.24 (0.17, 0.32) kg/m² less annual reduction in BMI, and reduced risk of MAKE (HR=0.68 (0.64-0.73)). SGLT2i use was associated with reduced risk of MAKE in eGFR <60 to <45 ml/min/1.73m² and in participants with and without albuminuria. The association was evident in per-protocol analyses which required continuation of the treatment. The association was evident in per-protocol analyses which required continuation of the treatment.

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

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 an ambulatory encounter with a primary care provider and a 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.

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

PO1017
Dulaglutide and Kidney Function-Related Outcomes in Type 2 Diabetes: Post Hoc Analysis from the REWIND Trial
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Background: Over the median follow-up of 5.4 years in the REWIND trial, which included participants with type 2 diabetes (T2D) and multiple cardiovascular (CV) risk factors, dulaglutide (DU) use was associated with a reduction in composite renal outcomes, defined as the first occurrence of new macroalbuminuria, sustained decline in estimated glomerular filtration rate (eGFR) of ≥30% (using the modification of diet in renal disease [MDRD] equation), or chronic renal replacement therapy. This posthoc analysis evaluated the potential effects of dulaglutide on renal outcomes using an alternative endpoint definition that is commonly used in renal outcomes studies; defined as the composite endpoint of sustained eGFR decline ≥40% (using the chronic kidney disease-epidemiology collaboration [CKD-EPI] equation), end-stage renal disease (ESRD), or all-cause death.

Methods: REWIND participants were randomized (1:1) to DU 1.5 mg once weekly or placebo. Cox proportional hazards model for time-to-first-event analysis was used to determine the risk of renal outcomes. Subgroup analyses were conducted by baseline eGFR and albuminuria status.

Results: At baseline, treatment groups had similar eGFR values (mean ± SD: DU = 77.6 ± 19.4 mL/min/1.73 m²; placebo = 77.1 ± 19.6 mL/min/1.73 m²). The incidence rate of the composite endpoint was significantly lower for the DU group compared with placebo. This effect was consistent regardless of baseline eGFR or albuminuria status (Table).

Conclusions: Treatment with DU 1.5 mg was associated with a 17% risk reduction in the composite renal outcome, suggesting potential delay in progression of diabetic kidney disease in patients with T2D at CV risk.

Funding: Commercial Support - Eli Lilly and Company

PO1018
Efficacy and Safety of Cotadutide, a Dual GLP-1 and Glucagon Receptor Agonist, for Patients with Type 2 Diabetes Mellitus and CKD
Victoria E. Parker,1 Thuong Hoang,1 Heike Schlichthaur,2 Yi-Ting Chang,3 Marcella Petrone,1 Lars Hansen,1 Philip D. Ambery,2 Hiddo J. Heerspink,3 Rory McErmimon,4 Lutz Jermutus,1 AstraZeneca, Cambridge, United Kingdom; 2Study Center, SMO MD GmbH, Magdeburg, Germany; 3AstraZeneca, Gothenburg, Sweden; 4University Medical Center, Groningen, Netherlands; 5School of Medicine, University of Dundee, Ninewells Hospital, Dundee, United Kingdom.

Background: Cotadutide is in development for nonalcoholic steatohepatitis and type 2 diabetes mellitus (T2DM). GLP-1 analogues have been shown to delay the development of macroalbuminuria in patients (pts) with T2DM. The glycemic and renal effects of cotadutide were assessed in a phase 2a, randomized, controlled trial.

Methods: The trial enrolled 41 pts with T2DM (HbA1c: a1g.5–a10.5%) and chronic kidney disease (CKD) stage G3 (estimated glomerular filtration rate [eGFR]: ≥30–60 mL/min/1.73m²), on insulin and/or oral therapy, with a BMI of 25–45 kg/m². Pts were randomized to once-daily subcutaneous cotadutide (n=21), titrated up to 300 μg, or placebo (PBO; n=20) for 32 days. Endpoints included glucose response via mixed meal tolerance test (MMTT), HbA1c, body weight (BW), eGFR, urinary albumin creatinine ratio (UACR), and C-peptide levels. The trial was powered based on a 2-sided alpha of 0.1.

Results: Cotadutide significantly reduced MTMM glucose AUC vs baseline (-26.7%, 90% CI: -34.6 to -18.8%) and vs PBO (35.7%; 90% CI: -8.3 to -11.2%; P<0.001), with a 35.2% reduction in insulin dose (P=0.012). Cotadutide significantly reduced BW (-3.7%) and HbA1c (+0.7%; both P<0.001). After 32 days of cotadutide treatment, no significant changes were observed in eGFR or blood pressure. Fasting C-peptide levels in the cotadutide arm increased significantly vs PBO (Δ: 0.07 μg/L, 90% CI: 0.06 to 0.10, P<0.001). No meaningful changes were observed in BW, eGFR, or UACR. C-peptide levels significantly increased (11 beats per minute; P=0.001) by day 32.

Conclusions: In pts with T2DM and CKD, cotadutide improved overall glycemic control and glaucoma responses to an MTMT with acceptable tolerability. Improvements in albuminuria suggest that cotadutide may be beneficial in this population to slow long-term progression of CKD. Further exploration of this effect is warranted.

Funding: Commercial Support - AstraZeneca
PO1021

Hemoglobin A1c 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 (HbA1c) 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 criterion and where the number of subjects receiving semaglutide with eGFR <60 mL/min/1.73m2 was ≥45. It included data for once-weekly subcutaneous semaglutide (SUSTAIN 4–6, pooled 0.5 and 1.0 mg; SUSTAIN 10, 1.0 mg only) and once-daily oral semaglutide (PIONEER 5 and 6). Within each trial, absolute estimated change in HbA1c from baseline to end of treatment (EOT) was compared between eGFR subgroups using a linear mixed model.

Results: Mean HbA1c at baseline ranged from 7.9% to 8.7% across the subgroups. Semaglutide significantly reduced HbA1c at a comparable magnitude across eGFR subgroups in all trials (mean reduction of 1.0–1.7% from baseline to EOT; p<0.048 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 - Novo Nordisk

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

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PO1023

Impacts of Glucagon-Like Peptide 1 Analogues and Sodium Glucose Cotransporter 2 Inhibitor on Type 2 Diabetes Patients with Renal Impairment

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Background: Diabetes mellitus (DM) is a progressive multifactorial disease associated with cardiovascular complications. To prevent the progression of cardiovascular complications in DM patients, we examined impact on cardiac function between glucagon like peptide-1(GLP-1) analogue and sodium-glucose cotransporter-2 (SGLT-2) inhibitors to treat type 2 diabetes patients with renal impairment.

Methods: A total of 156 type 2 DM patients with renal impairment were recruited for this study. All patients were divided into two groups according to the anti-diabetic agents at baseline : Group G; 0.9mg/day liraglutide, n=72, Group S; n=84; 5mg/day dapagliflozin, n=32. Blood glucose levels, glycosylated hemoglobin, was independently associated with greater UACR reduction (\(\beta\)-7.0\% for this study. All patients were divided into two groups according to the anti-diabetic agents at baseline : Group G; 0.9mg/day liraglutide, n=72, Group S; n=84; 5mg/day dapagliflozin, n=32. Blood glucose levels, glycosylated hemoglobin (HbA1c), serum creatinine, and albuminuria were obtained 12 months before and every 3 months for 36 months. Echocardiography, cardio-ankle vascular index(CAVI) were obtained every 12 months for 36 months.

Results: HbA1c and systolic blood pressure were significantly decreased after ADAs. The eGFRs were gradually decreased in both groups. Albuminuria was decreased significantly after initiation of ADAs. Left ventricular mass index (LVMI) and left atrial volume index (LAVI) were significantly decreased in both groups. Cardiac systolic function indicated by ejection fraction and diastolic function indicated by E/e’or left atrial dimension were remained or improved only in group G. Moreover, arterial stiffness indicated by cardio-ankle vascular index (CAVI) was improved in group G (Table1).

Conclusions: These findings suggest that liraglutide and SGLT-2 inhibitor for type 2 DM patients with renal impairment have similar effects on renal function including eGFR and albuminuria and left ventricular and atrial volume. However, liraglutide could provide more benefit for arterial stiffness than SGLT-2 inhibitors.

Table 1: Clinical Data

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

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PO1024

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 3rd 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 800-500 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.

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

Underline represents presenting author.
**PO1026**

**Effect of Oral Supplementation with Curcumin in Diabetic Subjects with Proteinuric Kidney Disease: A Randomized Controlled Trial**

Ana P. Hernandez-Martinez,1 Yao Cheng,1 Alfonso Giindl-Bracho,2 Alejandro Cabrera-Jara,2 Ana K. Fernandez-Yepes,2 Maria F. Martinez-Hernandez,2 L. Gabriela Sanchez-Lozada,1 Edilia Tapia,1 Francisco Eugenio R. Castellanos,1 Armando Rezquez-Zangreel,1 Magdalena Madero,1 1 Instituto Nacional de Cardiologia Ignacio Chavez, Mexico, Mexico; 2 Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, Tlalpan, Mexico; 3 Instituto Mexicano del Seguro Social, Ciudad de Mexico, Mexico.

**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/Nrf 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 gram/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 curcumin 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 83% had proteinuria > 1 gram/g. After 24 weeks of 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.

**PO1028**

**Preexisting CKD Increases Risk of Metformin Monotherapy Failure in US Veterans with Type 2 Diabetes**

Elvira O. Gosmanova,1,2 Darren E. Gemoets,1 Laurence S. Kaminisky,1 Csaba P. Koverydy,1,2 Aidar R. Gosmanov,1,2 Albany Stratton VA Medical Center, Albany, NY; 1 Albany Medical College, Albany, NY; 3 Memphis VA Medical Center, Memphis, TN; 4 The University of Tennessee Health Science Center, Memphis, TN.

**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/1.73 m2 who initiated MET monotherapy between 01/2010 and 03/2017. CKD3 was established as eGFR 30-59 ml/min/1.73 m2. MET monotherapy failure defined as the 1st >90 day gap in MET refill (MET discontinuation) or the addition of 2nd hypoglycemic agent (HA) during >3 yr follow up was compared between patients without and with CKD3 using univariate and multivariate Cox regression analyses adjusted for case-mix.

**Results:** The mean ± SD age for the total cohort was 59.4 ± 0.2 yrs, 94.3% were males, 79.9 ± 17.3% were Whites and Blacks, respectively. Preexisting CKD3 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 without and with 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 CKD 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 - Cyclerion Therapeutics

**PO1027**

**Effect of Pralirigacut, 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. Hamrahan,1 Ian H. de Boer,1 George L. Bakris,2 Phoebe Wilson,1 James D. Wakefield,1 Jelena P. Seferovic,1 Jennifer Chicking,1 Michael Cressman,4 Mark Currie,2 George T. Milne,1 Albert T. Profy,1 Cyclerion Therapeutics, Cambridge, MA; 2The University of Washington, Seattle, WA; 3The University of Chicago Medical Center Comprehensive Hypertension Center, Chicago, IL; 4 Covance Inc, Princeton, NJ.

**Background:** Impaired nitric oxide (NO) signaling has been implicated in the progression of diabetic kidney disease (DKD). Pralirigacut (PRL) is a soluble guanylate cyclase stimulator that amplifies NO signaling in vitro and reduces proteinuria and fasting plasma glucose in the ZSF1 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, serum uric acid creatinine ratio (UACR) 200-500 mg/g, hemoglobin Alc (HbAlc) <12%, systolic blood pressure (BP) 110-160 mmHg, on stable glucose-lowering and renin angiotensin system-inhibition therapy. Participants were randomized 1:1:1 to placebo (PBO), PRL 20 mg, or PRL 40 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], nominal p=0.03. PBO-adjusted CBF for other variables at week 12 (ITT) were: 24 h systolic BP -4.2 mmHg [-7.5, -0.8], 24 h heart rate 3.4 bpm [1.6, 5.2], HbAlc -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 pralirigacut 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:** Government Support - Non-U.S.

**PO1029**

**Utilization of Glucose-Lowering Medications Among US Medicare Beneficiaries with CKD Between 2007 and 2016**

Julie Zhao,1,2 Eric D. Weinhandl,1,2 Angelene M. Carlson,3 Wendy L. St. Peter,1,2 University of Minnesota, Minneapolis, MN; 3 Chronic Disease Research Group, Hennepin Healthcare Research Institute, 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.

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

Underline represents presenting author.
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 glucose-lowering renal medications. To test overall trends in glucose-lowering medication classes, linear probability models with adjustment for age, sex, race, income, and low-income status were used.

Results: Use of metformin, newer glucose-lowering medication classes (DPP-4 inhibitors, GLP-1 receptor agonists, and SGLT2 inhibitors), and newer insulin analogs (aspart, lispro, glulisine, detemir, glargine, degludec) showed statistically significant upward trends during the study timeframe. Sitagliptin was the most commonly prescribed DPP-4 inhibitor; use increased from 5.6% in 2007 to 15.0% in 2016. Use of liraglutide (approved in 2011) increased from 0.1% in 2011 to 6.0% in 2016. Compared with other GLP-1 receptor agonists, use of liraglutide (approved in 2010) increased more (0.3% in 2010 to 3.9% in 2016), and use was higher in 2015. Use of SGLT2 inhibitors (canagliflozin, empagliflozin, or dapagliflozin) remained very low but in 2016, use was increasing. Use of newer analog insulin therapy increased, especially insulin detemir (2.4% in 2007 to 11.7% in 2016). Insulin was the most highly used single medication class in 2016. The most highly used dual combination therapies in 2016 were metformin and sulfonylureas, metformin and insulin. Combination therapy was less common as CKD stage increased.

Conclusions: Use of metformin and newer glucose-lowering medication classes is increasing in CKD patients with type 2 diabetes. We anticipate that percentages of CKD patients using these newer agents will increase.

PO1030
Role of Roxadustat in Improving Erythropoiesis-Stimulating Agent (ESA)-Resistant Anemia in Patients on Maintenance Hemodialysis
Satoshi Funakoshi,1 Jyunichi Hashiguchi,1 Kenji Sawase,2 Taku Kawazu,3 Mineki Kitamura,1 Kanako Hayashi,1 Kosei Yamaguchi,1 Tomoya Ninomiya,2 Takashi Harada.1 Nagasaki University Hospital, Nagasaki, Japan; 2Nagasaki University, Kagoshima, Japan.

Background: Roxadustat, an oral hypoxia-inducible factor (HIF) prolyl hydroxylase inhibitor, is shown to stimulate erythropoiesis thus improving iron metabolism. Again, while hyperglycemic states are known to be associated with a decreased tissue hypoxia response, data that show that HIF has not been evaluated for its role in improving anemia in patients with or without diabetes in clinical settings.

Methods: A total of 64 hemodialysis patients being treated with epoetin α (9000 units weekly) participated in the study after giving informed consent. They were switched from intravenous epoetin α to oral roxadustat (100 mg 3 times weekly) therapy and were assessed for the improvement in anemia as well as changes for parameters of iron metabolism and C-reactive protein (CRP).

Results: The study included 39 patients without diabetes (mean age, 71.1 ± 12.1 years; mean diabetes vintage, 7.5 ± 7.4 years; mean GA, 16.2 ± 2.9%) and 27 patients with diabetes (mean age, 70.3 ± 10.3 years; mean diabetes vintage, 5.9 ± 5.5 years; mean GA, 24.9 ± 5.5%). As shown in Table 8, after 8 weeks the Hb concentration was significantly increased from 10.3 ± 0.8 g/dL at baseline to 10.7 ± 1.3 g/dL in patients without diabetes (P = 0.03) but was not increased in patients with diabetes (from 10.4 ± 0.6 at baseline to 10.5 ± 1.1 g/dL). Again, the serum iron, ferritin concentrations and the transferrin saturation ratio were decreased, irrespective of whether or not they had diabetes, with no change shown in serum CRP level.

Conclusions: Switching hemodialysis patients with ESA-resistant anemia from ESA to roxadustat led to improvement in anemia only in those without diabetes, while study results suggested the involvement of mechanisms, other than impaired iron utilization or inflammation, in the impairment of hematopoiesis in those with diabetes.

Funding: Private Foundation Support

Effects of Roxadustat on HD Patients without or with Diabetes

PO1031
Efficacy and Safety of Roxadustat in Patients with Dialysis-Dependent CKD, Anemia, and Diabetes Mellitus
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Background: Roxadustat is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor that stimulates erythropoiesis and improves iron metabolism. Diabetes mellitus (DM) is a growing health problem often associated with CKD. In patients with DM, 37-54% of patients on dialysis (Stages 4 and 5 CKD) have DM. Use of newer analog insulin therapy increased, especially insulin detemir (0.3% in 2010 to 3.6% in 2016), and use was higher in 2016. Use of SGLT2 inhibitors (approved in 2011) increased from 0.1% in 2011 to 6.0% in 2016. Compared with other glucose-lowering medication classes, linear probability models with adjustment for age, sex, race, income, and low-income subsidy (LIS) status were used.

Results: Use of metformin, newer glucose-lowering medication classes (DPP-4 inhibitor; use increased from 5.6% in 2007 to 15.0% in 2016. Use of liraglutide (approved in 2011) increased from 0.1% in 2011 to 6.0% in 2016. Compared with other GLP-1 receptor agonists, use of liraglutide (approved in 2010) increased more (0.3% in 2010 to 3.9% in 2016), and use was higher in 2015. Use of SGLT2 inhibitors (canagliflozin, empagliflozin, or dapagliflozin) remained very low but in 2016, use was increasing. Use of newer analog insulin therapy increased, especially insulin detemir (2.4% in 2007 to 11.7% in 2016). Insulin was the most highly used single medication class in 2016. The most highly used dual combination therapies in 2016 were metformin and sulfonylureas, metformin and insulin. Combination therapy was less common as CKD stage increased.

Conclusions: Use of metformin and newer glucose-lowering medication classes is increasing in CKD patients with type 2 diabetes. We anticipate that percentages of CKD patients using these newer agents will increase.

Funding: Private Foundation Support

Effects of Roxadustat on HD Patients without or with Diabetes

PO1032
Efficacy and Safety of Roxadustat in Patients with Non-Dialysis-Dependent CKD, Anemia, and Diabetes Mellitus

Diabetic Kidney Disease: Clinical - 2

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
POI034

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. We aimed to determine the independent relationship between MLR, all-cause and cardiovascular (CV) mortality in a large and ethnically diverse haemodialysis population.

Methods: Four cohorts were described by phases of haemodialysis 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, smoking status, body mass index, diabetes (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, consistent with the observed association with other markers of inflammation and malnutrition: lower albumin, phosphate and higher ferritin. Adjusted all-cause and CV mortality was observed to be higher in patients with higher MLR quartile both in the KM and spline analyses (Fig1/2).

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 haemodialysis 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.

POI035

Warfarin Increases the Risk of Vascular Calcification in Haemodialysis Patients: A Multicenter Case-Control Study

Rezzan Eren Sadioglu, Evren Ustuner, Ilhan Ergun, T. Eckerz, Gokhan Nergizoglu, Kenan Keven. 

Methods: This was a cross-sectional, observational, multicenter study. Vascular calcification (VC) were assessed using Adragao (AS; pelvis and hands) and Kauppila (KS; lateral lumbar spine) scores in 76 haemodialysis patients from six centers. There were 32 patients (4.5%) being treated with warfarin for at least 1 year out of a total of 711 haemodialysis patients and we included 44 control patients with matching parameters of age, sex and dialysis vintage to the study. Clinical characteristics, comorbid treatments, laboratory results were recorded and possible risk factors related to VC were analyzed.

Results: Of the patients, 47% were females, mean age was 65.8 ± 9 years, 23% were diabetics, their mean dialysis vintage was 68.39 ± 38.5 months and mean Kt/V 1.66 ± 0.27. No significant differences in clinical characteristics and basic laboratory results were found between control and warfarin group. In warfarin group, median Kauppila score was higher than control [11 vs 6.5 (25%-75% percentile, 5 vs 15), P = 0.032] and percentages of KS2 score ≥6 - patients were higher, as well (78.6% vs 50%; P = 0.029). Median Adragao score was not significantly different between two groups [7 vs 6, (25%-75% percentile 6 vs 8), P = 0.177]. Logistic regression analysis revealed that warfarin treatment was independently associated with Kauppila scores of ≥6 (OR 3.28, 95% CI 1.17-9.22, P = 0.024).

Conclusions: The results of this study showed that warfarin is a strong risk factor for vascular calcifications, especially in aorta of haemodialysis patients.

Table 1. Basic characteristics of the patients and the results of the study

<table>
<thead>
<tr>
<th>Patients (n</th>
<th>Age (years)</th>
<th>Gender</th>
<th>Race</th>
<th>DM (%)</th>
<th>Calcium (mmol/L)</th>
<th>Phosphorus (mmol/L)</th>
<th>Parathyroid hormone (ng/mL)</th>
<th>Serum creatinine (mg/dL)</th>
<th>Serum albumin (g/L)</th>
<th>Serum CRP (mg/L)</th>
<th>Calcium × Phosphorus Product (mg²/dL)</th>
<th>Kauppila score (mean±SD)</th>
<th>Kauppila score (median)</th>
<th>Adragao score (mean±SD)</th>
<th>Adragao score (median)</th>
<th>NLR</th>
<th>CRP</th>
<th>Serum creatinine (mg/dL)</th>
<th>Serum albumin (g/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>22 ± 12</td>
<td>66.8</td>
<td>57.7</td>
<td>30.0</td>
<td>7.4 ± 1.6</td>
<td>4.6 ± 1.5</td>
<td>29 ± 7.9</td>
<td>21.3 ± 9.6</td>
<td>3.9 ± 0.6</td>
<td>0.6 ± 0.1</td>
<td>38 ± 15</td>
<td>13 ± 12</td>
<td>12 ± 12</td>
<td>2 ± 1.2</td>
<td>2</td>
<td>1.7</td>
<td>2.9</td>
<td>3 ± 1</td>
<td>1.2 ± 0.1</td>
</tr>
<tr>
<td>Warfarin</td>
<td>30 ± 12</td>
<td>68.7</td>
<td>57.5</td>
<td>26.0</td>
<td>7.9 ± 1.7</td>
<td>4.7 ± 1.4</td>
<td>30 ± 6.1</td>
<td>22.2 ± 9.7</td>
<td>3.9 ± 0.6</td>
<td>0.6 ± 0.1</td>
<td>38 ± 15</td>
<td>14 ± 13</td>
<td>12 ± 12</td>
<td>3 ± 1.5</td>
<td>3 ± 1</td>
<td>1.6</td>
<td>3.6</td>
<td>3 ± 1</td>
<td>1.0 ± 0.1</td>
</tr>
</tbody>
</table>

POI036

Paradoxical Effect of Aldosterone on Cardiovascular Outcome in Maintenance Hemodialysis Patients

Kyu Sang Yun, Sun Ryoung Choi, Hayne C. Park, Do Hyong Kim, Aijn Cho, Juhee Kim, Jung Woo Noh, Youngki Lee, Hallym University Kangnam Sacred Heart Hospital, Seoul, Republic of Korea; Hallym University Dongtan Sacred Heart Hospital, Gyeonggi, Republic of Korea.

Background: Patients with end-stage kidney disease have an increased risk of cardiovascular (CV) events and left ventricular diastolic dysfunction (LVDD) is known to contribute to high occurrence of CV mortality. Although high serum aldosterone level is involved in the development of CV complications in general population, this association is unclear in patients undergoing hemodialysis (HD). We aimed to determine the impact of serum aldosterone on LVDD and CV mortality among HD patients.

Methods: We performed a prospective cohort study of maintenance HD patients without CV disease. Patients were divided into two groups according to the median level of serum aldosterone. All patients underwent echocardiography to evaluate diastolic dysfunction. Proportions of LVDD and CV mortality were compared between high and low aldosterone groups.

Results: We enrolled a total of 60 adult patients (mean age 57.9±12.1 years, male 30.0%). Low aldosterone group had an increased left ventricular diastolic dimension compared with high aldosterone group (52.2±8.4 vs. 30.3±5.2 mm, p=0.033). The E/e' ratio and the proportion of LVDD were significantly higher in the low aldosterone group than the high aldosterone group. Multivariate logistic regression revealed that low log-aldosterone (odds ratio (OR) 0.403; 95% confidence interval (CI) 0.180-0.862) and large left atrial dimension (OR 1.308; 95% CI 1.144-1.536) were independent risk factors for LVDD. During the mean follow-up period of 5.2 years, the cumulative incidence rates of CV mortality were significantly higher in low aldosterone group (log-rank test, p<0.027). In addition, cox regression analysis demonstrated that low serum aldosterone was an independent predictor of CV mortality in HD patients (hazard ratio 0.505; 95% CI 0.294-0.869, p=0.014).

Conclusions: Low serum aldosterone was not only associated with LVDD but also an independent predictor of CV mortality among HD patients.

Funding: Clinical Revenue Support
PO1037
Variations in the Thrombin Generation Profile and Clotting Factor Levels in the Patients Undergoing Maintenance Hemodialysis
Fakhra Siddiqui, Emily Bontecoe, Debra Hoppensteal, 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 their routine 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 compiled. Correlation analysis between peak thrombin and coagulation factors was carried out by using GraphPad Prism software.

Results: CKD-V 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 nM vs 168.3 nM) and AUC (589.8 nM*min vs 815.7 nM*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 exhibited increased levels of peak thrombin values which correlated with relatively higher levels of clotting factors suggesting a decreased activation of ETP. These studies indicated that a 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.

PO1038
Physical Activity and Mortality in Adults Undergoing Hemodialysis: A DIET-HD Cohort Study
Amelie Bernier-Jean,1 2 Germaine Wong,1 2 Valeria M. Saglimbene,3 6 Marcella Ruoso,1 Suetonia Palmer,1 6 Patrizia Natale,3 6 Vanessa Garcia-Larsen,3 6 David W. Johnson,1 7 Marcello Tonelli,1 7 Jonathan C. Craig,1 5 Giovanni F. Strippoli,1 3 School of Public Health, Faculty of Medicine and Health Sciences, University of Sydney, Sydney, NSW, Australia; 4Centre for Kidney Research, The Children’s Hospital at Westmead, Westmead, NSW, Australia; 5Diaverum Medical-Scientific Office, Diaverum, Lund, Sweden; 6Department of Medicine, University of Otago, Christchurch, New Zealand; 7Department of Emergency and Organ Transplantation, University of Bari, Bari, Italy; 8Program in Human Nutrition, Department of International Health, The Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; 9Department of Nephrology, Princ. Alexander Hospital, Brisbane, QLD, Australia; 10Australasian Kidney Trials Network, University of Queensland, Brisbane, QLD, Australia; 11University of Calgary, Calgary, AB, Canada; 12College of Medicine and Public Health, Flinders University, Adelaide, SA, Australia.

Background: People receiving maintenance hemodialysis (HD) are at higher risk of cardiovascular disease (CVD) and death. Regular exercise training reduces CVD mortality in people with coronary heart disease, but the potential survival benefits for adults undergoing HD are unknown. We assessed the association between self-reported physical activity (PA) and mortality in a very large cohort of people receiving HD.

Methods: DIET-HD is a prospective, multinational study of adults undergoing HD in Europe and South America. We classified participants as sedentary, exercises up to once a week (‘occasional PA’), or exercises twice a week or more (‘frequent PA’), using a self-reported question. We balanced the baseline characteristics, including socio-demographic factors, comorbidities, blood chemistry and dietary intake, across the PA groups using propensity scores. We conducted weighted Cox proportional hazards models with double robust estimation to assess the association between PA and mortality.

Results: Of the 8043 participants initially included in the DIET-HD study, 6147 (76%) had information on PA. 1226 (20%) exercised frequently, 1981 (32%) occasionally and 2940 (48%) were sedentary. During a median follow-up of 3.82 years (19 677 person-years), 2337 (38%) deaths occurred, of which 1050 (45%) were from CVD causes. After propensity score-weighting and adjustment for potential confounders, PA was associated with a lower risk of all-cause mortality, CVD mortality and non-CVD mortality (Table). We observed a dose-dependent effect of PA for CVD death.

Conclusions: Regular PA is associated with a lower risk of CVD mortality in adults receiving HD. Until randomized control trials assess the effect of PA on mortality in HD, it should be considered as part of the clinical management of HD patients.

Funding: Government Support - Non-U.S.
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 ≥18months, and a history of diabetes mellitus. Demographic characteristics, hemodialysis patterns, and overall survival were analyzed between the groups.

Results: The study included 8,955 patients (750 OL-HDF, 8,205 conventional HD) with a median follow-up of 2.58 (interquartile range 0.50–4.66) years. The mean age was younger and more male genders, and the dialysis vintage was slightly longer in patients with OL-HDF group compared with these 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 0.659, 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


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 471 HD patients who were tested for 11 SNVs in FOXO3, IGFBP3, Fabp1, PCSK9, ANGPLT6, and ANGPLT8 genes using HRM analysis and TaqMan assays. FOXO3, IGFBP3, L-FABP, PCSK9, ANGPLT6, and ANGPLT8 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 ANGPLT8 rs737337 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). rs737337 CC genotype was in particular a risk factor for cardiac (2e-4; 5.5–15.1; 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). ANGPLT8 rs737337 was also associated with an increased risk of diabetic nephropathy (OR 1.89; 95% CI 1.1–2.9; p = 0.02). Plasma ANGPLT8 levels were increased in patients diagnosed with CAD (p = 0.028). Carriers of IGFBP3 rs3110697 variant A allele had increased risk of cardiovascular mortality (HR 1.3; 95% CI 1.1–1.6; p = 0.02, adjusted pNS). 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 FOXP3 rs4946936 CT genotype had increased risk of cardiac death (HR 1.6; 95% CI 1.1–2.4; p = 0.03, adjusted pNS), whereas FOXO3 rs2802292 TT genotype was associated with decreased risk of vascular mortality (HR 0.4; 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: ANGPLT8 rs737337, IGFBP3 rs3110697, FOXP3 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-Quarter Change with Mortality in Maintenance Hemodialysis Patients

Takeshi Miyagi,1 Cachet Wenziger,1 Jui-Ting Hsiung,1 Yoko Narasaki,1 Yoshikazu Miyasato,1 Hiroshi Kimura,1 Kunitoshi Iseki,2 Ekamol Tantisattamo,1 Connie Rhee,1 Elani Streja,1 Kamyar Kalantar-Zadeh,3 ‘Harold Simmons Center for Kidney Disease Research and Epidemiology, Orange, CA; 2 Ryukyu Daigaku Igakubu Daigakuin Igaku Kenkyuka, Nakagami-gun, Japan.

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]/28. 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–<8.6, 8.6–<9.0, 9.0–<9.2, 9.3–<9.5, 9.5–<9.8. We estimated mortality rate 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 showed that patients with the lowest calculated SOsm had the highest hazard ratio after fully adjusted (Figure A). We observed a U-shaped association between all-cause mortality and per quarter change in calculated SOsm such that SOsm change levels ≥8.0 mOsm/Kg were 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) are collectively the fastest growing racial minorities in the US. While certain Asian subgroups and NHOPIs have a high prevalence of kidney disease risk factors, there are sparse data
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 treatment modality. A 3-months baseline period was defined as months 4 to 6 after hemodialysis initiation, all-cause mortality was noted during follow-up. Only patients who survived baseline were included. Censoring events were renal transplantation, modality change, or death. Patients were divided into 4 quartiles according to percentile rank of their comorbidity index (Group1: 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 death. Average annual mortality rates and survival using Log rank analysis corresponded to the sum of scores assigned to each factor. Patients were divided into 4 groups according to percentile rank of their comorbidity index (Group1: 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: Compared with White incident ESRD patients residing in the Mainland US, Asians and NHOPIs in the Mainland US had lower mortality risk: HRs (95%CI) were 0.47 (0.46–0.50) for Asians and 0.70 (0.67–0.73) for NHOPIs, 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. 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

PO1044
Association of All-Cause Mortality with Pre-Hemodialysis Pulse Pressure in Chronic Hemodialysis Patients
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Background: Pulse pressure (PP) reports cardiac and vascular conditions, where high PP values are associated with atrial fibrillation, arterial insufficiency, low arterial stiffness, low PP values may be associated with aortic valve stenosis, cardiac insufficiency. However, the association of pre-hemodialysis (pre-HD) PP with mortality among hemodialysis patients is not well understood. In this study, we aim to explore the extent to which PP is associated with mortality.

Methods: We analyzed pre-HD PP (calculated as pre-HD SBP minus pre-HD DBP) between 1/2001 and 12/2012 in hemodialysis patients treated in U.S. Fresenius Medical Care facilities. A 3-months baseline period was defined as months 4 to 6 after hemodialysis initiation, all-cause mortality was noted during follow-up. Only patients who survived baseline were included. Censoring events were renal transplantation, modality change, or study end. We built Cox proportional hazards models with spline terms, allowing us to model nonlinear effects of pre-HD PP as a continuous variable and its relationship with all-cause mortality.

Results: We included 152,625 patients. Mean age was 60.8 years, 59% were white and 56% were male. During a median follow-up of 26.0 months 40.4% patients died. We found that for patients with pre-HD PP between 49.2 mmHg and 74.7 mmHg, were associated with better survival. In contrast, a PP below 49.2 mmHg and above 74.7 mmHg were associated with higher mortality. Similar nonlinear effects are seen in SBP for a given pre-HD PP value (see Fig. 1). Figure 1: Association between pre-HD pulse pressure and all-cause mortality. HRs (solid line) and 95% CIs (dashed lines) of pre-HD pulse pressure. The tick marks on the x-axis represents individual patients.

Conclusions: The association of pre-HD PP with mortality is nonlinear, a better understanding will provide further insights into disentangling the associated mediators affecting its dynamics. Our findings may aid risk stratification.

Funding: Commercial Support - Fresenius Medical Care North America

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 (Group1: 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.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Conclusions: This new scoring system appears to be easily established at our clinics and may constitute a good predictor for all-cause mortality in our HD population.

The mortality parameters in the study groups

**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 for 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 finding suggests 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 choices. We assessed whether ESRD QIP scores and payment reductions aligned with facilities’ star ratings and with t-tests comparing mean QIP Total Performance Scores (TPS) among adjacent PR and star rating levels.

Methods: Payment year (PY) 2020 QIP scores and payment reductions (PR) and CY 2018 star ratings (1-5 stars) were obtained from DFC public data files. Comparisons between the two programs were assessed with cross-tabulations of PR categories and star ratings and with t-tests comparing mean QIP Total Performance Scores (TPS) among adjacent PR and star rating levels.

Results: Facilities with higher PY 2020 QIP scores tended to receive higher star ratings. 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 the ratings 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=PMOs)**

<table>
<thead>
<tr>
<th>QIP PR</th>
<th>Facility %</th>
<th>Mean TPS (SD)</th>
<th>Star Rating</th>
<th>Facility %</th>
<th>Mean TPS (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5%</td>
<td>39.4%</td>
<td>76.8 (7.9)</td>
<td>5%</td>
<td>21.6%</td>
<td>76.6 (7.5)</td>
</tr>
<tr>
<td>0%</td>
<td>24.0%</td>
<td>53.8 (12.8)</td>
<td>0%</td>
<td>29.0%</td>
<td>63.7 (9.6)</td>
</tr>
<tr>
<td>1%</td>
<td>12.0%</td>
<td>42.3 (12.8)</td>
<td>1%</td>
<td>33.6%</td>
<td>54.3 (10.3)</td>
</tr>
<tr>
<td>5%</td>
<td>4.3%</td>
<td>34.6 (14.6)</td>
<td>5%</td>
<td>7.9%</td>
<td>38.9 (17.3)</td>
</tr>
<tr>
<td>2%</td>
<td>1.3%</td>
<td>25.5 (15.7)</td>
<td>2%</td>
<td>2.6%</td>
<td>36 (13.0)</td>
</tr>
</tbody>
</table>

*Significant difference by t-test with PR≥0.05 vs. adjacent category.

**PO1049**

Comparison of 5-Year Survival Rate Between Hemodialysis and Peritoneal Dialysis Patients: A Prospective Cohort Study with Propensity Score Matching

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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 compared with HD group 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 = 0.041), 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 (Mg) is known to be positively associated with serum Mg levels in hemodialysis (HD) patients (pts). We aimed to study the associations between different Mg levels and mortality in HD pts.

Methods: We conducted a retrospective cohort study to examined the associations of different Mg levels (1.0, 1.5, or 2.0 mEq/L) and all-cause mortality. In-center HD pts treated in KfH and MONDO with constant Mg 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, catheter, and vintage) to create 4 matching groups: 1)Mg 1.0 versus 1.5 mEq/L (KfH and MONDO), 2)Mg 1.5 versus 2.0 mEq/L (only KfH), 3)1.0 versus 2.0 mEq/L (only KfH). The associations between different Mg levels and mortality after matching were evaluated with Cox proportional hazards models, Kaplan Meier survival curves, and the Log Rank test, respectively.

Results: We studied 32,117 pts from KfH [69 years, 64% males, 42% diabetics, 48% catheter; 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

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

Underline represents presenting author.
(16%), DMg 1.0: 12,508 (82%) and DMg 1.5: 222 (1%). Propensity score-matching created well-balanced cohorts with DMg of 1.0 v.s. 1.5 (KfH and MONDO), DMg 1.5 v.s. 2.0 and 1.0 v.s. 2.0 (KH), respectively. Survival analysis show that DMg 1.5 is not statistically associated with survival benefits compared to 1.0 in both data sets (Table 1, Figure 1 a, d). In addition, compared to both DMg 1.0 and 1.5, we do not observe a survival benefit of DMg 2.0 in KfH's data (Table 1, Figure 1b, c).

Conclusions: Increased DMg was not associated with a survival benefit in either the KfH or MONDO datasets. One of the limitations is the lack of detailed dialysate information. Further studies directly addressing the association between serum Mg and dialysate prescriptions.

PO1052

Electrolyte Changes in Contemporary Hemodialysis: An Analysis of the Monitoring in Dialysis (MID) Study
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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 pre-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 4.9mEq/L ±0.3, 0.7mEq/L±0.1, and 0.4g/dL±0.03, respectively), and potassium, magnesium, and phosphorus decreased immediately post-HD (mean -1.2mEq/L±0.1, -0.3mEq/L±0.03, and -3.0mg/dL±0.2, respectively). Hypokalemia and hyperphosphatemia 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 hyperphosphatemia 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.

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

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Metabolomic Analysis Fails to Identify Uremic Solutes 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, and lower serum albumin, body cell mass index (BCMI), lean tissue index, fat tissue index (FTI), femoral neck BMD, and right distal mid-third radius BMD.

Results: Of 593 uremic solutes analyzed using a metabolomics platform (Metabolon Inc.), 5 predominate (sodium, potassium, bicarbonate, calcium, and phosphate). plasma and UF were analyzed using a metabolomics platform (Metabolon Inc.). Solutes were first identified as uremic based on the finding of higher normal levels in all 36 HD patients and 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.

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

Characteristics

A.

B.

Predicted Change in Serum in Sodium

Predicted Change in Serum in Calcium

Average UF Peak Area Ratio of Itch to No Itch for each Solute

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), femoral spine, femoral neck, and right distal mid-third radius 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. 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.

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 (O2Sat), 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 O2Sat, interpreted as arterial O2Sat (SaO2) for those with a fistula or graft and as central venous oxygen saturation (SvO2) for those with a central venous catheter. For sessions with SvO2, we also calculated estimated upper body blood flow (eUBBF).

We extracted each parameter every 30 minutes through each treatment. We compared

The study was supported by Fresenius Medical Care Global Medical Affairs, Waltham, MA.
variables dependent on whether IDH occurred in the subsequent 30 minutes. Separate linear mixed models with session as random effect, with 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) and 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 (Fig1B). 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 hypotensive-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 (8) ( Fresenius Medical Care, Bad Homburg, Germany). Blood pressure was measured with OMRON monitors.

**Results:** The mean age of patients was 64 ± 13 years, mean dialysis vintage 63 (1-352) months, 61% were men, all patients had arteriovenous fistula as vascular access. ScvO2-mean (42%) patients were fluid overload (FO) with > 1.1 L 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 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±4.6 ml/kg/h. Patients with low initial PRR were more likely than patients with high initial PRR 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 had a 10 mmHg associated with symptoms. IDH-prone was defined as having >20% of treatments with IDH. Uni- 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 means±SD or aOR; 95% CI.

**Background:** Extracellular to Intracellular Water Ration in Hemodialysis Patients

**Results:** We studied 2,637 patients (61±15 yrs, 57% male, 51% white) with 184,044 total treatments, interdialytic weight gain (IDWG) 2.1±4.6 kg, and UFR 9.5±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±1.1 ± 10m, 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 multinobritdrinity 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 coagulation test results that had HA. Mean PRA was 3.3 +/- 7.7 ng/ml/hr & serum aldo was 2.9 +/- 1.6 ng/dL. All pts had failed low temperature dialysate, 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 from 1 & 6 months post-FC (Table 1). No changes occurred in UF volume. 4 pts have 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>
<th>Time Pre-FC</th>
<th>Mean ± SD</th>
<th>Post-FC</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mmHg)</td>
<td>117.9 (20.5)</td>
<td>131.1 (18.6)</td>
<td>130.1 (19.5)</td>
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<tr>
<td>DBP (mmHg)</td>
<td>64.9 (12.6)</td>
<td>71.7 (16.0)</td>
<td>70.6 (16.0)</td>
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<td>UF (ml)</td>
<td>1060 (14.5)</td>
<td>1225.1 (19.7)</td>
<td>1159.7 (12.2)</td>
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<tr>
<td>Pre-S-BP</td>
<td>58.0 (11.1)</td>
<td>65.2 (16.0)</td>
<td>60.4 (11.0)</td>
</tr>
<tr>
<td>Pre-D-BP</td>
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<td>1.0 (4.0)</td>
<td>1.0 (4.0)</td>
</tr>
<tr>
<td>Pre-UF (ml)</td>
<td>5.4 (9.3)</td>
<td>3.2 (3.1)</td>
<td>3.2 (3.2)</td>
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</table>

**PO1060**

**Feasibility and Benefits of Hemodialyzer Filtration of Contaminated Water in Poor Rural Communities in Ghana**

Friedrich K. Port,1,4 Jochen G. Raimann,1 Joseph M. Boaheng,1 Philip K. Narh,1 Seth Johnson,1,2 Linda L. Donald,2 Hongbin Zhang,3 Nathan W. Levin,1,3 Easy Water for Everyone, New York, NY; 2 Renal Research Institute, New York, NY; 3 City University of New York, New York, NY; 4 University of Michigan, Ann Arbor, MI; 5 Icahn School of Medicine at Mount Sinai, New York, NY.

**Background:** Contaminated water supplies for drinking water is 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 diarrhea, 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 diarrhea and death in 4 “study” villages that have access to river water. River water was pumped weekly into an elevated holding tank to be drawn by households of 8 villages that have no electricity during February to November 2018. In 3 “control” villages, the polluted water was not treated during the same 10 months. We calculated the monthly rate of diarrhea per village per month. 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.

**Results:** [1] Monthly rates of diarrhea in the study villages decreased from 18 to 5 per 1000 person-years 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 simple solution in entire rural villages in the absence of electricity.

The continuous function over >11 months indicates low cost of the device over time. The reduction in diarrhea 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 suggests wider application to other needy villages.

**Funding:** Private Foundation Support

**PO1061**

**Combining a Heparin-Grafted Dialyzer with a Citrate-Enriched Dialysate Offers Acceptable Dialysis Adequacy Avoiding Systemic Anticoagulation: Results of the Randomized Noninferiority Evoct Study**

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**Background:** The combined use of a heparin-grafted membrane with a citrate-enriched dialysate is a hemodialysis (HD) strategy with low circuit clotting 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 unfractonated heparin and bicarbonate-based dialysate (“evoceg”). 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 evoceg and 310 evohep sessions. Mean spKt/Vurea was 1.46±0.23 for evoceg and 1.50±0.24 for evohep sessions (p=0.06). The mean of the paired difference in 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). URD reduction rate (RR) was 71.5±5.5% vs 72.1±5.7% and time spent on reperfusion RR 37.4±6.8% vs 37.8±8.8% for evoceg and evohep sessions. Processed blood volume was 75.4±3L vs 75.8±5L and online Kt was 47.3±4L vs 48.3±4L for all evoceg and evohep sessions. Circuit thrombosis leading to premature treatment end occurred in 13/307 (4.2%) of evoceg sessions (n=6), but in none of the evohep sessions (p=0.0002), with a median 36(20-46)min treatment time shortening without impact on effective treatment times overall (236±12 vs 238±4min for evoceg vs retransfusion). Retransfusion failure occurred in 3/307 (0.98%) of evoceg sessions and none of the evohep sessions (p=0.25).

**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 evoceg 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 ≥18 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. 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 matched sampling and matching ratio of (1) duration of follow-up (at least 21 months of use in 9 villages.

**Results:**[1] Rates of diarrhea in the study villages decreased from 18 to 5 per 1000 person-years 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:** Cinacalcet use was not associated with an increased risk of GI bleeding among dialysis patients from DOPPS, an observational longitudinal data system of a random sample of patients from dialysis facilities in more than 20 countries.

**Funding:** Commercial Support - Amgen

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

Underline represents presenting author.

361
PO1063
Medium Cut-Off Dialyzer Improves Erythropoiesis-Stimulating Agent Resistance in a Hepcidin-Independent Manner in Maintenance Hemodialysis Patients
Jeong-Hoon Lim, Yong-Jin Kim, Hye-Yeon Jung, Ji-Young Choi, Sun-Hee Park, Chan-Duck Kim, Yong-Lim Kim, Jang-Hee Cho. Kyungpook National University Hospital, Daegu, Republic of Korea.

Background: The response to erythropoiesis stimulating agents (ESAs) is affected by inflammation linked 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, erythropoietin, 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 admission in dialysis patients with Medicare fee-for-service coverage, mostly because of increasing incidence of observation status admissions and ED visits.

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 51 age years, 45% males) was referred to estimate vitamin K status in healthy subjects. Vascular calcification was estimated with coronary artery calcium (CAC, n=237) and aortic valve calcium (AVC, n=223) among ESRD patients undergoing cardiac computed tomography scan.

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. 1 SD increase of dp-ucMGP associated with increased all-cause mortality (1.19 (1.01-1.46)), 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-uc-MGP levels were not associated with quantified calcification suggested by CAC (p=0.11, R2=0.30) and AVC (p=0.84, R2=0.12).

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.

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
Lu Dai,1 Longkai Li,1,2 Abdul Rashid T. Qureshi,1 Jonaz Ripsved,3,4 Torkel B. Brismar,1,4 Olof Heimburger,1 Peter F. Barany,1 Bengt Lindholm,1 Leon J. Schurgers,1 Peter Stenvinkel.1 1Division of Renal Medicine and Baxter Novum, Department of Clinical Science, Intervention and Technology, Karolinska Institutet, Stockholm, Sweden; 2Department of Nephrology, First Affiliated Hospital of Dalian Medical University, Dalian, China; 3Division of Medical Imaging and Technology, Department of Clinical Science, Intervention and Technology, Karolinska Institutet, Stockholm, Sweden; 4Department of Radiology, Karolinska University Hospital, Huddinge, Stockholm, Sweden; 5Department of Biochemistry, Cardiovascular Research School Maastricht, Maastricht University, Maastricht, Netherlands.

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 51 age years, 45% males) was referred to estimate vitamin K status in healthy subjects. Vascular calcification was estimated with coronary artery calcium (CAC, n=237) and aortic valve calcium (AVC, n=223) among ESRD patients undergoing cardiac computed tomography scan.

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. 1 SD increase of dp-ucMGP associated with increased all-cause mortality (1.19 (1.01-1.46)), 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-uc-MGP levels were not associated with quantified calcification suggested by CAC (p=0.11, R2=0.30) and AVC (p=0.84, R2=0.12).

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 Ardissino,1 Valentine Capone,1 Elisabetta Margiotta,2 Isabella Cropanese,1 Francesca Raffiotta,2 Giovanni Montini,1 Piergiorgio Messa,1 Pediatric Nephrology, Dialysis and Transplantation, Fondazione IRCCS Ca’ Granda, Ospedale Maggiore Policlinico, Milano, Italy; 2Nephrology, 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/100 g) 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 transplantation, COVID-19 infection or to documented non-adherence to the protocol. Observed mean (sd) DP were 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) (p=0.01) 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 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
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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 different significantly. 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 in 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 Ruffin,1 Lawrence Park,3 Michael M. Dagher,1 Christina M. Wyatt,2 Vance Fowler,2,3 Duke University Hospital, Durham, NC; 2Duke Clinical Research Institute, Durham, NC; 3Duke 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/quartiles 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,3 Martha L. Gruber,3 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 woman (ESRD secondary to type II diabetes and proliferative diabetic retinopathy) had a history of elevated intraocular pressure in both eyes with normal visual fields. She was referred to our unit for further management. Dioptric examination showed no evidence of glaucoma. A normal IOP was measured in both eyes. The patient had no significant past medical history, and was on regular hemodialysis without any significant medications. She returned for a follow-up visit 2 weeks later, and had an increase in IOP to 27 mmHg in the left eye and 28 mmHg in the right eye. She was further evaluated in the clinic with a normal visual field and no evidence of glaucoma. She was then referred to an ophthalmologist for further evaluation.

Discussion: The patient was seen by an ophthalmologist, who determined that the IOP was normal and there was no evidence of glaucoma. The patient was then referred to a glaucoma specialist for further evaluation.

PO1060
Hemodialysis-Associated Increased Intraocular Pressure: A Vision-Threatening Complication
Chad Y. Lewis,1 Nikhil Batra,2 Eric A. Steffen,3 Martha L. Gruber,3 Dartmouth College Geisel School of Medicine, Hanover, NH; 2Dartmouth-Hitchcock Medical Center, Lebanon, NH.

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Discussion: The patient was seen by an ophthalmologist, who determined that the IOP was normal and there was no evidence of glaucoma. The patient was then referred to a glaucoma specialist for further evaluation.
during HD. One proposed mechanism for increased IOP is as plasma urea is reduced, the aqueous humor lags, becoming hypertonic relative to plasma. The choroid may also thicken, obstructing outflow. We increased diuresis sodium and reduced HD time and dialysate flow. Other strategies include infusion mannitol or hyperosmolar glucose, ultrafiltration to increase plasma oncotic 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>Date</th>
<th>Pre-HD IOP (mm Hg)</th>
<th>IOP 3 hrs, after HD (mm Hg)</th>
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<th>% in IOP (mm Hg)</th>
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<td>122</td>
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<td>130/120</td>
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<td>36.6</td>
</tr>
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<td>5/22/20</td>
<td>117/105</td>
<td>130/96</td>
<td>2.6</td>
<td>13%</td>
</tr>
</tbody>
</table>

**Discussion:** 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 grading (VExUS) allow objective assessment of volume status using portal 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 exertions, 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 ~3cm 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.

**PO1070**

**Point-of-Care Ultrasonography to Assess Venous Congestion and Guide Ultrafiltration: Another String to Our Bow?**

Saquib Mahmud, Abhilash Koratala. Medical College of Wisconsin, Milwaukee, WI

**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 grading (VExUS) allow objective assessment of volume status using portal 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.

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**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?**

Claudia Torino,1 Rocco Tripepi,2 Maurizio Postorino,1 Giovanni Tripepi,2 Charalampos Loutradis,3 Pantelis Sarafidis,3 Francesca Mallamaci,1,2 Carmine Zoccali.1 1Nephrology Unit, GOM Reggio Calabria, Reggio Calabria, Italy; 2IFC-CNR, Reggio Calabria, Italy; 3Aristotleio Panepistimio Thessalonikes, Thessaloniki, Greece.

**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; 5-15; 16-30; >30 US-BL; 8-LIS score: <10; 10-20; 21-50; >50 US-BL). The prediction power of these scores was assessed by the explained variance ($R^2$).

**Results:** The 28-LIS score and the 8-LIS score were highly inter-related (p=0.03, 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. The $R^2$ of the 28-LIS score for death was 4.1% and that for CV events 4.6%. The corresponding $R^2$ 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 $R^2$ of the model including the 28-LIS score (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 C. 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 measurement of facility performance and to inform patient care.

**PO1075 Implication of Trends in Timing of Dialysis Initiation on Population Incidence of ESRD**

Chyi-yuan Hsu,1 Rishi V. Parikh,2 Leonid Pravoverov,2 Sijie Zheng,3 David T. Glidden,1 Thida C. Tan,1 Alan S. Go,1-3 University of California San Francisco, San Francisco, CA;1 Kaiser 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 1.163-1.481]), 11% (aOR 1.11 [1.03 to 1.20]) and 7% (aOR 1.07 [1.01 to 1.14]) respectively, adjusting for gender, age, 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.

**Discussion:** 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 AAKI initiative could potentially be achieved by changes in the timing of initiation of chronic dialysis.

**PO1076 The Impact of Serum Albumin Levels on Excess Hospital Spending**

Linda Ficociello,1 Melissa M. Rosen,2 Claudy Mullon,1 Robert J. Kossmann,2 Michael S. Anger,1 Fresenius Medical Care Renal Therapies Group, Waltham, MA;1 Fresenius Medical Care North America, Waltham, MA.

**Background:** National Kidney Foundation KDOQI guidelines recommend that hemodialysis patients have a 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 (MCO) 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 3.0-3.4 g/dL, sA of 3.0-3.4 g/dL, and sA ≤3.0 g/dL have 3.98, 7.65, and 7.8 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 reduced 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 aS level may result in excess healthcare spending of $5,662 for aS of 3.5-3.99 g/dL, $10,769 for aS of 3.0-3.49, and $10,980 for aS 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 $5,602, $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

POI077
A Pilot Randomized Control 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 Maouissa Donald,1 Brenda Hemmenga.1 University of Calgary Cumming School of Medicine, Calgary, AB, Canada; 2University of Alberta Faculty of Medicine and Dentistry, Edmonton, AB, Canada.

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 CPM-Performance Counts, participants were separated into 3 categories: sedentary, fairly active, or active if they walked more than 5,000, 5,000 to 10,000, or >10,000 steps per day respectively.

Results: Fifty-six patients were included in this analysis (54.12% years, 71% male, 66% black, 28.6% had diabetes and 23.2% CHF, dialysis vintage 5.8±5.8 years and body mass index of 28.0±7.0 kg/m²). Participants walked an average of 6,470±4,617 steps per day, median of 5,513 [IQR 3,043-8,268] steps/day. Of the 56 participants, 45% (n=25) were sedentary, 39% (n=22) were fairly active, and 16% (n=9) were active (fig.1).

Conclusions: This pilot project, still ongoing study enrolled HD patients from 4 clinics in NYC beginning in May 2018 and followed them up to 1 year. Patients a18 years, HD a3 months, able to walk, owning a smartphone, mobile tablet or PC were enrolled. They were provided with a wrist-based tracking device (Fitbit® Charge 2). We present baseline characteristics and PA levels of the first 7 days of wear. Based on their average daily step counts, participants were separated into 3 categories:sedentary, fairly active, or active if they walked less than 5,000, 5,000 to 10,000, or >10,000 steps, respectively.

POI078
Coffee and Headache in Hemodialysis Patients: The CoffeeHD Trial

Mabel Aoua,1,2 Najla Hilal,1 Chadia H. Beaini,1 Ghassan Sletlflay,1 Joseph Hajal,1 Celine El boueri,2 Dania Chelala,1 Saint-Joseph University, Beirut, Lebanon; Saint-George Hospital, Ajaltoun, Lebanon; 3Université Saint-Esprit de Kaslik, Jounieh, Lebanon; 4Bellevue 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/kg/hr. 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 (34% vs 37% respectively, p=0.522), nor the incidence of hypotension (27% 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.
PO1080
Feasibility and Acceptability of Symptom Monitoring with Feedback Trial (SWIFT) for Adults on Hemodialysis: A Pilot ANZDATA Registry-Based Cluster Randomized Trial
Rachel L. Morton,1 Kathryn Dansie,2 Paul N. Bennett,3 Emily Duncanson,2 Andrea R. Vescelius,1 Shilpa Jesudason,1 Karen K. Shah,1 Chris Brown,1 Sueotton Palmer,1 Fergus J. Caskey,1 Stephen P. McDonald,1,2 SWIFT NHMRC Clinical Trials Centre, Camperdown, NSW, Australia; 3 Australia and New Zealand Dialysis and Transplant Registry, Adelaide, SA, Australia; 4 Satellite HealthCare, San Jose, CA; 5 Princess Alexandra Hospital, Woolloongabba, QLD, Australia; 6 Royal Adelaide Hospital, Adelaide, SA, Australia; 7 University of Otago Christchurch, Christchurch, New Zealand; 8 University 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; 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 verify correct patients from ANZDATA, with a link 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.

PO1081
Physiological Pre-Dialytic Changes Could Mediate the Effects of Extreme Heat Events on Hospital Admission Risk in Hemodialysis Patients
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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, although 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 pressure (SBP) and interdialytic weight gain (IDWG) as mediators. The Prepare RCT integrated the Quintet Recruitment Intervention (QRI) – a complex

PO1082
Frequency, Risks, and Outcomes of Sepsis Hospitalizations in the ESKD Population in the United States
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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 <40; HR 1.30, 95% CI 1.24-1.36), dialysis 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 black 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 8.87-9.13).

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.

PO1083
Optimising Recruitment in Prepare for Kidney Care: A Clinical Trial Comparing Preparation for Dialysis vs. Responsive Management
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Background: Randomised Controlled Trials (RCTs) are core to evidence-based practice, but often close prematurely or are not attempted for fear of recruitment issues. Prepare for Kidney Care (‘Prepare’) randomises adults aged 80+ to 65+ with comorbidities to prepare for Renal Dialysis or Responsive Management—a form of conservative care. An RCT of this nature has never been attempted, with concerns about recruitment feasibility. The Prepare RCT integrated the Quintet Recruitment Intervention (QRI) – a complex
PO1084
Time Course of Tissue Sodium Flux in Maintenance Hemodialysis (MHD) Patients
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Background: Recent 2Na-MRI studies report that sodium can accumulate in tissues. MHD patients have higher tissue sodium concentration ([Na+]t) than healthy counterparts, while tissue [Na+]c can be partially reduced during hemodialysis (HD). This study aimed to evaluate the magnitude of tissue [Na+]c removed during HD and the time-course for its recalibration.

Methods: Seven HD patients (57% male; 66±12 yr; BMI: 36±10 kg/m²; spKt/V: 1.4±0.3; dialysate [Na+]: 136±1.0 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+]c 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+]c was also assessed at T1, T2, and T4 by colorimetric enzymatic assays (Piccolo). Repeated measures ANOVA and the Bonferroni correction were used to calculate differences in tissue [Na+]c over time.

Results: Tissue [Na+]c was reduced at the end of HD (T2) compared to baseline (T1) in the WL (P=0.006), MG (P=0.043), 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+]c at both T3 and T4 did not differ from baseline (all P>0.05), indicating that tissue [Na+]c returned to the baseline within 24 hours after last HD. In contrast, plasma [Na+]c did not change over time (P=0.067; Figure 1F).

Conclusions: We found that tissue [Na+]c 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+]c 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 anuric, 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: DNAs 137mEq/l: systolic 152±10, diastolic 78±9, DNAs 140mEq/l: systolic 154±10, diastolic 78±9. Post-dialysis: DNAs 137mEq/l: systolic 147±2, diastolic 77±8, DNAs 140mEq/l: systolic 151±3, diastolic 76±6. 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.

Funding: Government Support - India; Government Support - Non-U.S.; Private Foundation Support

PO1086
Low Sodium Dialysate for Hemodialysis Is Associated with Lower Blood Pressure and Interdialytic Weight Gain, but Not a Lower Pre-Dialysis Serum Sodium
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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) 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 sodium concentration during dialysis, 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) in HD patients on a high NaD (145) who transitioned to a low NaD (137-138)

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 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

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
null
Use of Predictive Analytics to Inform Integrated Care Programs to Reduce Hospitalizations Among Hemodialysis Patients

**Methods:** We reviewed electronic medical records of End-Stage Renal Disease Seamless Care Organization (ESCO) enrolled patients discharged home from acute-care hospitals between Nov 2018-Oct 2019 who returned to participating dialysis units. Patients readmitted ≤3 days, died, or entered hospice ≤30 days were excluded. Time-varying propensity score (from age, dialysis vintage, modality, cause and catheter use, prior hospitalization history, albumin, sex, marital status, and race) matched Cox models were constructed comparing hazard ratios for 30-day readmission between Full- and Partial-MTM exposure groups.

**Results:** MTM was provided in 1,752 discharges (456 Partial-MTM; 1296 Full-MTM). Of those, 455 Full- and 455 Partial-MTM cases were matched 1:1. Full-MTM had 25% lower risk for 30-day readmission even when compared to discharges that received partial-MTM services (HR 0.75; 95% CI 0.58-0.98). Full-MTM process was completed ≤14 days in 81% cases (n=1054). Of those, 444 early Full-MTM were matched to 444 Partial MTM cases and demonstrated a significantly lower risk for 30-day readmissions (HR 0.74, 95% CI 0.57-0.95), primarily driving the overall results.

**Conclusions:** Full MTM process is associated with lower 30-day readmission risk compared to Partial-MTM. The results are primarily driven by MTM process completion ≤14 days of discharge. These findings support that timely physician adjudication of pharmacists’ recommendations and subsequent actions (i.e. medication changes as needed) influence the effectiveness of MTM programs to impact readmission rates.

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**PO1092**

Healthcare Staff Acceptance of Ultrafiltration Rate Recommendations Made by a Novel Feedback Controller

**Methods:** We conducted a prospective, interventional study in chronic HD patients at 3 Dialysis Clinics in Manhattan. RBV was measured with the CLiC® device. CLiC® and Fresenius 2008FT HD machine data were fed into a research laptop running the UFR Feedback Controller software. UFR recommendations (generated every 10 minutes) were evaluated by dialysis nurses who then either implemented or rejected them as they deemed clinically appropriate.

**Results:** 56 HD treatments from 14 subjects had analyzable data. Out of 1,038 UFR recommendations, 926 (89.2%) were accepted, while 112 (10.8%) were overridden. For 25 HD treatments which had at least one recommendation overridden, we analyzed the direction and magnitude of disagreement between the Controller-suggested UFR and the implemented UFR (Fig. 1). From the overridden controller recommendations, 20 implemented UFRs were greater than the respective Controller-suggested UFRs, another 70 implemented UFRs were less than 100 mL/h lower than the Controller-suggested UFRs. Together, these two categories made up 83% of all “disagreements” between the nurse and the Controller. Of the total of UFR recommendations overrides, 59.6% were due to staff preference in the absence of clinical symptoms.

**Conclusions:** There was a high proportion (~90%) of Controller-UFR 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

**PO1093**

Intradialytic Online Multicomponent Total Removed Solute Monitoring in Spent Dialysate by a Novel Miniaturized Optical Sensor

**Methods:** Ten ESKD patients (6 M, 4 F; 60.2±16.8 y.o.) on chronic HDF were enrolled into the study. For each patient 5 midweek dialysis sessions (240min; HD: N=1, Qb=200mL/min, Qd=300mL/min, 1,5m2 ; HDF: N=4, Qb=500mL/min, Qd=500mL/min, V_dial=1.5L, 1.8m and 2.2m2) were included. Spent dialysate from the drain was monitored on-line by the miniaturized sensor prototype (Optoflux Technologies OÜ, Estonia). For the reference, samples from the spent dialysate drain tube of the HD machine were taken 70, 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 measured 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±112mmol and 512±87mmol for urea (R²=0.91), 423±72mmol and 421±75mmol for UA (R²=0.92), 201±90 and 231±40mg for B2M (R²=0.951), 60±33mmol and 61.6±32mmol for IS (R²=0.951), being not statistically different for any uremic 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.

**Background:** Urea is the most commonly exploited marker of dialysis adequacy, but also other uremic retention solutes accumulate in ESKD patients. Commonly, the uremic solutes are divided into three physicochemical types with the representative markers urea, uric acid (UA); indoxyl sulfate (IS); and β-microglobulin (B2M). Instead of total dialysate collection for quantification of the amount of uremic solutes removed during dialysis, an optical on-line monitoring has been proposed. The aim of this study was to evaluate intradialytic on-line multicomponent total removed solute (TRS) monitoring in the spent dialysate by a novel miniaturized optical sensor during hemodialysis (HD) and hemodialfiltration (HDF) with different settings.

**Funding:** Commercial Support - Fresenius Medical Care Deutschland GmbH, Bad Homburg, Germany; 1cuHN School of Medicine at Mount Sinai, New York, NY.
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 dialysate.

PO1094
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 cardiopulmonary 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.

PO1095
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 as 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 was defined in 30-minute intervals. Patients who experienced IDH were classified as early- or late-onset based on whether most sessions with IDH had incidents in the first 2 hours or not. Association of early-onset IDH with clinical parameters and mortality were explored with logistic regression and Cox proportional hazard models.

Results: We studied 4,348 patients and 785,682 sessions. For definitions 1 and 2, 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 occurred in the first 2 hours in 45% and 33% of IDH sessions, respectively. IDH incidence was not associated with time into HD using definition 1; a positive association was observed using definition 2. Adjusted hazard ratios for death comparing early-onset IDH with late-onset were 1.5 and 1.7 for definitions 1 and 2. Early-onset IDH was associated with female sex, higher age and UF 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.

PO1096
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 1.08) 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=0.001) 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 ≥18 years old.

Methods: In a cohort of incident dialysis patients ≥18 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

Nephrologists’ Practices, Perspectives, and Experiences Providing Care and Treatment Education to Patients with Varying Amounts of Pre-ESRD Care: A Mixed-Methods Study

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Background: A third of patients newly diagnosed with end-stage renal disease (ESRD) in the U.S. had minimal or no pre-ESRD nephrology care and “crashed” onto dialysis. Little is known about treating nephrologists’ practices and perspectives on renal replacement therapy (RRT) information delivery and decision-making for this subset of patients at the time of their ESRD diagnosis and RRT initiation.

Methods: A convergent mixed methods study design was used, and semi-structured interviews were conducted with nephrologists in Philadelphia and the surrounding region. Participants were queried on general practices and perspectives on RRT information delivery and decision-making practices for patients with varying amounts of pre-ESRD nephrology care and also queried on their experiences providing care to patients recently diagnosed with ESRD. Applied thematic analysis was used to analyze the qualitative responses and all quantitative data were fully described.

Results: A total of 15 nephrologists participated. Participants had been practicing nephrology for a median of 7 years and a third of participants were trainees at the time of the interview (i.e., nephrology fellows). The qualitative analyses revealed 12 themes, including: patients’ clinical presentation guides RRT initiation, RRT initiation often occurs urgently irrespective of pre-ESRD care, utilize direct communication style during diagnosis, reliance on other providers for patient education, challenges to providing patient education, desire improved access to educational resources, and desire engaging patients in shared decision-making for RRT selection and initiation. Notably, participants identified patient- and institutional-level barriers inhibiting their ability to provide quality care and education to patients presenting with ESRD diagnosis for RRT initiation.

Conclusions: Nephrologists face significant challenges in providing quality care to patients with varying amounts of pre-ESRD nephrology care. Increasing availability of nephrology-trained interdisciplinary staff in outpatient chronic kidney disease clinics and hospital settings to assist providers with the logistics associated with RRT education and initiation has the potential to improve care for patients newly diagnosed with ESRD.

Funding: NIDDK Support
POI100

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: 110 (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 hemodialfiltration. 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 1.3; 95% CI 1.0-1.6), internal jugular catheters (OR 3.3; 95% CI 1.0-1.9), and no history of hypertension (OR 4.7; 95% CI 1.4-16).

Conclusions: This study suggests a high rate 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.

POI101

Gram-Negative Bacteraemia in Haemodialysis Patients: Pathogen and Source Identification

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Background: Gram-negative bacteremia (GNB) in haemodialysis (HD) patients is associated with significant morbidity and mortality. Efforts to reduce rates of bacteraemia 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: On all confirmed bacteraemia 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 bacteraemias 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%).

Conclusions: E. coli bacteraemias remain a major cause of GNB in our HD population. Dialysis lines are a significant risk factor for bacteraemia, 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 1: Gram negative isolates from blood cultures

POI102

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 impendaneometry and quality of life KDOQOL-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 undermined. 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 (Q) 622.3; Xc (Q) 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 KDOQOL-SF 36 revealed scores greater than 60 for CKD symptoms and effects, with an SF-12 Physical Health Composite 83.6 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.

POI103

Feasibility of and Adherence to Using a Wrist-Based Activity Tracker in Hemodialysis Patients

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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 univariate 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
PO1104

Routine Measured Cardiac Troponin I and NT-ProBNP as Predictors of Mortality in Japanese Hemodialysis Patients: The Dialysis Outcomes and Practice Patterns Study

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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 cardiac disease. However, as the prevalence of atherosclerosis influencing lipid metabolism and exerting antioxidant and anti-inflammatory activities. Particularly relevant for HD patients is BB dialyzability. In non-dialysis patients, the risk of cardiovascular-cerebrovascular event. Use of high-dose statins has failed to identify hemodialysis patients with high risk of future cardiovascular events in hemodialysis patients. This study aimed to evaluate the potential of lipids to assess risk of future cardiovascular outcomes

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 hemocytes were stored at the baseline. Lipidomic analyses were performed on an Exion LC-system coupled with a QTRAP 6500 PLUS system. Principal component analysis and orthogonal project to late structures discriminant analysis, and was used to analyze the differences between patients in with(out)adverse cardiovascular-cerebrovascular outcome groups.

Results: A total of 45 plasma samples and 117 hemocytes samples were collected. 9 plasma samples and 28 hemocytes samples were from patients with cardiovascular-cerebrovascular events. 53% of patients were detected in plasma, 237% of patients were detected in erythrocytes. Compared with the patients without cardiovascular-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 38:9 (22:5), LPS 18:0, and lower level of erythrocytes Cer d1:6/2:0, Cer d1:8/1:8 and Cer d1:8/2:1:0 (Fold change >1.5 or <1/1.5, P value <0.05).

Conclusions: These findings revealed novel plasma and erythrocytes lipid predictors for cardio-cerebrovascular diseases in hemodialysis patients.

PO1107

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 dialyzable BB may also be increased. 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 patients 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% CL: 0.88-1.22) for ACM and 0.94 (95% CL: 0.80-1.11) for CVE. Significant heterogeneity was seen with F2 values of 86% and 84% for ACM and CVE respectively.
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-CKD) 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.

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 Access Phases
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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 stent, 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.

PO1110
Comparison of Mortality Risk Across 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 decade 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 (follow-up time median(IQR): 794(461,1244) days). Patients with the highest decile of either CysC or creatinine had the highest mortality risk compared to the reference. Conversely, risk of mortality was incrementally lower for each decade below the reference for CysC while lower creatinine deciles were associated with a null to higher risk of death [figure].

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.
PO1111 Comparative Mortality of ESKD from Nephrolithiasis or Urolithiasis in the United States
Jingvin Yan, Wolfgang C. Winkelmayer, Jingbo Niu. Baylor College of Medicine Margaret M and Albert B Alkek Department of Medicine, Houston, TX.

Background: Patient with nephro-/uroliathiasis (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; glucomerulonephritis; polycystic kidney disease (PKD); other urologic; and other/unknown/missing. 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))

<table>
<thead>
<tr>
<th>Cause of ESKD</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NL/UL</td>
<td>2.64 (2.57, 2.72)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.74 (1.67, 1.81)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.43 (1.37, 1.49)</td>
</tr>
<tr>
<td>CKD</td>
<td>1.32 (1.27, 1.37)</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>1.27 (1.22, 1.32)</td>
</tr>
<tr>
<td>PKD</td>
<td>1.25 (1.20, 1.30)</td>
</tr>
<tr>
<td>Other Urologic</td>
<td>1.18 (1.13, 1.24)</td>
</tr>
<tr>
<td>Other/Unknown</td>
<td>1.14 (1.10, 1.19)</td>
</tr>
</tbody>
</table>

Complete case analyses

PO1112 Sleep Patterns and Mortality Risk in a Prospective Hemodialysis Cohort
Amy S. You,1 Sara S. Kalantar,1 Antoney J. Ferrey,1 Miklos Z. Molnar,2 Ronald A. Fischman,3 Michael A. Fischman,3 Avedik Semerjian,3 Yalitzi Guererro,1 Tracy Nakata,1 Csaba P. Kovessy,7 Danh V. Nguyen,4 Kamyar Kalantar-Zadeh,4 Connie Rhee.1 1University of California Irvine, Irvine, Irvine, CA; 2University of Tennessee Health Science Center, Memphis, TN; 3Southland Renal Associates, Long Beach, CA.

Background: While sleep disorders are common in hemodialysis (HD) patients, 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. non-dialysis days, respectively. In analyses examining the association of sleep duration with survival on dialysis days, patients with shorter sleep duration (defined as ≤median) had higher mortality (ref: longer sleep duration >median): adjusted HR (aHR) (95%CI) 1.59 (1.09, 2.31) (Fig 1A). Similar findings were observed for patients with shorter sleep duration (defined as ≤median) on non-dialysis days (ref: longer sleep duration >median): aHR (95%CI) 1.51 (1.04, 2.19). When surveying patients with regards to having difficulty sleeping at night, those who reported a high frequency (often to almost always) had higher death risk (ref: never/rarely to sometimes): aHR (95%CI) 1.74 (1.17, 2.58). Upon surveying patients with respect to use of sleeping pills, those who reported using (sometimes to frequent use) had higher mortality (ref: never/rare use): aHRs 2.07 (1.08, 3.97) and 2.00 (1.22, 3.28), respectively (Fig 1B).

Conclusions: In HD patients, shorter sleep duration, frequent sleeping difficulty, 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

PO1113 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 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, 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

PO1114 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 clinics, 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.
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

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 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 ≥10s).

Results: 16 subjects studied were 54±11 years old, 63% males, 69% African Americans. SaO2 was 94±2±2.1%. “Sawtooth” patterns covered 19.1% of the recorded treatment time, whereas ODE made up only 0.3%. 9 out 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 vs. time in each status. Although ODE were rarely seen, 70% were observed during times when “sawtooth” patterns were also present.

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

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 with concomitant SDB and 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: Ovid MEDLINE, EMBASE, and the Cochrane Library were searched for eligible publications, including non-transplant CKD patients older than 18 years-old with co-existing SDB. CKD is defined in this study by estimated glomerular filtration rate of <60 mL/min/1.73m².

Results: Seven observational studies (n = 186,686) were included in the meta-analyses. 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 ± 0.6 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.

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

Jonas Hannestad, Anthony Kalife, Eva Czirr. Alkabest Inc, San Carlos, CA.

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
Selection of the Best Equation for Serum Osmolality Calculation in Hemodialysis Patients

Tsuyoshi Miyagi,1 Cachet Wenziger,1 Yoko Narasaki,1 Yoshikazu Miyasato,1 Hiroshi Kimura,1 Kunitoshi Iseki,1 Ekamol Tantisattamo,1 Connie Rhee,1 Elani Streja,1 Kamyar Kalantar-Zadeh,2 Harold Simmons Center for Kidney Disease Research and Epidemiology, Orange, CA; 1Ryukyu Daigaku Igakubu Daigakun Igaku Kenkyuka, Naojagumi-gun, Japan.

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 provided the best fit between measured and calculated SOsm: 2[Na, in mmol/L] + 8K, in mmol/L] + 8Glucose, 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.

Effect of Dialysate Potassium on Interleukin 6 During Hemodialysis in Patients with ESRD

Monika Aggarwal (Gupta),1 George M. Feldman,1 Naveen Samuel,1 Dipankar Bandyopadhyay2, Reuben P. Retnani,3 Shobha Ghosh,1,2 Hunter Holmes McGuire VA Medical Center, Richmond, VA; 1Virginia Commonwealth University, Richmond, VA.

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. Efflux 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 2.92kcal/L 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 pre-prescribed concentration for the remaining time Blood was drawn at 30, 60, 90, 120, 180, and 240 minutes after start of dialysis. Serum IL-6 was measured using ELSISA. 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

Table 1. Linear Mixed Model Serum IL-6

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimate</th>
<th>Std. Error</th>
<th>t value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interven A</td>
<td>0.465</td>
<td>1.246</td>
<td>0.371</td>
<td>0.712</td>
</tr>
<tr>
<td>Interven B</td>
<td>2.978</td>
<td>1.018</td>
<td>2.941</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Figure 1. Serum IL-6 at different timepoints between 2 Interventions(Mean±SE)

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 healthcare 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.

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 Khanum’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%).

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.

PO1122
Clinician Perspectives on Access to Kidney Replacement Therapy in Rural Communities
Nicole J. Scholes-Robertson, Talia M. Gutman, Allison Tong. Centre for Kidney Research, The University of Sydney School of Medicine, Sydney, NSW, Australia; Centre for Kidney Research, Westmead, NSW, Australia.

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 navigation 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 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

<table>
<thead>
<tr>
<th>Quote</th>
<th>Theme</th>
</tr>
</thead>
<tbody>
<tr>
<td>Every patient went to the clinic, all. They had people taking them. So they went to the clinic.</td>
<td>Overwhelming burden of travel</td>
</tr>
<tr>
<td>I don’t think they really get their full benefit. They’re just not taking it.</td>
<td>Financial burden</td>
</tr>
<tr>
<td>We’re everything by telehealth. (Urban District) and Nurse Outreach group from Rural District.</td>
<td>Complexity and rigidity of health system</td>
</tr>
<tr>
<td>They can’t stay in their home town. They actually wanted to move somewhere else, like a town.</td>
<td>Complexity and rigidity of health system</td>
</tr>
<tr>
<td>They’re not doing anything. They don’t have the capacity.</td>
<td>Complexity and rigidity of health system</td>
</tr>
<tr>
<td>They’re not doing anything. They don’t have the capacity.</td>
<td>Complexity and rigidity of health system</td>
</tr>
<tr>
<td>They’re not doing anything. They don’t have the capacity.</td>
<td>Complexity and rigidity of health system</td>
</tr>
<tr>
<td>They’re just not feeling well.</td>
<td>Complexity and rigidity of health system</td>
</tr>
<tr>
<td>They’re just not feeling well.</td>
<td>Complexity and rigidity of health system</td>
</tr>
<tr>
<td>They’re just not feeling well.</td>
<td>Complexity and rigidity of health system</td>
</tr>
</tbody>
</table>

PO1123
Estimation and Prediction of Prevalence of Patients Receiving Dialysis in China Based on Claims Data
Chao Yang, Jinwei Wang, Luxia Zhang, Ming Hui Zhao. China Kidney Disease Network (CK-NET) Work Group. Peking University First Hospital, Beijing, China; National Institute of Health Data Science at Peking University, Beijing, China.

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 and 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 age 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.

Figure 1. Prediction curve of prevalence and number of dialysis patients in China from 2013 to 2025

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

Abbreviation: PMP, per million population.

PO1124
Low Socioeconomic Status Increases Risk of Mortality and Hospitalization in Korean Maintenance Hemodialysis Patients
Jung Woo Noh, Hayne C. Park, Young Eun Kwon, Do Hyoung Kim, Aijon Cho, Juhee Kim, Kyu Sang Yoon, Youngki Lee. Hallym University Kangnam Sacred Heart Hospital, Seoul, Republic of Korea; Myongji Hospital, Goyang, Gyeonggi-do, Republic of Korea.

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 beneficiary). 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 93,100 person-year in 2013 and 106,100 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.

PO1125
Iron Overload in ESRD Treated with Dofexomazine for Chelation
Sylvester Barnes. Loyola University Health System, Maywood, IL; Edward Hines Junior VA Hospital, Hines, IL.

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 of blood from 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 consciousness. 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 sicksles. Iron was 13mcg/dl, transferrin 100, ferritin 4284ng/ml, and iron saturation 98%. Bone marrow biopsy was obtained showing normal cellular marrow for her age and iron laden macrophages. Hgb electrophoresis showed Hgb S 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 along with ESRD leading to transfusion dependence. The treatment of iron overload was used to confirm that AG was grafted to the PES successfully. Scanning electron microscopy(SEM) showed that the PES-AG membrane could decrease local thrombus formation SEM micrographs of PES and modified membranes.

PO1126
Role of Hemodialysis in Severe Ethanol Poisoning
Devin Driscoll,1 Griffin Bleecker,2 Alicen W. Zhen,1 Jean M. Francis,1 Aala Jaberi.1 1Boston Medical Center, Boston, MA; 2Boston University Medical Campus, Boston, MA.

Introduction: The treatment for acute ethanol intoxication remains largely supportive. About 1% of patients presenting with ethanol intoxication require the utilization of critical care resources. 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 unresponsiveness after 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 atrioventricular 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 60mg/dL/hr. Complications of prolonged intubation include cataract 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 Polyethersulfone Membrane with a Direct Thrombin Inhibitor to Decrease Local Thrombus Formation
Shuangshuang Fu, Yunmei Liang. Nephrology Department of Hunan Provincial People’s Hospital (The First-affiliated Hospital of Hunan Normal University), Changsha, China.

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 diseases. As dialysis patients are 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 polyethersulfone(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 antithrombosis 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
Detlef H. Krieter,1 Nicolas L. Kiefert,1 Marieke Rueh,2 Horst-Dieter Lemke,2 Christoph Wanner.1 1University Hospital Würzburg, Div. of Nephrology, Würzburg, Germany; 2ExcorLab GmbH, Obernburg, Germany.

Background: The mode a dialyzer or fractionator is operated may affect the fouling processes of the filter membrane and, hence, may determine its capacity 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 polyethersulfone 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; thermofiltration) and reversed plasma filtration flow direction (outside-in). The totally treated plasma volume was 1500 mL. Reduction ratios (RR) and sieving coefficients (Sv) at 300, 600, 900 and 1200 mL of treated plasma 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 modes (medium flow rate, 0.05±0.02 to, high flow rate, 0.08±0.01), Sv for LDL were significantly higher (P<0.001) in outside-in at 300 mL (0.21±0.03), Sv for LDL were also significantly higher (P<0.001) in both outside-in (0.19±0.07) and at high flow (0.17±0.02) conditions at 600 mL. For IgG at 900 mL, Sv for fibrinogen determined in outside-in (0.37±0.12) was superior to the low and high plasma flow modes (0.08±0.08 and 0.13±0.01, resp.). Several significant differences in Sv were identified at different plasma volumes within the same operation mode. No significant differences in RR were determined between operation modes.

Conclusions: 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 Sv did not translate into different reduction ratios.

Funding: Commercial Support - 3M Deutschland GmbH

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

- 380
PO1129

Abstract Withdrawn

PO1130

Online High-Volume Hemofiltration Reduces Pre-Dialysis Levels of Indoxyl Sulfate Compared with High-Flux Hemodialysis: Results from the HDFit Multicentric Randomized Controlled Trial

Jordan D. de Lima,1 Murilo H. Guedes,2 Silvia D. Rodrigues,1 Ana Clara S. Almeida,2 Ana Beatriz L. Barra,2 Maria Eugenia F. Canziani,1 Americo L. Cuvello neto,3 Carlos E. Poli de Figueiredo,2 Roberto Peccois-Filho,2 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 and pre-dialysis concentration of middle size molecules, little is known about its effect on concentration of protein-bound uremic toxins (PBUT) particularly in comparison to HD. Here, we investigated whether HDF impacts pre-dialysis plasma levels of the PBUTs indoxyl sulfate (IXs), p-cresyl sulfate (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 (HDFitclinicalTrials.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 diffuse 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 Jakopic, Martin Hren, Tina Strupnik Galufl, Masa Knehtl, Tadej Zorman, Nina Vodosek Hojs, Robert EKart, Radovan Hojs, Sebatian Beve. Univerzitetni Klinicien 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 it to conventional 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/FiO2), clinical parameters (mean arterial pressure (MAP), FiO2, 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 ± 31.8 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 levels (5.40 ± 4.74 mmol/L vs. 2.46 ± 1.74 mmol/L; p=0.010) and vasopressein dose (1.26 ± 1.1 vs. 0.88 ± 3.2 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.

PO1132

Clinical Safety of a New Hemodialyzer with the Surface Modifying Molecule Enexos™

Jill M. Meyer,1 Dylan Steer,2 Lisa A. Weber,3 Mayuri Thakuraria,4 Chiang-Hong Ho,5,6 Claus Mullon,7 Robert J. Kossmann,8 9California Institute of Renal Research, Chula Vista, CA; 9California Institute of Renal Research, San Diego, CA; 10Research Management Inc./Kansas Nephropathy Research, Wichita, KS; 11Fresenius Medical Care, North America, Waltham, MA.

Background: The new Optiflux Enexos™ dialyzer (OED) contains a fluorourethane surface modifying macromolecule (Enexos™) blended in the membrane during manufacturing. Performance and safety of the dialyzer were assessed in a multi-center, open-label study (NCT# 03536663). This sub-analysis reports additional safety results for OED.

Methods: Subjects enrolled in the study underwent 12 HD treatments on the Optiflux® F160NR followed by 38 HD treatments (visits 13-50) with the OED. Safety was assessed by evaluating: 1) hematology tests and serum chemistry measured pre and post HD at the first use of OED and then measured pre HD for subsequent visits at approximately 2 weeks intervals; 2) Complement activation and serum albumin measured pre and post HD at the first use of OED; and 3) Adverse events recorded during the study. 1171 subjects were included in the study of which 18 subjects (safety population [SPOP]) had at least one HD treatment with the OED for a total of 664 OED treatments. SPOP median age was 63.5 years, female (77.78%) and white (66.67%). Table 1 reports SPOP (n=18) mean (SD) for chemistry and hematology. An increase in mean serum albumin level from 3.94 to 4.23 g/dL was observed, but no overt complement activation was noticed. Thirty-two AEs (4.8%) and 3 SAEs were reported, none were device related. No deaths or AEs leading to study discontinuation occurred.

Conclusions: The novel Optiflux Enexos™ dialyzer was well tolerated in a clinical study including 664 HD treatments in ESRD patients.

Funding: Commercial Support - Fresenius Medical Care North America

PO1133

Changes in Sensitivity Patterns of Gram-Negative Isolates in Bacteraemic Haemodialysis Patients

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Background: Gram-negative bacteremia (GNBs) in haemodialysis (HD) patients are associated with significant morbidity and mortality. While there is a paucity of data around the quantitative impact of drug resistant organisms, it is clear that they result in increased mortality, longer length of illness and higher costs of delivering appropriate treatment. We aimed to determine the sensitivity patterns of GNBs in our HD center.

Methods: Data were collected from clinical records, electronic records, and the microbiology database of all bacteraemias in HD patients between 2007 and 2018. Results: 283 episodes of GNB occurred in 1361 patients over the 12-year period. Excluding Coli and Klebsiella Pneumonie were the dominant pathogens, accounting for 40.6% and 15.9% of bacteremia isolated respectively. Sensitivity pattern analysis reveals that Meropenem was almost universally effective against gram negative isolates, with little change over the study period. Similarly, Gentamicin had sensitivity rates of >80% each year except 2010 (50%). Co-Amoxiclav had a variable sensitivity profile and with little change over the study period. Similarly, Gentamicin had sensitivity rates of >80% each year except 2010 (50%). Co-Amoxiclav had a variable sensitivity profile and with little change over the study period.

Conclusions: Judicious antimicrobial use is a World Health Organisation objective in the fight against antimicrobial resistance. Our local HD policy includes Vancomycin and Gentamicin as empiric therapy. The emergence of Vancomycin-resistant enterococci and more recently staphylococci will influence our future use of Vancomycin. In our patient group, Gentamicin therapy remains effective. Carbenapen resistant organisms are a global health threat so whilst Meropenem is efficacious, it should be reserved for more severe infections or treatments. Resistance is increasing at a rate far greater than production of novel antimicrobials so antimicrobial stewardship is paramount; particularly in HD populations with high rates of infection, morbidity and antibiotic exposure.
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dysfunction to the development of premature biological aging and its related morbidities independent of chronological age. Our findings suggest a potential contribution of Nrf2 to antioxidative responses, declines with age and is implicated in the pathogenesis of 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 compared them 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), after multivariable adjustment, Nrf2 expression remained significantly and negatively associated with CDKN2A expression (beta 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.

POII134

Association Between Nrf2 and CDKN2A Expression in Patients with ESRD: A Pilot Study

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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), after multivariable adjustment, Nrf2 expression remained significantly and negatively associated with CDKN2A expression (beta 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.

POII135

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 in use and 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

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 domain in the spring 2019 survey period. Facility variables in 2018 included were: fall and spring ICH-CAHPS ratings; 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.

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. The assessment of performance via the area under curve (AUC) showed use of GLM modeling correctly predicted true/false positives in 73% of facilities. The assessment of performance via the area under curve (AUC) showed use of GLM modeling correctly predicted true/false positives in 73% of facilities.

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 (ICHD) and home hemodialysis (HHD) cohorts. Evaluation of patterns of weekly duration over time analyzed the 2000 to 2017 incident ICHD and HHD cohorts.

Results: Overall, 12,494 ICHD and 1,493 HHD prevalent patients in 2017 were included. Median weekly treatment duration was 13.5 (interquartile range (IQR) 12-15) hours for ICHD 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 ICHD and HHD. No center characteristics were associated with weekly duration. Variability in duration across centers was very limited in ICHD compared to HHD, with variation in HHD being associated with state. Duration did not vary significantly over time for ICHD, whereas longer weekly HHD treatments were reported between 2006 and 2012 compared to before and after this period.

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 ICHD.

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, but 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 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, K/TV, 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 minimum 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/ calcimimetics (29%). A projected total of $447,355 was saved.
Conclusions: Pharmacist in HD clinics has a positive influence on HD patients through medication management and cost savings.

PO1140
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 GALEN 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 higher serum potassium (B=0.04 mEq/L 95% CI 0.002 to 0.002 and 1.00, 95% CI 0.999 to 1.002, respectively). Higher potassium intake was not associated with all-cause mortality (hazard ratio [HR] 1.00 95% CI 0.999 to 1.002). The PD-efficacy relationship was better described by a linear model. Conclusions: Higher dietary intake of potassium is not associated with hyperkalemia or death in patients treated with maintenance hemodialysis.

Funding: Government Support - Non-U.S.

CACV: Coronary artery calcification score by volume

PO1142
Pharmacokinetics, Pharmacodynamics (PK-PD), and Exposure-Efficacy Evaluation from CaLIPSO, 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 with the aggregation and growth of ectopic hydroxyapatite (HAP), has showed a significant reduction in CVC progression in CaLIPSO, 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 CaLIPSO 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 (Cmax) and PD (ex-vivo inhibition of HAP crystalization in plasma), PK-efficiency and PD-efficiency was evaluated using linear and Emax models.

Results: The analyses included data from 56 patients. Cmax 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 CACs over 52 weeks per group are shown in the table. An Emax model described well the relationship between PK-PD (E_{max}=8.8%, E_{50}=75.9%, E_{EC50}=7.5 μM); and PK-efficiency (E_{max}=16.9%, E_{50}=14.5%, E_{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. E_{max} models showed a robust relationship between SNF472’s Cmax and both the ex-vivo inhibition of HAP crystalization and clinical efficacy measured by % change in CACV over 52 weeks. Higher SNF472 exposure and inhibition of HAP crystalization correlated with a reduction in CVC progression in ESKD patients on dialysis.

Funding: Commercial Support - Sanifit Therapeutics

PO1143
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 Assessment of Healthcare Providers and Systems (ICH-CAPHS) scores. Facility-level performance in CY17 on ESRD QIP measures for hypercalcemia, fistula, long-term catheter, comprehensive K/V, NIH strokebloodstream infection (BSI) standardized infection ratio (SIR), and standardized transfusion ratio (STIR) was assessed using tetratic. Associations between facility measure performance and outcomes were tested using Poisson models for SMR and SHR and Analysis of Variance (ANOVA) models for ICH-CAPHS scores.

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Results: For all ESRD QIP clinical measures, lower levels of performance were associated with higher relative risks (RR) for SMR and SHR (p<0.05; Table). For all clinical measures except STIR and NHSN BSIR, lower levels of performance were also associated with lower ICH-CAHPS QIP scores (p<0.05; Table).

Conclusions: The observed associations of facility performance on individual ESRD QIP clinical measures with mortality, hospitalization, and patient experience with care indicate that the program is incentivizing improvements in care that are related to important patient outcomes.

Funding: Other U.S. Government Support

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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 regarding medications and venous needle dislodgment risk assessment. 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.

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 cardiopulmonary resuscitation (26%); unexpected death (19%); nonconversion (9%); wrong medication/dosage (9%); hemolysis (7%); severe hypotension (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 hypotension (5%); seroconversion (9%); wrong disposable/dialyzer (9%); hemolysis (7%); severe anemia. Primary outcomes will be major cardiovascular events. The current analysis was assessing if Roxadustat improves prognosis in at least 250 dialysis patients with renal anemia.

Conclusions: Tracking of incidents has 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 Triglyceride

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Background: Roxadustat 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 iron markers in a real-world prospective observational cohort.

Methods: This is a multicenter, prospective, longitudinal observational cohort study assessing if Roxadustat improves triglyceridemia 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 last follow up. The serum ferritin at baseline and at the last follow up was 639.1±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 245 pg/ml, changes of ferritin were 245 pg/ml (95%CI: 117.6 to 373.46, p=0.001) and 362 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 361.12, 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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Underline represents presenting author.

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PO1146

Roxadustat in Treating Anemia in Dialysis Patients (ROAD): Short-Term Impact on Serum Iron Markers

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Background: Roxadustat 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 iron markers in a real-world prospective observational cohort.

Methods: This is a multicenter, prospective, longitudinal observational cohort study assessing if Roxadustat improves triglyceridemia 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 last follow up. The serum ferritin at baseline and at the last follow up was 639.1±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 245 pg/ml, changes of ferritin were 245 pg/ml (95%CI: 117.6 to 373.46, p=0.001) and 362 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 361.12, 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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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 was inversely correlated with NLR (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, …) underrunpinned 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
POI149
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

POI1150
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.
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 empirical 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, intervention pilot study in patients 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 3 h 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 range at 3 h 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 3 h 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 3 h.

Funding: Private Foundation Support

PO1153

A Novel Algorithm to Identify Presumably Fluid Overloaded Hemodialysis Patients

Priscila Preciado,1 Hanjie Zhang,1 Peter Kotanko,1,2 Renal Research Institute, New York, NY; 3Mount Sinai Health System, New York, NY.

Background: Adequate volume control is a major challenge in hemodialysis (HD) patients. Relative blood volume (RBV) monitoring evidence suggests that flat RBV curves are associated with significantly better survival. Our goal was to develop an algorithm that would require a much shorter observation period with clinically meaningful sensitivity and specificity to identify (presumably FO) patients with flat RBV profiles (RBV >92% at 3 hours). We categorized patients as either positive (mean RBV >92% at 3 hours) or negative. We computed sensitivities and specificities relative to the positive and negative cases for 1-15 HD sessions and various rates of treatments with flat RBV curves.

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.

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) questionnaire 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 ± 4.9 kg/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 ± 7.6 ml/kg/min, respectively, p=0.023). VO2peak correlated with ECW/TBW (r=−0.436, p=0.0001) and age (r=−0.483, p=0.001) in both groups and within each group. VO2peak correlated with interdialytic 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 pathophysiology.

PO1155

Simplifying the 28-Zone Lung Ultrasound Protocol

Monodou L. Sankó,1 Ivan Kuznetsov,2 Thomas C. Arnold, Cameron Baston, Nathaniel C. Resinger,2 Penn Medicine, Philadelphia, PA.

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.

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

Underline represents presenting author.
Methods: We analyzed an existing dataset of 28-zone BLS scores obtained from 106 patients on hemodialysis (HD) who were cared at our center at various times. 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 15-20, high: BLS >20) based on FO zone 1-8. Finally, we tested whether we could achieve better diagnostic performance with subsets 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 scans 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 produced resultant Cohen’s Kappa values of 0.74, 0.76, and 0.71 for the 4, 6, and 8 zone protocols, respectively. We identified an underscore 4-zone scan that gave a slight increase in 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-zone 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 Bacteraemias in Haemodialysis Patients: 12-Year Single-Centre Experience
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Background: Patients on haemodialysis (HD) are at increased risk of contracting infections. Gram-negative bacteraemia in HD patients is associated with early mortality. In our HD population, we looked at the incidence and clinical outcomes of gram-negative bacteraemias over 12 years.

Methods: Data were collected from clinical records and the hospital's microbiology database of all confirmed bacteraemias in HD patients between 2007 and 2018.

Results: 283 episodes of gram-negative bacteraemia 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 bacteraemias 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 bacteraemias 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=22), hepatobiliary 7.8% (n=22), chest 7.8% (n=22), gastrointestinal 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 bacteraemias 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 bacteraemias in our cohort appears to have plateaued, with bacteraemias originating from other sources such as the urinary tract and intra-abdominal accounting for a greater proportion of gram-negative bacteraemias in our cohort - a trend reflected in other similar observational studies in HD populations. Dialysis lines remain a significant risk factor for bacteraemia, lending further weight to the 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, Claudy Mullon. Fresenius Medical Care North America Ogden, Ogden, UT.

Background: Surface-modifying macromolecules (SMM) may improve the hemocompatibility of hemodialysis membranes. We report center for a total of 2800 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 15-20, high: BLS >20) based on FO zone 1-8. Finally, we tested whether we could achieve better diagnostic performance with subsets 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 produced resultant Cohen’s Kappa values of 0.74, 0.76, and 0.71 for the 4, 6, and 8 zone protocols, respectively. We identified an underscore 4-zone scan that gave a slight increase in 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-zone 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
Procalcitonin Is a Biomarker for Inflammation in Outpatient Hemodialysis Patients
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Background: Procalcitonin is a widely used test to distinguish bacterial infections from viral infections, but its level is influenced by kidney function. The normal range of procalcitonin levels in end-stage renal disease (ESRD) patients on hemodialysis (HD) is not well established. In this study, we evaluated the relationship between Procalcitonin 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 procalcitonin levels prior to dialysis. We evaluated whether procalcitonin levels were associated with clinical characteristics, laboratory parameters, and future hospitalizations and infections.

Results: In this cohort, the median procalcitonin level was 0.38 ng/mL with an interquartile range of 0.23 ng/mL and 0.54 ng/mL. The distribution of procalcitonin values are found in Fig. 1A. African Americans had a significantly higher procalcitonin level than non-African Americans (P= 0.02, Wilcoxon rank sum test). ESRD outpatients with the hypertension, diabetes mellitus, or HIV did not have significantly higher procalcitonin levels than those who did not (P > 0.05). Procalcitonin 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). Procalcitonin levels were not correlated with Kt/V, white blood cell count, and ferritin levels (P>0.05). ESRD outpatients who developed infections or who were hospitalized did not have significantly higher initial procalcitonin levels than those who did not (P > 0.05).

Conclusions: Procalcitonin levels are correlated with inflammatory markers such as CRP and albumin, suggesting its potential use to identify ESRD on HD at high risk for complications, especially in the era of COVID-19.

Funding: Private Foundation Support
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 levels. With active viral or bacterial infections, active cancer, inadequate KtV, use of medication or disease known to elevate PRL (hypothyroidism, chronic liver disease, macroadenoma), 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 levels.

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 KtV, 4 cancer, 3 less than 6 months on HD, 1 macroadenoma. Comparing data between patients with high (median) and normal (50th) PRL, no statistical difference was seen in terms of age, sex, BMI, etiology, time on HD, cholesterol, albumin, calcium, phosphorus, PTH, glycated hemoglobin, IL-2, IL-4, IL-17A, TNF-α, gamma interferon. There was a positive PRL correlation with serum levels of IL-6 (r=0.001, r<0.04); between PRL and IL-10, the correlation was negative and also statistically significant (p=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 Diagnostics Ltda, Private Foundation Support

Laboratory parameters of patients with high and normal Prolactin

<table>
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<th>Normal Prolactin</th>
<th>p-value</th>
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</table>

POI1611

Accumulation in Hemodialysis Patients of Solutes Secreted by the Native Kidneys

Seolhyun Lee,1,2 Christian G. Bolanos,1,2 Robert Maier,1,2 Natalie Plummer,1,2 Timothy W. Meyer,1,2 Tammy L. Sirich,1,2 Stanford Medicine, Stanford, CA; 1US Department of Veterans Affairs, Palo Alto, CA.

Background: The native kidneys rapidly clear numerous solutes by tubular secretion, a function not replicated by hemodialysis (HD). We examined which solutes are cleared by secretion accumulate to high levels in the plasma when kidney function is replaced by HD.

Methods: Metabolomic analysis was performed on plasma ultrafiltrate (UF) and urine from 16 control subjects (NL) and on plasma UF from 36 HD patients using an established platform (Metabolon). The fractional excretion (FE) for each solute was calculated as the urine to UF ratio relative to that of creatinine. The extent of accumulation in HD patients was calculated as the ratio of the average UF peak area for each solute in HD relative to NL subjects (HD/NL). An FE > 2 was considered evidence of secretion and only solutes detected in samples from all 16 NL subjects and 36 HD patients were analyzed.

Results: 26 solutes had FE greater than 2 (mean 4±2.7, range 2.0 to 14.2). HD/NL ratios were significantly higher for solutes with greater FE values as shown in the Figure (p=0.045, p<0.001). HD/NL ratios varied however among individual solutes with similar FE values.

Conclusions: Uremic solutes that are rapidly cleared by the kidneys tend to accumulate to high levels in HD patients. Non-renal clearance and differences in generation rate and distribution volumes may result in variable HD/NL ratios for solutes with similar secretory clearances in the native kidney.

Funding: Veterans Affairs Support

POI1160

Biphasic Dynamics of Inflammatory Biomarkers Following Dialysis Initiation: Results from the MONDO Initiative

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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 indicators, 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 ≥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 smooth 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 near comparable predictive power, this marker could be used as an alternative indicator of inflammation in resource-limited areas.
P01165

Disease Course of Hyperkalemia in Patients on Hemodialysis

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Zucker School of Medicine at Hofstra/Northwell, Great Neck, NY; 3Toki University School of Medicine, Isehara, Japan;
4King’s College Hospital Nephritis 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 (NCT00303521) 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 g 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 6.5–7.0 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

P01166

A USRDS Database Study on the Use of Pegloticase in Patients Undergoing Dialysis

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Background: Gout is a common co-morbidity of chronic kidney disease, but prevalence in dialysis patients is not precisely known. Oral urate-lowering therapy use is limited in patients with advanced renal disease, particularly end-stage. Pegloticase (PEGylated uricase) rapidly lowers serum uric acid, but phase 3 trials did not include dialysis patients. However, a phase 1 trial in non-gout patients showed that pegloticase efficacy and pharmacokinetics are not affected by dialysis. Beyond this, pegloticase use in dialysis-dependent patients is not reported in the literature. This United States Renal Data System (USRDS) study sought to better quantify and understand real-world use of pegloticase in patients undergoing dialysis.

Methods: Patients with advanced renal disease, who are dialysis-dependent, or who have undergone renal transplant are in the USRDS. USRDS patients who were administered pegloticase and undergoing dialysis were identified in 2012-2017 Standard Analytical Files. Parameters examined included demographics, comorbidities, dialysis type, number of pegloticase infusions, and time between pegloticase infusions.

Results: 58 dialysis centers reported on 136 patients. Pegloticase was most prescribed by rheumatologists (68%) and internal medicine physicians (7%). The majority of patients were white (61%) and male (73%) and patient age averaged 56.9 ± 16.8 years; all adult age groups were represented (18-44 years: 27%, 45-49 years: 35%, ≥56 years: 39%). Hypertension (74%) and diabetes (46%) were the most reported comorbidities. 9 patients (7%) were donor kidney recipients. More patients were undergoing hemodialysis (108 patients [79%]) than peritoneal dialysis (23 [17%]). Patients received 13.4 ± 19.1

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

Underline represents presenting author.
pegloticase infusions (median: 7, 46 [34%] patients a12) and median time between doses was 14 days (mean: 21 days). This treatment schedule reflected that of pegloticase labeling (biweekly infusions).

Conclusions: The literature contains few reports of pegloticase use in dialysis patients. Our real-world data suggest that pegloticase is well-tolerated in dialysis patients, as indicated by a median of 7 infusions per patient and the expected treatment schedule. Further research is needed to verify these findings.

Funding: Commercial Support - Horizon Therapeutics

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 not 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

Fig.1 Kaplan-Meier curve of time to withdrawal

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 of 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

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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%), gastric bypass (24%), and roux-en-Y gastric bypass (24%) were the most common procedures performed followed by gastric band or bilipancreatic 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<0.001; myocardial infarction 0.5-0.9% vs 0.1%; OR 3.4, 95%CI 2.0-5.8, P<0.001; pneumonia 0.3-0.9% vs 0.2-0.4%; OR 2.3, 95%CI 1.4-5.0; P=0.05) 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 Postdisalysis Fatigue and Recovery in Patients on Chronic Hemodialysis

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Background: The etiology of postdisalysis 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
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 pre and postdialysis serum levels of 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 2.30 [IQR: 0.00–4.30] on a scale from 1 to 5. Median TIRD was 120 min [IQR: 60–400]. 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 counterintuitive 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 fatigue experience in HD patients, as fatigue as response to treatment may have other determinants than a more chronically fatigue.

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-dilution hemofiltration (HDf) with FX120 (Fresenius Medical Care), HD with FX120, HD with Theranova 400 (Baxter), HD with Theranova 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 RR=(B0-B230)/B0, with correction for hemoconcentration using hemoglobin levels (Schneditz, ASAIO 2012).

Results: Twelve subjects completed the study (30% female, 43.8±7.7 years old). With B2M RR of 0.29 for MCO, 0.33 for HFPS; surface areas 1.7 m2 for Trp according to RR=(B0-B230)/B0, with correction for hemoconcentration using hemoglobin levels (Schneditz, ASAIO 2012)

Conclusions: Use of an MCO dialyzer may result in similar or greater Trp loss as use of an HFPS dialyzer with a much larger surface area. When considering the use of MCO dialyzers, clinicians should consider the potential impact on removal of salutary substances (incl. protein-bound substances), an area that deserves further research.

Funding: Private Foundation Support

Figure 2. Box-Whisker plot of Trp RR.

Figure 1. Design of clinical study.

POI172
Effect of Hemofiltration with Medium Cut-Off Dialyzer on Uremic Toxins Removal

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Background: To our knowledge no study has ever evaluated the use of middle cut-off membranes (MCO) with online hemofiltration (OL-HDF). This study aims to show if the combination of OL-HDF with MCO can achieve a higher reduction ratio of some uremic toxins in comparison to regular OL-HDF.

Methods: Patients from our hemodialysis unit were treated twice with four different modalities, namely combinations of post-dilutional OL-HDF or hemodialysis (HD) with a high-flux dialyzer (Cordura FX120, area 2.5 m2) or the MCO (Theranova 400; area 1.7 m2), respectively. We analyzed the reduction ratios (RR) of erythropoietin, beta2-microglobulin (B2M), phosphate, and urea.

Results: Twelve anemic patients were studied (6 females; mean age 43.8±15.8 years; HD vintage 35.7±27.9 months). Mean blood flow (Qb) was 367±23 ml/min, dialysate flow (Qd) was 493±57 ml/min, ultrafiltration volume was 2382±568 ml. B2M RR of 0.29 for MCO, 0.33 for HFPS; surface areas 1.7 m2 for Trp according to RR=(B0-B230)/B0, with correction for hemoconcentration using hemoglobin levels (Schneditz, ASAIO 2012)

Conclusions: Adding a medium cut-off (MCO) dialyzer to HDF does not add benefit. The B2M RR with HiFlEx exceeds the one of a MCO dialyzer. HDF provides benefit over HD between the B2M 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 sulphate (IS) and p-cresyl sulphate (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 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 sulphate (PhS), as well as serum from hemodialysis patients, were adjusted to a pH of 4 to 11, and the concentration of the free form of PBUTs was measured.

Results: Albumin partially unfolded at pH <4 or >12. Calorimetric analyses revealed weakened interaction between IS and albumin at pH <5 or >10. The concentration of free IS in the presence of albumin was significantly increased at pH 4 (89.49±13.85 μg/dL) and pH 11 (22.45±13.85 μg/dL) compared to pH 7 (17.20±8.75 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±3.3 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 towards 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 model 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 ml/min/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) showed 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 (P), Vitamin D (Vit D), parathyroid hormone (PTH), Albumin (Alb), Ferritin, C-reactive protein (CRP) were measured. HOME-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, BF-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 BF-Ins had significant difference (Table). The trajectories of Uric Acid level prior to dialysis transition are shown.

Conclusions: IR-Ins, BF-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 (VitD).

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=0.49) 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 VitD 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

Comparison between groups

<table>
<thead>
<tr>
<th>Metric</th>
<th>CAD (n=64)</th>
<th>AAD (n=68)</th>
<th>p-value</th>
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<tr>
<td>iPTH BL</td>
<td>137 ± 41</td>
<td>172 ± 51</td>
<td>0.01</td>
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<tr>
<td>iPTH FU</td>
<td>125 ± 36</td>
<td>143 ± 55</td>
<td>0.001</td>
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<tr>
<td>sCa BL</td>
<td>9.3 ± 1.1</td>
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<tr>
<td>sCa FU</td>
<td>9.4 ± 1.2</td>
<td>9.3 ± 1.1</td>
<td>0.48</td>
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</tbody>
</table>

*p<0.05 from paired t or McNemar’s test
+2 sample t test and repeated measures logistic regression for continuous and categorical variables

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
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 which 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 model the mean difference (95% confidence interval (CI)) in β2M levels between HDF and HD.

Results: A total of 195 patients (mean age 53±15 years, albumin 4.0±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 patients. Compared to HDF, in the HD arm monthly mean pre-dialysis β2M levels were 1.57 μg/mL (95% CI 0.102 to 3.12) higher. In other words, HDF reduced mean circulating β2M levels over time compared to HD. (Figure).

Conclusions: In this post-hoc analysis of the HDFit trial, we describe for the first time that high-volume HDF substantially 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

Effect of Intradialytic Exercise on the Removal of Tissue Sodium During Hemodialysis
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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 intradialytic cycling (IDC) potentiates the removal of tissue [Na⁺] during HD.

Methods: Seven HD patients (sex: 57% male; age: 60±12 y; BMI: 36±10 kg/m²; spKt/V: 1.4±0.32; dialysate [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 proximal (MG) and lateral (LG) gastrocnemius, soleus (Sol), tibialis anterior (TA), and the whole lower leg (WL) were quantified from MRI images by trend analysis. Plasma [Na⁺] was also assessed by a 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=.036) and Sol (P=.016), with the EX treatment attenuating the drop in [Na⁺] during HD compared to the CON condition in both WL and Sol (Figure A-B). [Na⁺] of MG (P=.002), LG (P=.001), TA (P=.001), and plasma (P=.042) were reduced during HD, but these changes did not differ by treatment (treatment x time interaction P = N.S. for all; Figure C-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

PO1179

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 patients 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 latent-band exercise. Hand grip strength (HGS) and leg muscle strength (LMS) showed good correlation (r = 0.715, p < 0.001). HGS (25.1 ± 18.6 kg, p = 0.01) but LMS did not show statistical significance (29.3 ± 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 home or group exercise and introduce new feasible form of exercise for HD patients.

Table 3. Multiple linear regression analysis of the factors related with hand grip and leg muscle strength

<table>
<thead>
<tr>
<th></th>
<th>Hand grip strength</th>
<th></th>
<th>Leg muscle strength</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>21.80</td>
<td>0.001</td>
<td>28.07</td>
<td>0.068</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>0.63</td>
<td>0.54</td>
<td>0.57</td>
<td>0.56</td>
</tr>
<tr>
<td>Age (year)</td>
<td>-0.371</td>
<td>0.15</td>
<td>-0.352</td>
<td>0.15</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>0.069</td>
<td>0.1</td>
<td>0.125</td>
<td>0.15</td>
</tr>
<tr>
<td>Exercise (yes/no)</td>
<td>0.335</td>
<td>0.016</td>
<td>0.257</td>
<td>0.08</td>
</tr>
<tr>
<td>Serum albumin (mg/dL)</td>
<td>0.624</td>
<td>0.78</td>
<td>0.02</td>
<td>0.82</td>
</tr>
<tr>
<td>Serum creatinine (mg/dL)</td>
<td>0.141</td>
<td>0.11</td>
<td>0.104</td>
<td>0.26</td>
</tr>
<tr>
<td>hs-CRP (mg/L)</td>
<td>-0.035</td>
<td>0.70</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BMI: body mass index, hs-CRP: highly sensitive C-reactive protein.
PO1180
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)DMX 4.5, CI 2.2 to 6.8 points/100: low certainty evidence), depressive symptoms (SMD 0.73, CI 0.39 to 1.07: moderate certainty evidence), pain (MD 0.8, CI 0.3 to 1.1: low certainty evidence), functional capacity measured in terms of the 6 Minutes-Walk Test (MD 49.9 meters, CI 37.2 to 62.6: moderate certainty evidence) and the Sit-To-Stand test (MD 0.4 cycles, CI 0.1 to 0.7: low certainty evidence). The impact on depression was greatest for those who had maintained exercise beyond 4 months (SMD 1.26, CI 0.72 to 1.80). We could not draw conclusions 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.

PO1181
Comparative Risk of Fall-Related Fractures Among Hemodialysis Patients Newly Initiating Zolpidem vs. Trazodone Therapy
Magdalene M. Assimon, Jennifer E. Flynn1. University of North Carolina at Chapel Hill, Chapel Hill, NC.

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 resultant 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 hospitalised 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 prescribed higher zolpidem dosages (1.92 [1.4, 3.2]) 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, 3.7]). 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

PO1182
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 measured 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 y, 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 47% 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 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 is a key target for intervention required for diagnosis.

Funding: Private Foundation Support
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 gap between nephrologists and other kidney health 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 (pmp) and nephrology trainee density was 1.42 pmp. High-income countries reported the highest densities of nephrologists and nephrology trainees (23.15 pmp and 3.83 pmp, respectively), whereas low-income countries reported the lowest densities (0.24 pmp and 0.11 pmp, respectively). Compared to higher income countries, more low-income countries reported shortages of all types of ESKD healthcare providers, including nephrologists, transplant surgeons, peritoneal and hemodialysis access surgeons, and peritoneal and hemodialysis 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 ± 15 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, ≥55yrs: 55 ± 15). Sex was associated 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

Jun Yin,1 Jin-mei Yin,1 2Third Affiliated Hospital of Sun Yat sen University, Guangzhou, China; 3the Fifth Affiliated Hospital of Sun Yat sen University, Zhuhai, China.

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, Zarit Burden Inventory Scale, and Warwick-Edinburgh Mental Well-being Scale.

Results: The total score of psychological detachment of caregivers in maintenance hemodialysis patients was 1.52 ± 0.74 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)

Rafael C. Green,1,2 JiYoon B. Ahn,1 Laura Plantinga,1,3 John Sperati,1 Khaldet Abdell-Kader,1,4 Mara McAdams-DeMarco,1 Kelly H. Beers,1,5 Sandeep S. Soman,1,6 Michael J. Choi,1,7 Bernard G. Jaar,1,2 National Kidney Foundation Education Committee 1National Kidney Foundation, New York, NY; 2Johns Hopkins University, Baltimore, MD; 3Emory University, Atlanta, GA; 4Vanderbilt University Medical Center, Nashville, TN; 5Albany Medical College, Albany, NY; 6Henry Ford Hospital, Detroit, MI; 7MedStar Georgetown University Hospital, Washington, DC.

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 (a1 PCP visit) 1 year before and 1 year after dialysis start among adults age ≥67 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, 5% 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, Medicaid 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,
from more rural areas, or had functional impairments. Research to understand the barriers to PCP use may inform interventions to improve delivery of primary care for these vulnerable populations.

**Funding:** Private Foundation Support

Factors Associated with Continuity of PCP Care and Initiation of PCP Care after Starting HD

**PO1188**

**Status and Trajectory of Patient Activation Among Incident Dialysis Patients in the United States**

Wael F. Hussein,1,2 Anna R. Carrasco,1 Paul N. Bennett,1,3 Emily Watson,1 Sumi J. Sun,1 Brigitte Schiller,1,2 Satellite Healthcare, San Jose, CA; 3Stanford University School of Medicine, Palo Alto, CA; 4Deakin University Faculty of Health, Burwood, VIC, Australia.

**Background:** Patient activation (PA), a measure of knowledge, skills and confidence in managing one’s health, is associated with healthy behaviors, better disease management and improved health outcomes. We investigated the status and correlates of PA among end-stage kidney disease (ESKD) patients at dialysis initiation, and changes in PA after the first 3 months of dialysis.

**Methods:** Adult ESKD patients commencing dialysis at 25 in-center hemodialysis (ICHD) and 12 home dialysis facilities completed the Patient Activation Measure 13-item instrument (PAM-13) at dialysis initiation (t0) and month 4 (t1). Logistic regression was used to examine factors associated with high PA levels at t0 (PAM levels 3 and 4). Paired t-test was used to examine changes in PAM scores from t0 to t1.

**Results:** 227 patients completed the survey at t0 between Jun-Nov 2019; 166 (73%) on ICHD and 61 (27%) on home dialysis, mean age 60 ± 15 years. At t0, mean PAM scores were 65.1 ± 16.8; and 44% of patients had low activation. Mean PAM scores were 63.7 ± 17.3 and 69.4 ± 14.5 in ICHD and home patients respectively. In the adjusted model, higher education level and longer pre-ESRD nephrology care were associated with high PA at t0, while increased age was associated with lower odds of high activation – Figure 1. There was no significant change in PAM scores among 182 participants who completed the survey at t1 (mean 64.8 ± 17.8, mean change: -0.3 ± 17.3, p = 0.80).

**Conclusions:** Low activation is common among incident dialysis patients and is more common among those on ICHD. Patient activation does not seem to improve over the first 3 months of dialysis with current practice.

**PO1189**

**Fully Immersive Virtual Reality-Based Mindfulness Intervention in Hemodialysis Patients: A Pilot Study Assessing Safety and Utility**

Brett Burrows,1 Matthew H. Browning,2 Killivalavan Solai,1 Drew Fast,1 Natalia O. Litbarg,1 Judith T. Moskowitz,4 Kenneth R. Wilund,1 Rosalba Hernandez.1 1University of Illinois at Urbana-Champaign, Urbana, IL; 2Clemson University, Clemson, SC; 3University of Illinois at Chicago College of Medicine, Chicago, IL; 4Northwestern University Feinberg School of Medicine, Chicago, IL.

**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 full 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 an average of 5.03/7.0 and a System Usability Scores of 82.8/100.

**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.

**PO1190**

**Skin the Fat: PLEX for Hypertriglyceridemia-Induced CRRT Clotting**

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**Introduction:** CRRT filter clotting remains a significant barrier to providing adequate dialysis in critically ill patients. Clotting leads to reduced clearance and volume removal, blood loss in the circuit, and increased nursing workload. Elevated triglycerides have been reported to result in filter clotting. Here, we present a case of CRRT circuit clotting in a patient with familial hypertriglyceridemia-induced pancreatitis.

**Case Description:** A 46-year-old man with obesity, hyperlipidemia, recurrent pancreatitis secondary to hypertriglyceridemia, and DMII presents with 2 days of abdominal pain. CT abdomen showed pancreatitis necrosis and stranding prompting admission for pancreatitis. Hospital course was complicated by hypoxic respiratory failure requiring intubation, shock, and oliguric AKI requiring initiation of CVVHD. Shortly after initiation of CVVHD, the filter and tubing clotted with a milky yellow substance. This recurred after circuit exchange and use of regional anticoagulation with Citrate Dextrose 3%. Triglyceride level returned at 3,668 mg/dL (reference range: <150 mg/dL). Given the severe hypertriglyceridemia and inability to effectively provide RRT, he underwent one session of therapeutic plasma exchange (PLEX) with subsequent fall in triglyceride levels to 433 mg/dL. Further CRRT was then effectively provided with typical filter and circuit life.

**Discussion:** This case highlights the impact of elevated triglyceride levels on CRRT filter life. Prior case reports have described clotting and shortened filter life in the setting of lipid infusion and propofol-induced hypertriglyceridemia despite regional Citrate anticoagulation. Triglyceride levels fell and clotting resolved with cessation of the infusions in both situations. In the setting of a non-iatrogenic etiology of elevated triglycerides, we suggest consideration of anticipatory plasma exchange to avoid CRRT filter clotting and to be able to provide more effective dialysis.

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**Figure 1:** Adjusted odd ratios of high activation among incident dialysis patients

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

*Underline represents presenting author.*

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Medical Center, Charlottesville, VA.

Given these medications are renal failure given the drug’s pharmacokinetics. Both acyclovir and valacyclovir are toxicity is more likely to present in patients with acute or chronic keratitis and discharged home.

An additional session of hemodialysis was performed due to persistent altered mentation symptoms resolved. The following morning a repeat acyclovir level was 1.1 mcg/mL. After a four-hour session of hemodialysis her mental status improved, and her movement initiation was elevated at 2.6 mcg/mL (typical therapeutic level 0.14 – 1.2 mcg/mL). 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 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 the 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.


Introduction: After implementation of standard protocols for new start dialysis, Dialysis Disequilibrium syndrome has become rare. Patients with preexisting neurologic damage, head trauma or stroke are more vulnerable to this complication. We present a case report of a patient who had a “near miss” safety event after starting intermittent hemodialysis in the setting of a traumatic brain injury (TBI). His deterioration on dialysis is not fully explained by the current leading theory on the pathogenesis of this syndrome (theory of “reverse urea effect”) implying that either a multifactorial etiology is implicated or that impaired cerebral autoregulation may play a more significant role than previously believed.

Case Description: A 70 year old male was hospitalized after being involved in a motor vehicle accident. He suffered multiple injuries including cardiac arrest from which he was revived. TBI and acute kidney injury (AKI) requiring initiation of hemodialysis using the new start protocol. Trends of intracranial pressure (ICP), cerebral perfusion pressure (CPP) and heart rate (HR) before, during and after intermittent hemodialysis showed clear worsening of these parameters after beginning dialysis with subsequent improvement after discontinuing dialysis (Figure).

Discussion: This case points toward a change in the pattern of presentation of DDS, requiring new guidelines focusing on dialyzing vulnerable TBI patients. These guidelines include early initiation of dialysis, selection of CVVH as preferred modality given reduced dialysis dependency in AKI patients, adjusting dialysis settings to minimize urea clearance per unit time, utilizing ICP monitoring when available, using hypertonic saline to maintain serum sodium > 155 mmol/L and avoiding central lines on contralateral side to an internal jugular dialysis catheter to preserve cerebral venous return. The establishment of these guidelines may help reduce the risk of poor outcomes in this population.

Rescue Hemodialysis for Paroxysmal Hyperammonemic Encephalopathy Sans Cirrhosis Ativa Chachar, Brian Simba, Waqas Memon, Graham T. Gipson, Niraj R. Kothari. Virginia Commonwealth University, Richmond, VA.

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 catastrophes. 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 fulminant 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.

A Case of Polysulfone Membrane-Induced Thrombocytopenia Ivan L. Claudio-Gonzalez, Sarah Nicholls, James T. Someren, Susan M. Wall. Emory University Emory College of Arts and Sciences, Atlanta, GA.

Introduction: The development of biocompatible hemodialysis membranes has been a major advance in the treatment of renal failure. Newer, synthetic membranes such as polysulfone are considered to be more biocompatible than the older cuprophane or cellulose membranes. However, polysulfone dialyzers can interact with and thereby

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only Underline represents presenting author.
reduce platelet counts. A few isolated case reports have observed thrombocytopenia in patients after initial dose adjustment. Although etiology remains unclear, there was suspicion for drug-induced liver injury caused by hydralazine and high dose statin. Patient had a planned liver biopsy however he decompensated rapidly, and had a cardiac arrest which led to his demise.

**PO1197**

**Life Finds a Way: Two Successful Pregnancies in a Woman Without Kidneys**

Anna K. Curtis, 1 Christian C. Lamb, 2 Sarah Atallah, 1 Amit J. Patel. 1 University of Missouri Kansas City, Kansas City, MO; 2US Army Brooke Army Medical Center Medical Library, Fort Sam Houston, TX, USA.

**Introduction:** Bilateral nephrectomy is a controversial and rarely used approach to control refractory hypertension in patients with anuric 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 advancements in pharmacotherapy.

**Case Description:** The patient is a 31-year-old African American woman 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 dyspnea. 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 neonatal intensive care unit (NICU) where her baby 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 challenge with this case is the need to distinguish aHUS from 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 dyspnea. 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 neonatal intensive care unit (NICU) where her baby 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.

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mutant surface proteins. The detectable HBsAg is thus a mixture of wild type and variants, whereas the detectable anti-HBs are only against wild type viruses. These patients are still in the chronic HBV infection category as they typically do not progress to active disease, however acute infection is possible. Given our patient’s low HBV DNA (< 10,000 IU/ml) and mild transaminitis, she fits the chronic, inactive carrier state. Appropriate infection control precautions for HD were taken as established for chronic HBV infection patients.

Case Description: A 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 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.

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.

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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 thirteen documented reports of patients suffering from cerebral herniation secondary to DDS with poor outcomes.

Case Description: A 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 right-sided fasciculations and gaze palsy. The follow-up head magnetic resonance imaging (MRI) showed resolution of the midline shift and tonsillar herniation.

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PO1203

Association Between Serum Alkaline Phosphatase Levels and Stroke Risk in Patients Receiving Maintenance Hemodialysis: The Q-Cohort Study

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Background: 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 subdistribution 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 follow-up 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

Baylor University Medical Center at Dallas, Dallas, TX.

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 (Kt/V) of 0.5. Her weight was 60 kg. 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 Ki/V and URR is provided by the equation: ki/V = In (1-URR). A URR of 40% is roughly equivalent to a ki/V of 0.5. Thus, targeting a ki/V of 0.5 is a reasonable goal for the initial treatment. ki can be plotted on the nomogram in figure 1 (used with permission) for a given dialyzer koA and blood flow rate. Using a 400 koA dialyzer at a blood flow rate of 200 ml/min for 120 minutes in a patient with a V of 30 l, the estimated ki/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.
PO1205
Ultrafiltration 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 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 dialysate 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, UF, isolated ultrafiltration, or a sequential therapy modes.

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: mode (HD, UF, Only, and Sequential therapy (HD—UF only, UF only)—UF only), 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 to high venous and arterial pressure.

Results: Thirty simulated treatments were performed. Twenty-four treatments were performed with Qb from 150-250ml/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 (~ 400ml 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
Shilpi Shah, Angelina Edwards. University of Texas Health Science Center at Houston, Houston, TX.

Introduction: Despite its life-sustaining potential, prolonged dialysis and inadequate clearance of middle molecules can have untoward consequences. Largely underdiagnosed, 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) to lambda (λ) light chain ratio of 10.9. Bone marrow biopsy was normal but patient was found to have elevated serum β2 microglobulin (β2-m) 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 A (SAA) and κ light chain and λ light chain (AL). Further testing identified the amyloid protein as κ light chain (κ-chain). Retrospective history revealed he had suffered years of joint pain, especially in his shoulders, and had bilateral carpal tunnel surgery. He was chronically dependent on hydrocodone but since transplant he no longer experienced pain. Nadir serum creatinine was 1.3 mg/dl and repeat β2-m level decreased to 4.1 μg/mL.

Discussion: Present on all cell surfaces, β2-m is freely filtered then reabsorbed and catabolized in proximal tubules. Prolonged reduction in glomerular filtration leads to accumulation and deposition of amyloid fibrils particularly in periarticular structures, leading to debilitating arthritis. Although no precise treatment for DRA exists, transplantation leads to renewed clearance and dramatic improvement in symptoms. This case reiterates the importance of remaining alert for such diseases in patients with prolonged dialysis vintage.

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PO1207
Baclofen Pump Causing Electroencephalography Seizures
Niraj K. Yadav, Janame J. Kottekay, Josephine Abraham. University of Utah Health, Salt Lake City, UT.

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 lorazepam. Initial labs showed lactate 11.9 mmol/l, PCO2 30 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 mg/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
Wala Abusalah, Heather R. LeKowitiz. Newark Beth Israel Medical Center, Newark, NJ.

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.

Congo Red Staining in Vessel Wall Demonstrates Amyloid Deposition
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 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 HBsAg is positive, further testing is recommended 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 but Not with the Volume of Urea Distribution
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 + 1.12x [1 if male, 0 if female] – 0.06x age (yrs) – 0.08x spKt/Vurea + 0.009x Creat (pre-dialysis). Regression lines were created for each parameter over the 24 months. Slopes in the change of 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 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

Create a table to show the comparisons of slope of regression lines for stated factors.

PO1210
Crit-Line Blood Volume Monitoring in a Community Hemodialysis Unit
Carl E. Dukes, Carl E. Dukes, MD PA, San Antonio, TX.

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 a specific Crit-Line Blood Volume monitoring site, were included in this analysis. Time was divided into 1-month Baseline, 3-month training period, and 7-month follow-up period. 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 medications were discontinued. Thereafter, the other anti-hypertensive medications such as beta-blockers and RAASI agents were reduced or discontinued.

Results: Patients (n=38) were on average 63 years old, with a HD vintage of 5 years and BMI of 27.44 kg/m^2. 58% of patients (n=22) were females. Percentage of patients identified as black/African American and 40% identified as Hispanic/Latino. Most patients (74%) had pre-HD systolic BP at baseline in the hypertensive range. 41 patients had BP Med information. 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%) their BP medication. Patients able to discontinue the medications, had the largest decrease in post-HD weight.

Funding: Commercial Support - Fresenius Medical Care Renal Therapies Group

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

Underline represents presenting author.
PO1213

Use of Triferic and Outcomes of Hemodialysis-Dependent Patients: Initial Analysis Using 2016-2017 USRDS

Yi Zhang,1 Marc L. Hoffman,2 Ajay Gupta,3 *MTTP, Bethesda, MD; 2Rockwell Medical Inc, Wixom, MI

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 year study, 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 and 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 cohort study suggests that use of ferric pyrophosphate citrate as an 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 variety 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

Hiroshi Kimura,1 Cachet Wenziger,2,3 Jui-Ting Hsiung,1 Connie Rhee,1 Elani Streja,1 Csaba P. Kovovsky,1,2 Kamyar Kalantar-Zadeh,1 Harold Simmons Center for Kidney Disease Research and Epidemiology, Orange, CA; 2The University of Tennessee Health Science Center College of Medicine, Memphis, TN; 3Memphis VA Medical Center, Memphis, TN

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 (GNIr) 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 GNIr with decline in RKF were retrospectively examined across three strata of GNIr [low (GNIr <92), middle (GNIr 92-98), high (GNIr >98) GNIr 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 GNIr groups.

Results: The median GNIr and baseline KRU were 107.7 and 3.4 ml/min/1.73m², respectively. Lower GNIr 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 GNIr 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 GNIr groups, reference: high GNIr group]. KRU trajectories showed greater KRU decline over time in lower GNIr.

Conclusions: Lower GNIr 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

Yoshikazu Miyasato,1 Cachet Wenziger,1 Jui-Ting Hsiung,1 Elani Streja,1 Connie Rhee,1 Csaba P. Kovovsky,1,2 Kamyar Kalantar-Zadeh,1 Harold Simmons Center for Kidney Disease Research and Epidemiology, Orange, CA; 2The University of Tennessee Health Science Center College of Medicine, Memphis, TN; 3Memphis VA Medical Center, Memphis, TN

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. Besides, we compared the mortality predictability of PNI and its components (serum albumin levels and total lymphocyte count) using the receiver operating characteristic curve (AUROC), net reclassification improvement (NRI) and integrated discrimination improvement (IDI).

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-mix 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 (0.74-0.750), 0.743 (0.739-0.748), 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); 0.034 (0.023-0.045), 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

Anirudh R. Gong, Michael J. Ross, Corinne Levitus, Montefiore Medical Center Jack D Weiler Hospital, Bronx, NY

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 tunneled HD catheter. The patient had HCV-induced cirrhosis and had been receiving outpatient ciprof 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 medications and receiving continuous infusion of dextrose solution and repeated boluses of 50% dextrose. Prior to receiving HD, serum insulin was elevated at 42 nl/ml and 148 nl/ml despite hypoglycemia and c-peptide was 40mg/ml consistent with excessive endogenous insulin secretion. The patient was suspected to have cipro-induced hyperinsulinaemia. Emergently HD was performed to
increase clearance of ciprofloxacin and insulin. After 1 HD session, insulin level decreased to 14.6 with improved BG levels. The patient was subsequently managed 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 had a history of cipro-induced endogenous insulin secretion, it is likely that this reduced insulin in our patient by reducing cipro-induced endogenous insulin secretion and via clearance of insulin.

Methods: Twelve HD patients had 3 low sodium meals/day (Mom Meals, Inc) delivered to their homes for 4 weeks. On average they were on 17 medicines among which NRS-T (mean = 1.2), NRS-X (mean = 2.2; p<0.05) significantly reduced nausea and vomiting scores. Thirst and xerostomia were measured at three time points: baseline (BL), after 4 weeks of low sodium meals (INT), and 4 weeks post-meals (POST[SAA1]).

Results: Patients’ mean thirst during the day, thirst after HD, thirst’s influence on social life, dry mouth feeling, total XI, NRS-T, NRS-X scores were significantly lower between INT compared to BL (MeansSD scores from BL to INT: 3.1±2.1; 3.5±2.2; 1.3±0.9; 2.9±1.9 to 1.5±0.5; 28.5±12 to 19.3±3 on the scale of 1-5; 6.3±2.8 and 5.5±3.1 on the scale of 0-10, respectfully; p<0.05). The score of thirst’s influence on social life and NRS-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; p<0.05). NRS-T is significantly lower in POST compared to BL (MeansSD scores from BL to POST: 6.3±4 to 4.5±2; 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.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
POI1221

**Surprise Question: A Mortality Predictor in Hemodialysis Patients?**

**Patrícia Valerio,1,2 Ana Farinha,1,2 Centro Hospitalar de Setubal EPE, Setubal, Portugal; 3Fresenius 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% 2.47-30.34) 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±5.5 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**

**Hiroshi Kimura, John Sy, Connie Rhee, Elani Stejca, Kamyr Kalantar-Zadeh. Harold Simmons Center for Kidney Disease Research and Epidemiology, Orange, CA.**

**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.
**PO1224**

**Optimal Patient Positioning for Chest Compressions in Dialysis Clinics: A Randomized Cross-Over Simulation Study**

Patrick H. Pan, 1,2 Kevin T. McNamara, 1 Duke University School of Medicine, Durham, NC; 1Duke Clinical Research Institute, Durham, NC; 2Durham 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 backpack (baseline); 2) on the floor; 3) in a reclined dialysis chair; and 4) in a reclined dialysis chair with a backpack placed underneath. The sequence of manikin positions was randomized to reduce carryover effects and assessments were conducted a 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 MTSs 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:** Patient 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

**Figure 1:** Summary of Results

**PO1225**

**The Plasma Factor Beta-2 Microglobulin Drives Cognitive Impairment in ESRD**


**Background:** Our goal is to decode changes in the plasma proteome in age and disease to identify novel therapeutic targets. We and others have shown that administration of aged human plasma in young immunodeficient mice results in impaired neurogenesis and cognition. We are now extending these findings to plasma from end-stage renal disease (ESRD) subjects undergoing hemodialysis (HD). The prevalence of chronic kidney disease increases with age, and hemodialysis patients have a high incidence of cognitive impairment. The causes for this cognitive impairment are not fully understood and we hypothesize that plasma proteins, specifically beta-2-microglobulin (b2M) are a detrimental factor in HD patients. The Plasma Factor b2M was administered IP to wild-type (WT; C57BL/6) mice, followed by similar analyses.

**Methods:** B2M was administered IP to wild-type (WT; C57BL/6) mice, followed by behavioral testing, and histological and molecular analyses. B2M was administered IP to wild-type mice (WT; C57BL/6) with median hemodialysis vintage of 2.93 years (IQR: 1.76, 5.63) with median HD vintage of 2.93 years (IQR: 1.76, 5.63) with median HD vintage of 2.93 years (IQR: 1.76, 5.63), with median HD vintage of 2.93 years (IQR: 1.76, 5.63) was 3.19 years (IQR: 1.96, 4.51). The median HD vintage among all subjects was 3.19 years (IQR: 1.96, 4.51). In the subsequent multivariate analysis, including all variables that showed significance in the univariate analysis, excluding Fe, age, and induced calcification were observed. In the univariate logistic regression analysis, CACS ≥ 400 had a significant association with TSAT ≥ 20%. Fe ≥ 80 μg/dL, age, and dialysis vintage (P<0.05). In the univariate logistic regression analysis, CACS ≥ 400 had a significant association with TSAT ≥ 20%. Fe ≥ 80 μg/dL, age, and dialysis vintage (P<0.05).

**Conclusions:** Patient 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

**PO1227**

**Valvular Heart Disease in Prevalent Haemodialysis Patients**

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**Background:** Valvular heart disease is observed in patients with Chronic Kidney Disease. Recent large studies found a prevalence rate of 14%-16% of valvular heart disease (VHD) in haemodialysis patients (2014 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 haemodialysis 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, 4.51). In the multivariate analysis, including all variables that showed significance in the univariate analysis, excluding Fe, age, and dialysis vintage (P<0.05). In the univariate logistic regression analysis, CACS ≥ 400 had a significant association with TSAT ≥ 20%. Fe ≥ 80 μg/dL, age, and dialysis vintage (P<0.05). In the univariate logistic regression analysis, CACS ≥ 400 had a significant association with TSAT ≥ 20%. Fe ≥ 80 μg/dL, age, and dialysis vintage (P<0.05). In the univariate logistic regression analysis, CACS ≥ 400 had a significant association with TSAT ≥ 20%. Fe ≥ 80 μg/dL, age, and dialysis vintage (P<0.05).

**Conclusions:** Patient 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:** Private Foundation Support

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Underline represents presenting author.
PO1228

The Effect of Intradialytic Potassium and Magnesium Fluctuations on Cardiovascular Functioning in ESRD Patients Undergoing In-Center Hemodialysis

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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 hyper-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># HD (population)</th>
<th>Mean Pot K (mmol/L)</th>
<th>Mean Post K (mmol/L)</th>
<th>Mean Pot Mg (mmol/L)</th>
<th>Mean Post Mg (mmol/L)</th>
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<td>3.6 (3.3)</td>
<td>2.2 (2.0)</td>
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<td>3.1 (3.1)</td>
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<td>3.4 (3.3)</td>
<td>2.1 (1.7)</td>
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<td>3.3 (3.1)</td>
<td>2.3 (2.2)</td>
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</tbody>
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PO1229

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

PO1230

Inpatient Dialysis Provider Type and Duration of Hospital Admissions of Dialysis Patients

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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 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.
PO1231

The Impact of CRRT Modality on Filter Life

László Magy, Iro Honkanen, Rebecca L. Hegeman, Chou-Long Huang, Prerna Kumar, Swie Zin Mar Winhtutoo, 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 hemocencentration within the circuit, whereas CVVH is subject to hemocencentration 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 hemocencentration. We hypothesize that filter life is longer in patients treated with CVVH than CVVHD.

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

<table>
<thead>
<tr>
<th>Variable</th>
<th>CVVH (n=67)</th>
<th>CVVHD (n=63)</th>
<th>p value</th>
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<tbody>
<tr>
<td>Age (yr)</td>
<td>70 ± 6.3</td>
<td>73 ± 10.6</td>
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</tr>
<tr>
<td>Male (%)</td>
<td>9 (13.4%)</td>
<td>7 (11.1%)</td>
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<td>Hypernatremia (%)</td>
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<td>0 (0%)</td>
<td>0.20</td>
</tr>
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<td>Black (%)</td>
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<td>2 (3.2%)</td>
<td>0.41</td>
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<td>Diabetes (%)</td>
<td>1 (1.5%)</td>
<td>2 (3.2%)</td>
<td>0.41</td>
</tr>
<tr>
<td>Diabetes (mEq/L)</td>
<td>3 (4.5%)</td>
<td>3 (4.7%)</td>
<td>0.66</td>
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</tbody>
</table>

PO1232

Acute Dialysis in a High-Dependency Unit: A New Service with a Long-Term Legacy

Nasreen Samad,1,2 Frazel Anci,1 Nick Lever,2 Ian R. Carrasco Barber.3 Barts Heath NHS Trust, London, United Kingdom; Queens Hospital, London, United Kingdom.

Background: Continuous Renal Replacement Therapy (CRRT) in the intensive care unit (ICU) was restricted to the limit during the COVID-19 pandemic. COVID-19 was combined with acute kidney injury (AKI) and intensive care in 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 Queen’s Hospital, Romford, UK, was without critical nerves to develop a viable urgent alternative treatment. 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 plumbing work, machines and consumables. In the interim 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 Norepinephrine up to 0.6mcg/kg/min. Dialysis treatment was provided 6 days a week 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 COVID-19 patients were receiving dialysis requiring Acute Kidney Injury (AKI) therapy. 45 sessions were provided (range 1-19 sessions per patient). Of the 12 patients 4 died, of whom 4 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.

PO1233

Predictors of 30-Day Hospital Readmission Among Minority ESRD Patients Receiving Maintenance Hemodialysis

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Background: End-stage renal disease (ESRD) is one of the most prominent disparities as racial/ethnic minorities are 1.5-4 times more likely than others to develop ESRD. Among ESRD patients receiving haemodialysis, more than 1/3 of hospital discharges are followed by a readmission within 30 days. These subsequent readmissions are associated with increased healthcare costs and poor health outcomes. Therefore, knowing the incidence and risk factors for readmission are crucial steps needed for necessary prevention. This retrospective study aims to identify predictors with hospital readmission and outpatient care that contribute to 30-day hospital readmissions among minority ESRD patients receiving maintenance hemodialysis within an outpatient dialysis center located in the District of Columbia.

Methods: Data from electronic medical records were taken for patients who have had at least one hospital admission between January 1, 2017 and August 31, 2019. Descriptive statistical analysis was conducted for all study variables. Univariate and multivariable logistic regression analyses with 30-day readmission as the dependent outcome were conducted to identify and assess predictors of 30-day readmissions.

Results: A total of 969 patients were included in the study. Among these patients, 49 (51%) had 30-day hospital readmission. Overall, patients were predominantly African American (86.5%), age between the age of 60-69 (29.2%), and with a diagnosis of hypertension (89.6%). A diagnosis of secondary hyperparathyroidism, serum calcium < 8.5mg/dL at time of discharge, and serum PTH < 150pg/mL are significantly associated with higher readmission rates in multivariable analyses (p < 0.05). Gender, race, a weekend discharge, and serum phosphate at time of discharge were not associated with 30-day readmission.

Conclusions: Overall, the study findings provide some insight into risk factors associated with 30-day readmissions in minority patients receiving maintenance hemodialysis. These findings suggest that secondary hyperparathyroidism and chronic kidney disease mineral bone disorder (CKD-MBD) markers predict readmissions. Identifying inpatient and outpatient strategies to mitigate risks and prevent readmissions may improve outcomes among this high-risk ESRD population.

PO1234

Role of Lung Ultrasonography to Predict Intradialytic Hypotension in ICU Patients

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Background: Lung ultrasonography has emerged as a valuable tool in the assessment of volume status in hemodialysis (HD) patients. A-line profile noted on lung ultrasonography denotes low wedge pressure while B-line profile is associated with hypervolemia. We hypothesized that patients with A-line profile are more likely to experience intradialytic hypotension (IDH).

Methods: We identified all patients admitted to the Medical ICU at two tertiary care facilities in the Northwell Health system between Jan 1st, 2016 and Sep 23rd, 2019 in whom hemodialysis was performed and a lung ultrasound was documented the same day. We manually reviewed clinician documentation and included patients whose lung ultrasound findings demonstrated A-line profile or B-line profile. Patients with other lung ultrasound findings were excluded. IDH was defined as a decrease in systolic BP by ≥ 20 mmHg with a failure to meet UF goal or increase in pressor requirement during HD or associated symptoms of hypotension. In total 105 dialysis treatments were reviewed, 78 were included for analysis. Northwell IRB exempted the study for full IRB review.

Results: There were 55 treatments with A-line profile and 50 treatments with B-line profile on POCUS. The incidence of IDH in HD treatment with A-line profile and B-line profile was 50.9% and 21.7% respectively. 13 HD treatments with A-line profile and 1 B-line profile had an increase in pressor requirement.

Conclusions: Lung ultrasonography provides a quick and effective means of assessing volume status. Our data suggest that IDH occurs more frequently in patients with A-line profile compared to those with B-line profile. Further research should focus on describing the relationship between lung ultrasound and IDH.

PO1235

Relationship Between Cardiac Output (CO) and Estimated Upper Body Blood Flow (eUBBF) During Hemodialysis (HD)

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Background: Cardiopulmonary monitoring during HD could improve outcomes. Upper body oxygen consumption, arterial and central-venous oxygen saturation and hemoglobin concentration are used to calculate eUBBF (Rosales 2019). We studied the association between eUBBF and CO during HD.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Methods: In patients with central-venous catheter we measured central-venous oxygen saturation and hemoglobin levels during HD using the Crite-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 discernible 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.

POI1236
Point-of-Care Ultrasound Findings Among Dialysis Patients with COVID-19

Background: Dialysis patients are vulnerable in the COVID-19 pandemic due to advanced age, comorbidities, and obligate travel with frequent healthcare contacts. Point-of-care cardiac and lung ultrasound (US) has been used to enhance the physical exam in dialysis patients and is a potent tool for assessment COVID-19, comparing favorably to invasive mechanical ventilation and 56% intensive care unit admission. 23 (68%) had pleural effusions, 8 had pleural effusions (3 bilateral). 17 had an ejection fraction (EF) >55%, 3 had EF 30-55%, 1 had 36% required invasive mechanical ventilation and 56% intensive care unit admission. 23 patients had cardiac US. 17 had an ejection fraction (EF) >55%, 3 had EF 30-55%, 1 had 36% required invasive mechanical ventilation and 56% intensive care unit admission. 23 (60%) were discharged with mean length of stay 10 days.

Conclusions: We showed a high prevalence of thickened pleural lines, subpleural consolidations, and multifocal or confluent B-lines among dialysis patients with COVID-19. Most had a normal or collapsed IVC and intact cardiac function. Pleural and pericardial effusions were uncommon. More study is needed to determine whether US findings can help guide fluid management in dialysis patients.

POI1237
Accelerated Renal Replacement Therapy: Single-Institution Experience in Calculating Delivered Clearance During the COVID-19 Pandemic
Jans J. Cho, Shubha Ahy, Cybele Ghossein. Northwestern University Feinberg School of Medicine, Chicago, IL.

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 RRT 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 delivered 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 + Qf x FUN/BUN / weight /24 and calculated using the following formula K= Qd + Qf x FUN/BUN / weight /24. Qd >spent dialysate Qr= replacement fluid rate and Quf = net fluid removal rate. FUN = effluent 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.

POI1238
Can COVID-19 Personal Hygiene and Social Distancing Reduce Bacteremia and Peritonitis Rates in Dialysis Patients

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 haemodialysis(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 decolonisation 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.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO1239

Effect of Lockdown to Stop Spread of COVID-19 on Physical Activity Levels of Hemodialysis Patients
Maggie Han,1 Priscila Preciado,2 Ohmar Thwin,1 Xia Tao,1 Mirell Tapia,1 Lemuier Rivera Fuentes,1 Anirush U. Patel,1 Mohamad I. Hakim,3 Lelia Tisdale,1 Stephan Thijssen,1 Peter Kotanko,1,2 Renal Research Institute, New York, NY; 1Icahn School of Medicine at Mount Sinai, New York, NY.

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±11.6 years old with a diagnosis 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
Hamwon Shin, Miiryung Kim, Jun Young Lee, Jae Won Yang, Jae seok Kim, Seung-Ok Choi, Minseob Lee, Jun Youngang, Jae seok Kim, Wonju Severance Christian Hospital, Wonju, Gangwon-do, Republic of Korea.

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 could help keep patients at home longer. Understanding the reasons for exit from HHD may lead to strategies to reduce patient loss.

Methods: A retrospective cohort study of adult HD patients who entered training for HHD between January 1 2013 to December 31 2018 in AKC-S, followed until exit study end date. Reasons for technique failure (TF) identified, with KM estimates used to determine technique survival, and Cox proportional hazard model used to determine risk factors for TF.

Results: 147 patients entered the HHD program-48(33%) women; 44(30%) DM, 38(25.9%) CAD, 14(9.5%) CVD, mean age of 54(13) years. 12(8.1%) did not complete training. Overall time in program 28 +/- 20 months, average training time 6.7 +/- 3.3 weeks. Reasons for exit include transplant 24(16%), death 6(4.5%), TF 32(24%). TF reasons include medical 9(39.1%), psychiatric 2(8.7%), social 3(13.0%), safety 4(17.4%). Patient request 4(17.4%), change to PD 1(4.3%). Technique survival at 1, 2, and 5 years 91%, 85%, and 63%. Risk factors for TF include DM 2.36(1.06, 5.28) p= 0.036, CVD 4.34(1.8, 10.5) p=0.001 and a longer training time 1.18(1.07, 1.30) p=0.001.

Conclusions: First circuit clotting was significantly related to serum bicarbonate (r=0.454, p=0.005) and creatinine levels (r=−0.359, p=0.026). Blood pressure, infection, blood flow of circuit showed no relationships with circuit lifespan. The use of heparin and nafamostat increased circuit lifespan compared to non-anticoagulant.

PO1241

Home Hemodialysis Patient Loss: A Quality Improvement Initiative to Review Technique Failure in Alberta Kidney Care - South
Bailey Paterson,1 Victoria Riehl-Tonn,2 Elena Qirjazi,1 Jennifer M. MacRae.1
1University of Calgary Cumming School of Medicine, Calgary, AB, Canada; 2Mount Royal University, Calgary, AB, Canada.

Background: The number of dialysis patients has increased 15% over 5 years in Alberta Kidney Care South (AKC-S) with most patients pursuing in-centre hemodialysis. Although home hemodialysis (HHD) offers advantages of improved quality of life for patients and cost savings for programs it has grown at a slower rate. To increase the number of HHD patients, programs need to promote more patients to start on HHD and reduce the number of patients leaving HHD. Understanding the reasons for exit from HHD may lead to strategies to reduce patient loss.

Methods: A retrospective cohort study of adult patients who entered training for HHD between January 1 2013 to December 31 2018 in AKC-S, followed until exit/ study end date. Reasons for technique failure (TF) identified, with KM estimates used to determine technique survival, and Cox proportional hazard model used to determine risk factors for TF.

Results: 147 patients entered the HHD program-48(33%) women; 44(30%) DM, 38(25.9%) CAD, 14(9.5%) CVD, mean age of 54(13) years. 12(8.1%) did not complete training. Overall time in program 28 +/- 20 months, average training time 6.7 +/- 3.3 weeks. Reasons for exit include transplant 24(16%), death 6(4.5%), TF 32(24%). TF reasons include medical 9(39.1%), psychiatric 2(8.7%), social 3(13.0%), safety 4(17.4%). Patient request 4(17.4%), change to PD 1(4.3%). Technique survival at 1, 2, and 5 years 91%, 85%, and 63%. Risk factors for TF include DM 2.36(1.06, 5.28) p=0.036, CVD 4.34(1.8, 10.5) p=0.001 and a longer training time 1.18(1.07, 1.30) p=0.001.

Conclusions: First circuit clotting was significantly related to serum bicarbonate (r=0.454, p=0.005) and creatinine levels (r=−0.359, p=0.026). Blood pressure, infection, blood flow of circuit showed no relationships with circuit lifespan. The use of heparin and nafamostat increased circuit lifespan compared to non-anticoagulant.

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Underline represents presenting author.
Figure 1. Cumulative Incidence of Competing Risks.

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 a132 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

Drew Hager,1 April Bertrand,1 Nickie L. Cool,1 Thomas W. Ferguson,1 Claudio Rigatto,2 Navdeep Tangri,2 Clara Bohm,2 Michelle S. DiNella,2 Paul Komenda,1 Winnipeg Regional Health Authority, Winnipeg, MB, Canada; 3University of Manitoba, Winnipeg, MB, Canada; 4Seven Oaks General Hospital, Winnipeg, MB, Canada.

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 complex medical conditions 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.

PO1244

Timed Repetitive Controlled Rotations of the CAR-170-C NXSTAGE Chronic Cartridge Hemodialysis Filter: An Original Newfangled Maneuver toEnable 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 Warfarin, on maintenance daily Home Hemodialysis (HHD) with a NxStage machine, developed intra-abdominal abscess and sepsis following an urgent laparoscopic appendectomy. He required emergent pericardiocentesis 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 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.

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

Underline represents presenting author.
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 co-morbid, 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±6.8, 66% 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 5%, PTH resistance 11%, 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.

PO1248

Binding of TonEBP and β-Catenin to the E-Cadherin Promoter Is a Key Process of Hypertonicity-Induced Phenotype Transition of Peritoneal Mesothelial Cells (MCs)

Background: Epithelial-to-mesenchymal transition (EMT) of MCs is considered as an early mechanism of peritoneal fibrosis. Tonicity-responsive enhancer binding protein (TonEBP) is a transcriptional factor that enables cellular adaptation to hypertonic osmotic
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-γ-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 α-smooth muscle actin (α-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 SMIT, 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 β-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 β-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.

PO1250

Geographic Variation of Home Dialysis Utilization in the United States Eric D. Weinhandl,2,12 David T. Gilbertson,1 James B. Wetmore,3,1 Kirsten L. Johansen,1,3,14 Chronic Disease Research Group, Minneapolis, MN; 2 University of Minnesota, Minneapolis, MN; 3 Hennepin Healthcare, Minneapolis, MN. 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 assessed 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 ascertainment the dialysis modality—in-facility hemodialysis, home hemodialysis (HHD), 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) of 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% (10.0% HHD, 12.2% 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 errors, 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 were revised 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

In the revised SHDR, expected home dialysis utilization also reflects race and payer.

PO1252

Higher Utilization of Peritoneal Dialysis Following the Executive Order on Advancing American Kidney Health Eric D. Weinhandl,1,2 David T. Gilbertson,1 James B. Wetmore,3 Kirsten L. Johansen,1,3 Chronic Disease Research Group, Minneapolis, MN; 2 University of Minnesota, Minneapolis, MN; 3 Hennepin Healthcare, Minneapolis, MN. Background: On July 10, 2019, the president of the United States issued an Executive order which set the goal for 80% of patients to receive treatment at home or a transplant by 2025. To achieve this goal, providers and payers will not only need to encourage the use of PD but also will need to mitigate PD technique failure (TF). McGill et al. (AJKD, 2019) found that 6 out of 7 patients who start treatment with PD experience TF and will switch to hemodialysis (HD) within five years. Of patients who switch, Jaar et al. (BMJ Nephrology, 2009) found that 20% did so by 6 months. Improving PD treatment time is important for patient quality of life and reducing healthcare costs. The goal of this study was to model Medicare cost savings associated with extending patient time on PD.

Methods: Using USRDS data, we calculated total Medicare spending per patient per day to be $226.71 for PD and $266.26 for HD, respectively. We estimated potential savings if treatment with PD could be extended each month up to 1 year using a base case of an incident ESKD patient who transitions to HD after receiving PD for 6 months. We assumed that during this year patients neither had a transplant nor died and that patients received HD once they stopped PD. Results: Extending PD beyond 6 months for incident patients could result in potential savings to payers. Extending PD by 1 month, 2 months, 3 months, 4 months, 5 months, or 6 months could save $1,203.05, $2,406.10, $3,609.15, $4,812.20, $6,015.25, or $7,218.30, respectively per patient. We found that if a patient could avoid TF, $14,436.59 could be saved annually.

Conclusions: Extending the PD treatment time beyond 6 months has the potential to reduce treatment costs by $1,203.05-$7,218.30 for patients on PD 1 month to 6 months longer, respectively. Annually, avoiding TF could result in savings of $14,436.59. Multiple risk factors are associated with TF. Focusing on identifying and addressing modifiable conditions can help keep more patients dialyzing at home.

Funding: Commercial Support - Fresenius Medical Care North America Renal Therapies Group
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

### POI1254

#### Disparities in Home Dialysis and Links to Kidney Transplantation: Inequities Among African American ESRD Patients in Detroit, Michigan

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#### 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.

#### Funding: NIDDK Support
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 recorded, 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 patients 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). Few 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 initial PD prescription patterns, there have been reductions in cycler volume, total number of exchanges, and prescriptions for 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

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: VIPKHD, 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 catheter 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 VIPKHD (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 12/31/2017, 37 patients were on CCPD with good adequacy, 29 discharged. 1 Recovery, 7 Transplant, 3 Relocation, 4 Declined, 1 Hospice, 15 Dropouts (5 peritonitis, 1 tunnel infection, 2 leaks, 1 inadequate dialysis, 3 disability, 1 burnout). Performance rates per 100 ESRD patient years (VIPKHD 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, ceflection and collaboration, promotes shared decision-making and facilitates timely access to integrated, longitudinal, patient-centered care.

Funding: Clinical Revenue Support

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 euveloria. All patients were initially started on manual exchanges every 1-2 hours (Total volume 12.5L to 24 hours) and eventually most were changed to automated PD (Total volume 18-20L/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, phosphorus, 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: Acute PD 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 in treatment related complications compared to non-obese patients. Acute PD should not be restricted based on elevated BMI.

Peritoneal Dialysis - 1

Comparing Mortality of Peritoneal and Hemodialysis Patients in an Era of Medicare Reform

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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
the relative mortality of PD and HD if PD is increasingly used by sicker patients. This study examines the competing risks 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 2-year 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 to 1.04 for 900 incident cohort). Mortality differences between PD and HD did not change over time (p=0.23).

Conclusions: Growth in PD initiation over time occurred without changing the patient mix towards sicker patients. After adjusting, 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 use.

Funding: NIDDK Support

PO1260
Duration of Serum Phosphorus Control Associated with Overall Mortality in Patients Undergoing Peritoneal Dialysis
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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, 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 following-up point - baseline SP level) / baseline SP level. Duration of SP control (months) = PD vintage when patients reached hyperphosphatemia - PD vintage when patients' SP 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 = 0.003]. The longer SP controlled duration, the lower overall mortality. We should controll SP were tightly associated with overall mortality, PD withdrawal and combined endpoint. The longer SP controlled duration, the lower overall mortality. We should controll SP levels as early and as long as possible.

Conclusions: In PD patients, the level of SP and the degree of change after dialysis - PD vintage when patients reached hyperphosphatemia - PD vintage when patients' SP decreased to less than 1.78 mmol/L after PD.

PD vintage when patients' SP decreased to less than 1.78 mmol/L after PD.

PO1261
Urgent-Start Peritoneal Dialysis and Outcomes
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Background: Many patients start dialysis without adequate pre-dialysis planning, and generally initiate hemodialysis using a central venous catheter (HD-CVC). A minority utilize urgent start peritoneal dialysis (USPD), where a peritoneal dialysis catheter is placed without the usual 2-4 week waiting period. Few analyses have compared outcomes between patients utilizing these two dialysis initiation routes.

Methods: All data for this retrospective study were derived from deidentified electronic health records. Patients who initiated dialysis via HD-CVC during 2018 were matched 1:1 to patients who initiated dialysis using USPD during the same period on the basis of insurance type, etiology of end-stage kidney disease, race, and presence of diabetes. Hospitalization, mortality, and scores on the Kidney Disease Quality of Life (KDQOL) survey were evaluated from dialysis initiation through the first of death.

PO1262
Efficacy of Statin Use in Patients Undergoing Peritoneal Dialysis
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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: From a total 612 PD patients between 2006 and 2018 in 2018 (example: HR, 0.93; 95% CI, 0.84 to1.04 for 2018 cohort). 331 (53.6%) patients were men. The number of statin uses was 390 (63.5%) and the number of patients who use statin before starting PD was 311 (50.8%). The use of statin (as2 ±2 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.

PO1263
Mortality and Hospitalization in a Large International Peritoneal Dialysis Institution During 2018
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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/episode/ year and risk 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), RO (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 HR (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% (cardiac 33% of causes); other unknown 6% 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 10.7% (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 homogenous 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.
Association Between Peritoneal Dialysis (PD) Patient-Reported Family Member Assistance and Peritoneal Dialysis Morbidity Persistence

Nashville, TN
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Background: Increasing the number of dialysis patients who start and maintain home therapy is an urgent national priority. PD patients perform their own dialysis procedures at home. Family members may assist with moving dialysate bags, catheter care, dialysis machine set-up and connections, and medication administration. Understanding and supporting caregivers is an important driver of successful home dialysis, necessary to inform program content and activities. This study describes associations between patient reported family member assistance with healthcare tasks, and morbidity persistence.

Methods: Prospective, single site, cohort study of adults receiving PD for kidney failure. A baseline survey assessing family assistance with healthcare tasks at home was administered during a routine outpatient visit. Longitudinal data were tested using Chi-squared (SPSS) for associations between patient reported family member assistance, and PD morbidity persistence at six months.

Results: This sample of N=100 patients was 57% male, 31% African American, and 4% Hispanic/other. Average age was 56 years. 16 years. Most patients reported a family member provided help at home (65%). Among those reporting family member assistance, 20% reported help administering insulin, 65% reported help with the PD procedure, 54% managed medications, and 59% provided wound care. Also, 16% reported help with one or two tasks, 28% help with three tasks, 25% help with five tasks. Patients who self-identified as Black/Hispanic reported less family member assistance than whites (51% vs 71%, p=0.04). In the 74% of the initial sample who completed 6 month follow-up, for patients reporting any family assistance compared to those reporting none, there was a trend toward higher PD morbidity persistence (86.4% vs. 70.4%, p=0.092).

Conclusions: Optimizing family assistance may be a strategy to promote PD morbidity persistence. More work is needed to better characterize the caregiver role and its impact on health outcomes specific to home dialysis.

Patient Outcomes of a Two-Exchange Assisted Continuous Ambulatory Peritoneal Dialysis (CAPD) Programme for Frail Older Patients

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Background: Recognising the burden that hospital haemodialysis (HD) places on frail people in terms of time away from home, transport and haemodynamic shifts, we developed a 2-exchange assisted CAPD programme to enable frail people to receive a home-based therapy. Eligible patients include frail, mostly elderly patients who are symptomatic from advanced kidney disease and have residual kidney function. The focus of the programme is to optimise patients’ symptoms while avoiding a high treatment burden.

Methods: In this observational study, all 2-exchange aCAPD patients attending for routine review are approached for assessment. Frailty is assessed with the Edmonton Frail Scale (EFS), cognitive function with the Montreal Cognitive Assessment (MOCA), treatment satisfaction (treatment-related Quality of Life Questionnaire (RTSQ)) and symptoms with the Palliative Outcome Scale-Symptom Renal (POS-S Renal). Data was collected via patient interviews and chart review.

Results: Of the 17 patients currently receiving 2-exchange aCAPD, results have been collected from 47% (N=8) to date. Mean age is 82 years (77-90) and 50% are male. Mean number of co-morbidities is 4.4. Mean time on 2-exchange aCAPD was 9 months (0-24). 63% had at least mild frailty with an EFS >8/17 (3-11). 75% had memory impairment with a MOCA <26/30 (8-30). Median number of hospital admissions was 1 (0-13). 38% had travelled outside of the UK (with family support) since commencing aCAPD. 85% reported high satisfaction with treatment with a RTSQ of >55/66 (median 62). Patients reported a low symptom score with a median POS-S Renal of 14.5 (7-27). Pain, lack of energy and poor mobility were the most commonly reported symptoms.

Conclusions: Our results demonstrate a frail, elderly population with multiple co-morbidities. Although our population number is small and they are not matched to the assisted PD and HD populations published in the FEPOD study they do compare favourably in terms of the RTSQ score; median of 60 vs 55 for assisted PD and 60 vs 51 for HD. Our population was compared in 2010 with the POS-S Renal symptom scores of 14.5 vs 14 for assisted PD and 14.5 vs 16 for HD. This indicates that 2-exchange aCAPD could potentially become the dialysis modality of choice for the frail, older person requiring dialysis.

A Snapshot for Peritoneal Dialysis Clinic Visits: Addressing Hospitalization Rates with a Checklist

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Background: Readmission rates are a component of quality metrics in home dialysis follow-up. Common causes of peritoneal dialysis (PD) related hospitalizations have been elucidated through National Readmission Database review. However, a systematic 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 exacted. 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 clinical 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%), bacterial peritonitis (19%), electrolyte derangement (17%), hypotension (13%), new-onset hypertension (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.

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<0.001). 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.

Outcomes of Urgent-Start Peritoneal Dialysis in a Retrospective Cohort

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Background: Peritoneal dialysis (PD) has shown to have early survival benefit and increased patient satisfaction when compared to in-center hemodialysis. Despite this, 86% 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 ensue 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 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. Reasons for transition from PD to hemodialysis (HD) were obtained. Median time from catheter placement to initiation of dialysis was 5 days. Major complications including peri-catheter leakage occurred in 3 patients (7.5%), catheter malfunction in 7 patients, and hospital admissions within the first 4 weeks occurred in 3 patients (7.5%) 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 HD or RRT.

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.

POI1269
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 examination showed a maintained general status, diffuse non-pulpable purpura and tonsillolaryngopharyngitis. Laboratory testing revealed an elevated c-reactive protein and pancytopenia. Malaria prophylaxis (A-P) had been prescribed by his general practitioner on return from Kenya with a diffuse erythematous rash, dysphagia, fever and weight loss. Malaria infection was ruled out through blood smear analysis. Broad spectrum antibiotics were administered for tonsillolaryngopharyngitis. Bone marrow examination showed a megaloblastic anemia. Besides, he developed a diffuse nonscarring hair loss within weeks.

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 DNA synthesis pathway.

Conclusions: More cases of A-P related toxicity should be reported on peritoneal dialysis patients.
Conclusions: 24-hour ambulatory pulse pressure is the most significant predictor of peritonitis 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.

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PO1273
Differences in Protein Energy Wasting Indicators by Peritoneal Transport Type: A Cross-Sectional Study with Automated 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, 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 transporter peritoneal 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, 35.1 ± 13.3 years; dialysis duration, 7 ± 4.3 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 hypoalbuminemia and inflammatory state in CKD patients on automated peritoneal dialysis. HT patients are at an increased risk of 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 2019 the U.S. 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 contribute to modality failure and reluctance to opt for PD when starting dialysis. A

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)
Keith McCullough,1 Jeffrey Perl,2 Muthana Al sahlawi,3 Neil Boudville,4 Yasuhiko Ito,5 Talergonsak Kanjanabuch,1 Beth M. Piraino,5 Douglas E. Schauble6 Martin J. Schreiber,5 Isaac Teitelbaum,5 Graham Woodward,5 Junhui Zhao,1 Ronald L. Pisoni.1 1Archer Research Collaborative for Health, Ann Arbor, MI; 2St. Michael’s Hospital, Toronto, ON, Canada; 3Chulalongkorn University, Bangkok, Thailand; 4University of Pittsburgh, Pittsburgh, PA; 5University of Colorado, Denver, CO; 6University of Western Australia, Perth, NSW, Australia; 7St. James’s University, Leeds, United Kingdom; 8Aichi Medical University, Nagakute, Japan; 9DaVita Inc, Denver, CO; 10University of Pennsylvania, Philadelphia, PA.

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
Anubha Muneja,1 Shilpa Arora,2 Frank J. O Brien,3 Daniel W. Coyne,1 Daniel Picus.1 1Washington University in Saint Louis, Saint Louis, MO; 2Rush University Medical Center, Chicago, IL.

Background: Peritoneal Dialysis (PD) is a favored treatment modality for patients with end-stage kidney disease. PD catheter Complications on adequate 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–Aug 2019 were included in the analysis. GP with a PACS and employed

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Repeat Peritonitis: A New Reality After Staphylococcus aureus Carriage Surveillance Implementation
Marina Reis, Ana Marta Gomes, Daniela Lopes, Clara Santos, João C. Fernandes. Centro Hospitalar Vila Nova De Gaia/Espinho, Vila Nova de Gaia, Portugal.

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 (11.8% 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<0.001) as Streptococcus 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=0.013) 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, Streptococcus became more frequent than SA in repeat group, peritonitis outcomes became more favorable but repeat peritonitis rate increased. We believe that as measures to prevent SA infections are implemented more programs will face this reality.

Repeat Peritonitis Causative Microorganisms

![Graph showing percent distribution of causative microorganisms](image)

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 technical failure. Data reporting to individual PD home programs on PTN rates is desired to drive a proactive and permanent approach to prevent technical failure. We considered older age, female sex, obesity, diabetes mellitus, diverticulosis, and constipation to be the most important risk factors for endogenous peritonitis in patients undergoing PD. Therefore, we added these six factors as confounding factors into our multivariate logistic regression model.

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 the most recent calendar month filled with the most current PTN rate at that event. We queried our EMR after 07/30/2013 to preferentially concentrate the inoculum. We used univariate logistic regression models for the above-mentioned risk factors for endogenous peritonitis (p = 0.0036) in our multivariate logistic regression model.

Conclusions: Because smoking and constipation are significant independent risk factors for endogenous peritonitis in PD patients. The management of constipation 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
Sunil Shergaw, Jie Ouyang, Angelica C. Grussner, Subodh J. Saggi. SUNY Downstate Health Sciences University, Brooklyn, NY.

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 an 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 07/30/2013 (5-10 ml) of a cloudy cloudy PD fluid was injected into an aerobic and an anaerobic blood culture bottle.

Conclusions: 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 PF 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 sets within EMR systems to close this gap ultrasound. Repeat microbiology studies showed fungal elements in the PD fluid, later identified as Penicillium species mold. 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 drainage. His course was further complicated by recurrent upper 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 leak, solved after transtentorialysis for 2 months. In 2002 she was admitted with complete spontaneous PC expulsion (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. CASE3: 62 year-old woman with CKD due to anti-glomerular basement membrane disease. She received induction treatment with high-dose steroids and cyclophosphamide. She presented Pseudomonas aeruginosa solved after a course of topical antibiotics as well as external cuff shaving. In 2019 she developed again ESI with Pseudomonas aeroginosa, and despite topic treatment as per antibiotic exit site cultures remained positive. One month later she presented a spontaneous expulsion of the PC. A contralateral PC was placed without further infectious complications. These risk factors should be identified and kept in mind to prevent the catheter extrusion.

PO1284
Polymicrobial Peritoneal Dialysis Peritonitis due to Eggertghella lenta, Parabacteroides Species, and Bacteroides distansion
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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 identifiable 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 cell count of 22,000 cells/ul. He was treated with intraperitoneal amikacin and cefazidime with improvement in abdominal pain and cell count downtrended to 2700/ ul on Day four he was discharged with continued IP antibiotic administration. He was re-admitted in two days for worsening abdominal pain with a cell count of 14,000/ ul. Patient had been correctly administering IP antibiotics with the assistance from his family members. CT abdomen pelvis with intravenous and oral contrast showed small bowel ileus likely due to the peritonitis. At this time the peritoneal catheter was removed and he was converted to hemodialysis. The peritoneal fluid cultures on Day 7 revealed Eggertghella Lenta and Parabacteroides distansion. After a straight Tenckhoff PC, his initial PD fluid culture prior to transfer from outside hospital was positive for Candida parapsilosis and Bacteroides distansion. Sensitivities were reported for only Eggertghella Lenta and Parabacteroides species and they were both sensitive to metronidazole. Antibiotics were broadened to intravenous vancomycin, cefazidime and metronidazole with clinical improvement in his abdominal pain and ileus. He was discharged with continued IP antibiotic administration.

Discussion: To our knowledge, this is the first case of bacterial peritonitis from Parabacteroides species and Bacteroides Distansion. There is only one case report of Eggertghella Lenta causing PD peritonitis and in this case extracorporeal removal was slow growing and this highlights the potential need for anarobic coverage in PD peritonitis without early pathogen isolation and/or failure of initial empiric treatment.
A Rare Case of Trichoderma-Related Peritonitis in a Patient on Peritoneal Dialysis
Ramya Bachu, Stefan C. Hemmings, Suman Siddamreddy. Baptist Health - UAMS Medical Education Program, North Little Rock, AR.

Introduction: Trichoderma 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 white 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 rebound tenderness, rigidity, and guarding. 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 Trichoderma 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, thrush-like plaques all over the peritoneum. IV amphotericin B was added to inpatient antifungal regimen. However, he continued to deteriorate and elected to go home on hospice and passed away soon after.

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 Trichoderma spp have shown resistance to fluconazole and 5-fluorocytosine but show intermediate susceptibility to Amphotericin B, Itraconazole, Ketocanozole 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 infection. More research is needed to guide early diagnosis and guide effective treatment of this rare fungal disease with high mortality.

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

Underline represents presenting author.
the identification of novel molecular biomarkers of peritoneal EMT may facilitate the diagnosis and management allowing early initiation of treatment targeting peritoneal fibrosis. Hylaroranon (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 expression in peritoneum of ESRD patients.

Methods: Peritoneal MCs isolated from overnight dwells dialysates 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 (Ibogen, 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 and in their isoforms determined 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-SMA, and fibronectin were ameliorated by siHAS2, but not by siHAS1. HAS inhibitor induced changes in cell morphology and the expression of E-cadherin, TGFβ1 and α-SMA, and fibronectin were ameliorated by siHAS2, but not by siHAS1. HAS inhibitor (4-methylumbelliflorone; 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 4 weeks in mice. The numbers of TGFβ positive cells, a smooth muscle actin (αSMA) or F4/80 positive cells were significantly decreased in Am80 treated group. KLF5 was expressed in αSMA, F4/80 or CD31 positive cells. Western blotting for KLF5 showed the tendency that KLF5 expression was decreased in higher concentration of Am80 in mouse fibroblasts stimulated by TGFβ1-in vitro.

Conclusions: These results indicate the KLF5 might not only associate phenotypical differentiation from fibroblasts to myofibroblasts but also regulate inflammatory responses and angiogenesis. Am80 is a promising 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 PLL 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 from January 2014 to December 2019. PPC was calculated as dividing 24h dialysate protein loss by serum total protein. LBMI was assessed by BIA and LBMI was calculated dividing LBMI by body height square. 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±0.8, nGFR 6.7±4.1 mL/min/1.73m2 and D/P creatinine ratio 0.63±0.01. The median PPL and PPC were 5.2(3.8-6.7) g/day and 0.5(0.3-0.7) mL/min/1.73m2, respectively. PPC was significantly positively associated with LBMI (r=0.401, P=0.001) and BSA (r=-0.327, P=0.007), but not with BMI (r=-0.109, P=0.381). Compared with conventional body indexes, LBMI had better performance in predicting higher PPC. Multiple linear regression model, when adjusted for gender, nGFR (PD), and diabetes, showed that older age (β=0.288, P=0.018), higher D/P creatinine ratio (β=-0.232, P=0.050) and higher LBMI (β=0.334, P=0.014) were independent predictors of PPC.

Conclusions: Higher LBMI is a marker of better nutritional status, which is associated with better survival in PD patients. In this study, higher LBMI was independently associated with higher PPC, partly by explaining conflicting results on the impact of higher PPC 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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1Plantin, support patient questionnaire, we used logistic regression to analyze binary outcomes employment (full- or part-time versus unemployed), depression (CES-D a10 vs. <10), and functional status (a11 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: 7.4-11.2]) 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 difference of 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 baseline patients and 532 (19%) PD and 573 (22%) HD patients were lost to follow-up due to 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 if either PD or HD on 12 months. This information, when shared with patients choosing a dialysis modality, could result in an increased uptake of PD.

Funding: Commercial Support - Global support for the ongoing DOPPS Programs is provided without restriction on publications by a variety of funders. For details see https://www.dopps.org/AboutUs/Support.aspx

PO1293
H2S May Inhibit Peritoneal Dialysis-Related Fibrosis Through the Sulfhydrylation Regulation of PSMA7
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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, low 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 that H2S may affect the fibrosis by regulating the level of sulfhydrylation, 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 inhibitor PAG group. The expression of pyroptosis associated proteins, inflammatory factors and fibrosis related pathways in different groups were compared. The changes of protein sulfhydryl sulfhydration level were analyzed by HPLC/MS/MS. The target protein and related pathway protein were up/down regulated by siRNA and the 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-smad3). 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 plasmids. The expression level of NLRP3 was up/down regulated 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.

POI1294
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 subscale of KDQOL-SF. Cox proportional hazard models were fitted to examine the association between fatigue and 12-month mortality.

Results: We included data from 1,388 PD patients (mean age 58.5±15.4 years, 64% had RRF). 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.

POI1295
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.

Methods: All patients were in the ICU with COVID related hypoxic respiratory failure and acute kidney injury (AKI). 635 patients who received PD were treated for 16 hours per day in the prone position to improve oxygenation. The mean age was 54.6. The average BMI was 35.5. Patients were on mechanical ventilation 12-33 days. 3/6 patients were on CVVH however, switched to PD due to clotting. Patients were on PD for an average of 9.3 days. All PD catheters were placed at the bedside using an open cut down technique. PD was started the same day using manual exchanges. Dwell volume was gradually increased to 2 L. Exchanges were performed q1h while supine and q2h while prone, a total of 4-6 exchanges/day. The PD team coordinated timing with the prone team and ICU nurses to allow the continuation of the PD treatment. Patients were monitored clinically for abdominal distention and changes in respiratory mechanics.

Results: All 6 patients remained on PD for the duration of the hospitalization. There were no incidences of bowel injury, hemorrhage, exit-site infections, or peritonitis. None of the patients had any catheter malfunction. Leaking was addressed with temporarily reducing the dwell volume. Patients experienced slow draining which was due to kinking of the tubing during prone positioning. All patients were able to continue receiving PD without interruptions. Either no change or improvement in ABG and ventilator settings was noted after prone positioning and PD.

Conclusions: Due to COVID related surge, we saw a significant number of patients in the ICU with severe acute respiratory failure requiring prone positioning who also developed AKI requiring RRT. We were able to successfully provide acute PD in ventilator-dependent prone patients suffering from CRAKI. This required a team effort and some modifications in the conventional PD prescription.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author. 426
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 episode 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 55.4±15 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.

Funding: Government Support - Non-U.S.

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%). Multivariate 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.
PO1301
Plasminatic 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 2.1±0.37 mg/dL and high-sensitivity C-reactive protein (hs-CRP) 10.8±4 mg/L. 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 poorer nutrition, increased fat mass and inflammation. Dietary effects are also well described in relation to obesity in PD. In conclusion, hypoMg appears 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 observed lowest detectable level of bacterial contamination by ten-fold dilution.

**Results:** The lowest detectable concentrations of bacteria are summarized in Table 1. The true Limit of Detection (LoD) for each species is between 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 platelets 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 (54.2%); 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.

**PO1304**
Quality Improvement Initiative: Suboptimal Utilization of Loop Diuretics in Peritoneal Dialysis Patients
Zeynala Al hadhrami, Omar M. Ghadieh, Edward A. Biersc, Queen’s University, Kingston, ON, Canada.

**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/24 hrs when increased altrilfiltration 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, mean ± SD, range), and the proportion of pts on diuretics when PD volume status was controlled.

**Results:** Of 428 patients, 213 pts received loop diuretics (50%). The mean total daily dose of loop diuretics was 107.6 ± 102.4 mg/day (range 0 – 1360 mg/day). The proportion of pts on loop diuretics was 59.5% in pts with urine output ≥ 200 mL/day vs 25.9% in pts with urine output < 200 mL/day (p = 0.0001).

**Conclusions:** Loop diuretics are used suboptimally in PD patients. The algorithm developed in this study can guide the rational use of loop diuretics in PD patients.
frequency) and the pill count before and 3 months after the intervention. In the algorithm, Furosemide prescriptions of 40 mg tablets were 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 27 %, OD 73 %, and median 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.

PO1305
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 examination. Mean age was 55 ± 15, 28% were female, 15% 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.

Funding: Commercial Support - Satellite Healthcare

PO1306
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.

PO1307
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 15.0, 28.2, 34.7, and 69.6/1000 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.
Methods: We have reviewed electronic charts of patients on PD in the last 8 years in our hospital. We compared 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 peritonitis.

Results: The median follow-up was 36 (17,71) 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=0.022). Initial 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 peritonitis (17.6% 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. The choice of DMTs varied from 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 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 60%, and 46% prone for a home therapy). Early referral (>12 m. in clinic before DMT started): 51%. Aids used included written information (97% of pts), DVD in 27% and HD/Peritoneal Dialysis - 2

PO1311

Peritoneal Dialysis in the Setting of Acute Brain Injury, an Underappreciated Modality

Elaina Wang,2 Ankur Shah.1 1Brown University Warren Alpert Medical School, Providence, RI; 2Division of Nephrology, Rhode Island Hospital, Providence, RI.

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 CCPD 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 tenkoff catheter, we had to make PD for peritoneal dialysis. We continued 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 ischaemia 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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Background: 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.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only Underline represents presenting author.
Blood Urea Nitrogen/Creatinine Ratio and Mortality in Patients on Peritoneal Dialysis
Xianfeng Wu, Junnan Wu, Niansong Wang. Affiliated Sixth People’s Hospital, Shanghai Jiao Tong University, Shanghai, China.

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 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 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 NYHA 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.

PO1314
Abstract Withdrawn

PO1315
Between Gradients and Ratios
Nidrit Bohra, Abigayle Sullivan, Haseeb Chaudhary. Reading Hospital, Reading, PA.

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 pleuropertitoneal 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.

Discussion: Previous reports have concluded that the incidence of pleuroperitoneal fistula is higher in PD patients compared to the general population. The incidence of pleuroperitoneal fistula in patients on CAPD has been reported to range from 0.05% to 1%. The incidence of hydrothorax in PD patients has also been reported to be 0.05-0.12%.

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).
POI1318

Ochrobactrum Peritonitis in Peritoneal Dialysis: A Rare Case and Literature Review

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Introduction: Ochrobactrum are gram-negative facultatively anaerobic, motile bacilli typically isolated in aqueous environments. Reported 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 Antiropi peritonitis and review the literature on similar cases.

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 effluent culture. He was empirically initiated on intraperitoneal ciprofloxacin and no other previous PD complications. A peritoneal effluent sample showed 347 nucleated white blood cells. He was empirically initiated on intraperitoneal ciprofloxacin and fluconazole, and he completed the antibiotic course with resolution of symptoms and peritoneal leukocytosis.

Discussion: We present the 8th case of Ochrobactrum Anthropsi peritonitis in a peritoneal dialysis patient. Zero of the published cases were associated with bacteremia. Attempted treatments have typically included carbapenems, aminoglycosides, gentamicin, 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.

POI1317

Late Onset of Sweet Hydrothorax: A Rare Complication of Peritoneal Dialysis

Amel L. Taha, Tyler Andrea, Swati Arora, Harry K. Williams, Bhavna Chopra. Allegheny General Hospital, Pittsburgh, PA.

Introduction: Peritoneal dialysis (PD) has a variety of complications, with diaphragmatic leak causing pleural effusions occurring in 1.6% of cases within 30 days of initiation of PD. We present a case of late-onset right sided pleural effusion, 14 months after initiation of PD, due to spontaneous pleuro-peritoneal leak and the course leading to this rare diagnosis.

Case Description: A 34-year-old female with polycystic kidney disease, bilateral native nephrectomies, and failed kidney transplant receiving PD presented with three days of right sided chest tightness and shortness of breath associated with ultrafiltration failure on PD. Chest x-ray on admission showed a large right-sided pleural effusion (Figure 1A). The patient received PD using 2.5% dextrose dialysate. 2 hours after catheter placement was performed with placement of a chest tube. Fluid analysis revealed a transudative effusion, with glucose of 322 mg/dL with corresponding plasma glucose of 147 mg/dL, consistent with dianeal solution in pleural space. Figure 1B demonstrates passage of the radiotracer from the peritoneal cavity (B) to the pleural space (A), suggestive of right-sided pleuro-peritoneal fistula (C). PD was discontinued and the patient was transitioned to hemodialysis (HD).

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.
patients who are asymptomatic i.e. without abdominal pain or cloudy dialysate effluent. We will be able to detect elevation of their effluent dialysate, tailored at the time when 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 strips 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 61.4 (± 14.7) 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?

Adil Ghaffar, Laura J. Maursetter, Neetika Garg. University of Wisconsin System, Madison, WI.

**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 and Dialysis 20 years ago was referred to our clinic to have VZV encephalitis evaluated. Lumbosacral 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 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 admission, 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 in these patients to use these strips at home to help rule out PD-related peritonitis in a more efficient manner.

**Conclusion:** Our patient’s neurologic symptoms started after an inappropriately high dose of valacyclovir, and low protein binding, valacyclovir is highly dialyzable. Hemodialysis can be helpful in these patients to use these strips at home to help rule out PD-related peritonitis in a more efficient manner.

PO1321

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 (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:** 15237 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 associated with all-cause mortality.

**Results:** 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

PO1322

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 organisms, mitochonric acid (MA-5), which is the active form of the plant homoeoindole-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/6 mice. MA-5 was administrated at 2 mg/kg by gavage every day. Control mice received only a vehicle
Longitudinal Changes in the Use of Peritoneal Dialysis Assistance for Patients Maintained on Peritoneal Dialysis

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Background: Home dialysis therapies such as peritoneal dialysis (PD) offer flexibility and improved wellbeing for older individuals. However, a substantial proportion require assistance with personal care and health self-management. The study objective was to assess the nature of, and need for, assistance with PD management tasks changes over time. We hypothesized that patients and families would require less assistance as they become more familiar with PD management.

Methods: Using a multicentred, prospective observational study design, we recruited patients aged ≥50 years initiating PD. Patients underwent formal evaluation at baseline using validated components of a Comprehensive Geriatric Assessment. They then completed a monthly questionnaire for 6 months about their need for assistance with PD management tasks.

Results: 111 patients (age 69 ± 10 years, 68% male, 56% diabetic) were followed for a total of 609 patient-months. Assistance for PD management tasks remained generally stable throughout follow-up, and did not vary according to age, frailty, functional dependence or cognitive impairment. The proportion of patients needing assistance varied widely across the 13 different PD management tasks, but the proportion of patients needing help for each task remained relatively stable across time (Figure 1). Of those who needed assistance, 40% had help from a family member and 33% were helped by nurses. The family/nurse caregiver ratio for the different tasks did not change over time.

Conclusions: Our results suggest that MA-5 alleviates peritoneal fibrosis with the reduction of macrophages infiltration. Thus, MA-5 may have a therapeutic potential in the progression of peritoneal fibrosis as well as kidney disease models.

PO1325

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 (CVD), and vascular access (VA) related) would be related within 6 months, 1 year, 3 years, and 5 years would be assessed.ITT analysis based on patients' first AVF or AVG placed 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%) had AVF placed and 9,043 (23.9%) 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 than AVG (RR 0.75 (95% CI: 0.71 - 0.80) 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; 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.

PO1326

Implementing Multidisciplinary Pre-ESRD Program to Improve Vascular Access in New-Start Dialysis Patients

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Background: Tunneled 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.

Initial Vascular Access

<table>
<thead>
<tr>
<th>Access Type</th>
<th>2013 (%)</th>
<th>2017 (%)</th>
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<tr>
<td>TDC Only</td>
<td>54</td>
<td>49</td>
</tr>
<tr>
<td>AVG Only</td>
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<tr>
<td>PD Only</td>
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Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
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/AVF 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 PV A 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, AVF patients improved serum albumin by 0.33 gram/dl (p=0.001) 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<0.0003, 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 Venogram 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 based 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 in 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

William Weitzel,1,2 Nirmala Rajaram,1,2 Lenar T. Yessayan,7 Yihao Zheng,3 Brian Thelen,1,4 Timothy Morgan,1 James Hamilton,1 Miguel A. Funes-Lora,2 Veterans Affairs Ann Arbor Health System, Ann Arbor, MI; 3University of Michigan, Ann Arbor, MI; 4Worcester Polytechnic Institute, Worcester, MA; 5Michigan Technical Research Institute, Ann Arbor, MI.

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
data provides a contact-free method to ascertain \( Q_a \) and to indirectly indicate the degree of stenosis. Further study is needed to standardize the quality of video and streamline the methodology.

POI1330

Relationship of Vascular Access Flow and Stenosis Detected by Frequency Domain Analysis of Videos Taken with a Smartphone

Fansan Zhu, Lin-Chun Wang, Alhajj Cherihi, Vaibhav Maheshwari, Ohnmar Thwin, Lela Tisdale, Xia Tao, Paulo Paneque Galuzio, Norbert Sataninberg, Dean C. Preddie, Peter Kotanko,renal Research Institute, New York, NY; AzuraVascular Care, New York, NY; Icahn School of Medicine at Mount Sinai, New York, NY.

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 (\( Q_a \)) with 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). \( F_{\text{Max}} \) and \( F_{\text{Min}} \) were 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 (\( F_{\text{HR}} \)).

Results: The differences between \( F_{\text{Max}} \) and \( F_{\text{HR}} \) were 1.14±0.74 Hz and 1.38±1.44 Hz, respectively. \( \Delta F \) was associated with \( Q_a \) pre- (Fig 1(a)) and post-intervention (Fig 1(b)). \( \Delta F \) increased most when \( Q_a \) increased from pre- to post-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 \( \Delta F \) between pre- and post-intervention. The difference between \( F_{\text{Max}} \) and \( F_{\text{HR}} \) was associated with % stenosis (Fig 1(d)).

Conclusions: The relationship between \( F_{\text{Max}} \) and \( F_{\text{HR}} \) suggests that the signal of \( F_{\text{Max}} \) represents an important hemodynamic component of \( Q_a \). \( \Delta F \) may be used as an index to predict low levels of stenosis. The use of frequency domain analysis from video image

POI1332

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 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 therapy group including only patients who received the drug for 30 days or more. The primary outcome was the primary patency of VA. Effect of nitrate treatment was examined using Kaplan Meier analysis and Cox proportional hazard, after adjusting for covariates.
Results: A total of 7,428 participants were included in this study, and nitrate therapy was noted in 7.7% of total patients. 1,178 patients demonstrated an increase in circulating immune cells. After ANCOVA analysis, nitrate therapy was lower proportion of angioplasty than non-user (log-rank, P<0.001). The risk of angioplasty was low in patients receiving mononitrate and nicorandil (hazard ratio (HR) 0.18, [95% confidence interval 0.07-0.43]; HR 0.15, [0.06-0.41]). But, nitrates and molsidomine were not associated with the risk of angioplasty. Multivariate Cox proportional analysis revealed that nitrate therapy with mononitrate and nicorandil had a decreased risk of angioplasty after adjustment for age, sex, hypertension, and diabetes (HR 0.17, [0.05-0.53]; HR 0.14, [0.04-0.45]).

Conclusions: We conclude that while using Ticagrelor in patients with ESRD on HD is safe, the 3 patients demonstrate a therapeutic superiority in preserving the patency of AVF using this drug compared to placebo. This study is limited by the number of patients and more studies may be warranted in the future.

Funding: Commercial Support - AstraZeneca

Outcomes

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Platelets</th>
<th>Ticagrelor</th>
<th>Placebo</th>
<th>Δ platelets (µL/mm^3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention period</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 week</td>
<td>15,180</td>
<td>15,985</td>
<td>15,180</td>
<td>0.00</td>
</tr>
<tr>
<td>2 weeks</td>
<td>15,180</td>
<td>15,985</td>
<td>15,180</td>
<td>0.00</td>
</tr>
<tr>
<td>3 weeks</td>
<td>15,180</td>
<td>15,985</td>
<td>15,180</td>
<td>0.00</td>
</tr>
<tr>
<td>4 weeks</td>
<td>15,180</td>
<td>15,985</td>
<td>15,180</td>
<td>0.00</td>
</tr>
<tr>
<td>5 weeks</td>
<td>15,180</td>
<td>15,985</td>
<td>15,180</td>
<td>0.00</td>
</tr>
<tr>
<td>6 weeks</td>
<td>15,180</td>
<td>15,985</td>
<td>15,180</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Over 10 weeks of treatment, there was no significant change in platelet counts between the Ticagrelor and Placebo groups. However, a slight decrease in platelet counts was observed in the Placebo group compared to the Ticagrelor group.

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 needle 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 were 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 dislodgements were recorded in the hemodialysis unit room during the first three months. In the study period, we conducted the integrated program and reduced the incidence of needle removal and blood leakage.

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.

Methods: This was an observational study examining 35 patients receiving chronic hemodialysis with PHA using 15-g needles for ≥3 months. Control patients were randomly selected from the dialysis unit and 1:1 matched for age, sex, and race. The mean age of patients was 73 yrs, 97% were males, 63 and 31% were Whites and Blacks, respectively. The mean (SD) hemoglobin concentration and platelet count were 10.4 (1.0)g/dL and 184 (77)×10^9/L, respectively. Sixty and 74% of patients were on oral antplatelet agents and intradialytic heparin. The mean (SD) BT after arterial and venous needle removal with additional (2-1) minutes increments, if needed. The mean BT for arterial and venous sites were calculated for each patient over 1-month period. Associations between BT and baseline characteristics were evaluated using adjusted regression analysis.

Results: The mean age of patients was 73 yrs, 97% were males, 63 and 31% were Whites and Blacks, respectively. The mean (SD) hemoglobin concentration and platelet count were 10.4 (1.0)g/dL and 184 (77)×10^9/L, respectively. Sixty and 74% of patients were on oral antplatelet agents and intradialytic heparin. The mean (SD) BT after arterial and venous needle removal with additional (2-1) minutes increments, if needed. In the adjusted analyses, there was a strong correlation between arterial and venous BT (r2 = 0.98, p<0.016), however, no correlations were seen between arterial and venous BT and any baseline variables (Tables).

Conclusions: In this study, BT after dialysis needle removal was between 10 and 15 min in patients with stable PHA. Future studies are needed to understand what changes in BT may predict PHA dysfunction.
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 (NIH). 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 peripherally 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 NIH 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 (4.20-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 NIH 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.

PO1338

Geometry and Interuser Variability of Arteriovenous Fistulas in Mice and Rats

Hannah M. Northrup1, Isabelle D. Falzon,1 Savanna Cahoon,1 Yan-Ting E. Shiu,1 Maheshika S. Somarathna,2 Timmy C. Lee,1,2 1University of Utah, Salt Lake City, UT; 2Veterans Affairs Medical Center, Birmingham, Birmingham, AL.

Background: Arteriovenous fistula (AVF) maturation failure is a significant and unresolved clinical issue. Although rodent models have been used extensively to investigate the pathology and treatment of AVF maturation failure, the literature has largely relied on histology to analyze rodent AVF remodeling. Information regarding three-dimensional (3D) AVF lumen geometry in live animals is lacking. Our group has developed a magnetic resonance imaging (MRI)-based protocol to quantitatively characterize 3D AVF lumen geometry in mouse and rat AVFs. Inter-user variability was also determined.

Methods: Carotid-jugular AVFs were created in C57BL/6 mice (n=21). Femoral AVFs were created in Sprague Dawley rats (n=7). Both had the arterial-side-to-venous-end configuration. Black blood MRIs were taken at 7 or 21 days post-AVF creation. Two users reconstructed the AVF lumens and computed the cross-sectional lumen area, anastomosis angle, nonplanarity angle magnitude, and tortuosity, using a centerline-based approach.

Results: Mice had a greater anastomosis angle (94.29° vs. 38.75°) and tortuosity (0.42 vs. 0.035) than rats (p=0.05). The nonplanarity angle magnitude was similar for mice and rats (~8.5°). Geometries of mouse and rat AVFs from the two users are overlaid in Figure 1. Inter-user variability were predominately small, indicating the reliability and reproducibility of our protocol.

Conclusions: Our work is the first detailed study of luminal changes in rodent AVFs using MRI. The anastomosis angles of mouse and rat AVFs are similar to human brachioccephalic AVFs (~70-90°) and radiocephalic AVFs (~30-60°) in the literature, respectively. These data support the clinical relevance of our rodent AVF models and set the stage for future studies on how these geometrical parameters affect AVF maturation and the mechanisms leading to geometrical changes.

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

PO1339

Longitudinal Geometry of Pig Arteriovenous Fistulas (AVFs)

Savanna Cahoon,1 Isabelle D. Falzon,1 Yan-Ting E. Shiu,1 Alfred K. Cheung,1,2 University of Utah, Salt Lake City, UT; 2VA Salt Lake City Health Care System, Salt Lake City, UT.

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 magnitudes 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 6 wk. 0.10 of the proximal artery (24.0 ± 17.3 mm² vs. 28.0 ± 5.60 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 ± 0.06 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 radioccephalic 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

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 (AVF) 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 groups were 152 versus 137 (P-value = 0.57) for AVF 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 AVF 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 DCC group could be the reason for this observation.

Target Lesion Patency Outcomes

<table>
<thead>
<tr>
<th>Type of Access</th>
<th>Diameter of Lesion (mm)</th>
<th>Drug Coated Balloon</th>
<th>Non Drug Coated Balloon</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVF</td>
<td>5.2</td>
<td>2.1</td>
<td>3.4</td>
<td>0.01</td>
</tr>
<tr>
<td>AVG</td>
<td>5.0</td>
<td>2.1</td>
<td>3.4</td>
<td>0.01</td>
</tr>
</tbody>
</table>

PO1343

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, Stephan Thijsen, 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 (FMG, 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 eUBBB provide shorter 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>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient 1</td>
<td>2.0</td>
<td>66.4±1.5</td>
<td>66.4±1.7</td>
<td>0.12</td>
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<tr>
<td>Patient 2</td>
<td>2.4</td>
<td>63.5</td>
<td>63.8±1.8</td>
<td>0.05</td>
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<tr>
<td>Patient 3</td>
<td>7.9</td>
<td>71.8±0.6</td>
<td>71.9±0.6</td>
<td>0.06</td>
</tr>
<tr>
<td>Patient 4</td>
<td>13.6</td>
<td>66.8±0.8</td>
<td>67.4±0.2</td>
<td>0.01</td>
</tr>
<tr>
<td>Patient 5</td>
<td>13.7</td>
<td>64.6±6.4</td>
<td>64.6±6.4</td>
<td>0.01</td>
</tr>
</tbody>
</table>

*Patient 2 had only the average of 1-week assessments prior intervention. Data are expressed as mean, standard deviation, minimum and maximum values.

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>2.8±1.2</td>
<td>10.9±4.7</td>
<td>0.09</td>
</tr>
<tr>
<td>30</td>
<td>2.1±1.1</td>
<td>11.9±6.7</td>
<td>0.01</td>
</tr>
<tr>
<td>60</td>
<td>2.3±1.5</td>
<td>11.6±8.5</td>
<td>0.04</td>
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<tr>
<td>90</td>
<td>3.5±1.5</td>
<td>12.2±2.9</td>
<td>0.06</td>
</tr>
<tr>
<td>120</td>
<td>3.3±1.5</td>
<td>13.3±4.2</td>
<td>0.01</td>
</tr>
<tr>
<td>180</td>
<td>3.2±1.5</td>
<td>13.5±3.5</td>
<td>0.01</td>
</tr>
</tbody>
</table>

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, brachybasilic 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 arteriostomy 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 an 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 (Gupta), George M. Feldman,1 Naveen Samuel,1 Reuben P. Retnam,2 Dipankar Bandypadhyay,2 Shobha Ghosh,1,2 Hunter Holmes McGuire VA Medical Center, Richmond, VA; 1Virginia 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
Assessment of Arteriovenous Fistula Dysfunction with Access Stenosis in Hemodialysis Patients Using Smartphone Videos

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Background: Hemodynamically relevant stenoses in arteriovenous fistulas (AVF) lead to a reduction in access flow rate (Q_a). 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 Q_a measurements were conducted before and after the intervention by an iPhone 6S. Q_a was measured by HVT100 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±14 years, HD vintage 4.1±3.5 years). Post-intervention Q_a (1638±714 ml/min; P<0.01, paired t-test) was on average 1.23-fold higher than pre-intervention Q_a (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 Q_a 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.
Efficacy and Long-Term Patency of Kissing Stent Technique for Endovascular Reconstruction of the Axillary Vein: A Case Report with Long-Term Follow-Up
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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 use of kissing stent technique (KST) to reconstruct the AXV.

Conclusions: KST for EVR of the Axillary vein is technically feasible and has long term efficacy.

Funding: Other U.S. Government Support

Partially migrated stent

Conclusions: KST for EVR of the Axillary vein is technically feasible and has long term efficacy.

Funding: Private Foundation Support

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 (0.8% 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
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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 or standard of care alone. There were no statistically significant differences in the baseline demographics and data between the two groups except for ethnicity (p<0.017). Patients were followed on average for 15.2 months. There were significantly less per patient thrombotic events (Poisson rate) in the surveillance group (0.12/patient) as compared to the control group (0.23/patient) (p=0.012). There was no significant difference in total number of procedures 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 a 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

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,1 Alissa Kapke,1 Jeffrey Pearson,2 Adebola O. Adeleye,2 Delia Houselaw,3 Eric W. Young,4 1Arbor Research Collaborative for Health, Ann Arbor; 2Centers 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-FFS) to all ESRD patients, revised numerator 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.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Results: We identified 425 individuals on HD. Of these, there were 141 ambulatory TTEs, of which 64 TTEs 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 TTEs, 19 had one or more parameters indicating RVD. Select findings with bivariate analysis are presented in Table 1. Continuous variables are expressed as means (S.D.) and analyzed by ANOVA. By multivariate logistic regression, diastolic vantage <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 TTEs 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

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>RVD Positive</th>
<th>RVD Negative</th>
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</thead>
<tbody>
<tr>
<td>Age</td>
<td>65 ± 12</td>
<td>70 ± 15</td>
</tr>
<tr>
<td>Gender</td>
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<td>50% Female</td>
</tr>
<tr>
<td>Blood Pressure</td>
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<td>120/80</td>
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<tr>
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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 HDU personnel 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 the 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 patients’ feedback, knowledge and needs, and also on practice guidelines and best practice recommendations from CDC, KDOI, and ORN. Nursing education involved updating nursing policies, and a nursing catheter care certification program. 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 “infection 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 who had received enough teaching about catheter care knew how to keep catheter clean and dry, recognize complications and not adjust catheter by themselves. Eighty-nine percent of patients found the education/training easy to understand and feasible tool to help patients understand proper care of their dialysis catheters.

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 Tunned Dialysis Catheters with Exposed Cuff and Risk of Subsequent Catheter-Related Bloodstream Infection

Zachary J. Bauer, Aecan Hana, Christopher Kassab, Amulya Rajagopal, Lalathaksha Murthy Kumbar. Henry Ford Hospital, Detroit, MI.

Background: Tunneled dialysis catheters (TDC) are prevalent in patients with end stage renal disease (ESRD) on hemodialysis (HD). Exposure of catheter cuff leads to increased 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 included TDCEx 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 CR, 0.64 (95% CI, 0.24-1.14) 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, insignificant 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=0.026]. 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, 0.53-3.51; P=0.442). Catheters with infection compared to TDCEx for mechanical dysfunction had a significantly increased IR at 90 (HR, 2.36; 95% CI, 1.01-5.37; 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

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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 in reducing the risk of CRBSI were assessed.

Methods: From inception to April 2020, we looked for relevant clinical controlled trials in the following databases: EBSCO, PubMed, Cochrane CENTRAL, MEDLINE, EMBASE, clinicaltral.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=0.0001). 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.

CR

PO1353

The Catheter Tip Position as the Main Non-Infectious Cause of Catheter Replacement Survival

Joan G. Navarro gallery, 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). Novel anatomic variables analyzed

Methods: Our objectives: Identify risk factors associated with CR. The Cath were placed guided by ultrasonus (US). We analyze age, gender, height, previous number of blood punctures, jugular vein (JV) collapsibility, lab tests, blood pressure, 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 (UCID), JV and Carotid diameter and distance between JV 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

PO1354
NitriCap Hemodialysis Catheter Insert to Prevent Catheter-Related Bloodstream Infection

Background: Tunneled 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 weeks to assess its bacteriocidal activity.

Methods: Two cm long inserts using S-nitrosoglutathione (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 (NitriCap) 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 with NO releasing inserts (NitriCap) and in sheep for two weeks to assess its bacteriocidal effects.

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 AVG, 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 dependency was similar between A VF and A VG, 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 dependency was similar between A VF and A VG, respectively, at 1m after placement; 23.3% vs 64.3% at 3m; 16.4% vs 28.9% at 6m; >3.4 cm CR

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.

PO1355
Catheter Dependency After Vascular Access Placement Among Elderly Patients on Hemodialysis: An Intention-to-Treat Analysis

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 that 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 AVG, 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 dependency 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 groups (24.8% in AVG vs 27.8% in AVG by 12m; 42.4% in AVG 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.
is associated with adverse events such as bloody shunting, internal hemorrhage, and hypotension.

Methods: This is a single-center, retrospective study of patients treated for HD catheter dysfunction. The medical records were reviewed for demographic data, catheter dysfunction symptoms, and outcomes.

Results: A total of 159 HD catheter dysfunction cases were identified. The most frequent symptoms were hematoma (52.8%) and malposition (40.7%). The primary interventions were removal (51.8%) and mobilization (27.8%). The mean catheter dysfunction duration was 14 days. The catheter survival rate was 65.7% after a year.

Discussion: HD catheter dysfunction is a common complication. Early recognition and appropriate management can improve patient outcomes. The choice of intervention should be guided by the severity of the complication and the patient's clinical status.

PO1358

Use of Diphenhydramine as Adjutant to Conscious Sedation in Patients Undergoing Interventional Nephrology Procedures

Background: Benzodiazepines and opioids are commonly used for conscious sedation during interventional nephrology procedures but are associated with adverse events such as bradycardia and respiratory depression. We are proposing to use Diphenhydramine as adjutant medication to decrease the required dose of benzodiazepine and opioid.

Methods: We compared patients who received conscious sedation with IV midazolam and IV fentanyl as per standard practices to patients who received IV diphenhydramine prior to IV midazolam and IV fentanyl. Level of sedation was managed as per guidelines of moderate sedation. Data collected included baseline patient characteristics, dose of midazolam and fentanyl used, 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 conscious sedation. Demographically the diphenhydramine use significantly reduced midazolam (2.2 mg vs 2.88 mg, p value <0.001) and fentanyl (88.2 mcg vs 102.07 mcg p value 0.005) dose requirements during procedures. It was not associated with increased rates of bradycardia and hypoxia. When comparing who administered sedation, physician administered sedation was associated with lower midazolam (2.18 mg vs 3.37 mg, p value < 0.001) and fentanyl (09.29 mcg vs 105.97 mcg, p value 0.04) dose 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.
PO1361
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) 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 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 passed 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 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 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 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).

Discussion: DSS is a rare malformation which may impact the preference of dialysis access site and type in ERSD 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.

PO1362
Missed Central Venous Stenosis Causing Unilateral Arm Swelling
Sylvester Barons, 1,2 Loyola University Health System, Maywood, IL; 3 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.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Discussion: These two cases showed that prolonged dialysis access thrombosis can be complicated with arterial embolic events that require high suspicion and immediate treatment.

POI1364
Associations Between Length of Dialysis Facility Ownership and Vascular Access
David T. Gilbertson,1,2 Yi Peng,1,2 William Eggert,1,2 Mahesh Krishnan,3,4Chronic Disease Research Group, Minneapolis, MN; 2Hennepin Healthcare Research Institute, Minneapolis, MN; 3DaVita HealthCare Partners, Denver, CO.

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

% of Patients With a Catheter ≥90 Days

<table>
<thead>
<tr>
<th>% of Patients With a Catheter ≥90 Days</th>
<th>Year Prior</th>
<th>Year Acquired</th>
<th>Year After</th>
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<td>11.4%</td>
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<tr>
<td>Not owned by LDO</td>
<td>12.0%</td>
<td>11.8%</td>
<td>12.0%</td>
</tr>
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</table>

% of Patients With AV Fistula in Use

<table>
<thead>
<tr>
<th>% of Patients With AV Fistula in Use</th>
<th>Year Prior</th>
<th>Year Acquired</th>
<th>Year After</th>
</tr>
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<tr>
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<td>Not owned by LDO</td>
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POI1365
Data-Backed Multidisciplinary Care Substantially Improves Renal Replacement Therapy Outcomes
Xiuyan Wang,1 Olle Fielding,1 Jung Hoon Son,1 Edward M. Lee,1 Andrew Bohmar,1 Frank Liu,2 Jeffrey L. 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

POI1366
Education and Experience Gained Through Nephrology Business Leadership University (NBLU) Provide Valuable Benefits to Graduating Nephrology Fellows: A Survey-Based Study
Diana Mahbod,1 Manasi Bapat,1 Samir Nangia,1,2 Dallas Renal Group, Dallas, TX; 2Texas Christian University, Fort Worth, TX; 3East 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 fellowship programs 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.
PO1367

Medicine Residents’ Perception of the Nephrology Specialty

Georges Nakhour,1,2 Ali Mehdi,1,2 Jonathan T. 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 Bierer,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 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, 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 greatly 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 Launera,1 Kurtis Pivert,1 Stephen M. Sozio,2 (American Society of Nephrology, Washington, DC; Johns Hopkins University, Baltimore, MD; 1Duke 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 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 greatly 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.

PO1369

Association Between Different Payment Models, Workload, and Job Satisfaction of Nephrologists in Lebanon and Jordan

Mabel Aoun,1,2 Nour Bretche,1 Kassem M. Kassak,1,2 (Saint Joseph University, Beirut, Lebanon; American University of Beirut, Beirut, Lebanon.

Background: The main challenges that nephrologists are facing worldwide are lower income, dissatisfactory payment models, long work hours and burnout. This study aimed to identify factors associated with nephrologists’ satisfaction in Lebanon and Jordan.

Methods: An online survey was sent to all 250 Lebanese and Jordanian nephrologists, including data on demographics, education, academic activities, job satisfaction, burnout, workload and reimbursement.

Results: A total of 59 nephrologists responded. Mean age was 46.9 ±12.5 years, 39% women. Respondents reported low rates of satisfaction in job opportunities (20%), income (25%) and administrative support (32%). On the other hand, 68% reported that nephrology is stressful. High satisfaction rates were found in relationship with patients (78%) and colleagues (73%). Income was significantly higher among males than females (p < 0.001). Satisfaction towards income was significantly lower in females, mean score difference 0.71 ± 0.30 (95%CI: 0.10,1.32; p=0.024). A greater proportion of male over female practitioners wanted to follow above the 40-dialysis-patient regulation (p=0.001) and preferred pay-for-performance over fee for service. Satisfaction with income and work-life balance was positively correlated with age and young nephrologists had significantly lower satisfaction with job opportunities (11%). Driving over 1 hour daily to work was significantly associated with dissatisfaction in work-life balance (p<0.029), stress and burnout (p=0.016). Using regression analysis, longer delay in payment predicted worse work-life balance among Lebanese nephrologists (p=0.04). Compared to male practitioners, female practitioners spent more time on teaching (p<0.001), and more female had academic rank and publications (p<0.001). Gender discrimination was perceived significantly among women.

Conclusions: Unfair and delayed reimbursement is associated with dissatisfaction among the surveyed nephrologists. Gender differences are very significant with lower income and satisfaction rates among women. Similarly, it seems that the younger generation perceives low job opportunities. Decision makers need to urgently empower women, address payment delays conduct market analysis and accordingly regulate nephrologists’ entry to avoid oversupply or unemployment.

PO1370

Evaluating Nephrology Competency in General Pediatrics

Amrit Kirpalani,1,2 Natasha Jawa,1 Charushree Prasad,1 Adelle R. Atkinson,1 Mark E. Feldman,1 Justin M. Jeffers,1 Damien G. Noone,1 (Hospital for Sick Children, Toronto, ON, Canada; London Health Sciences Centre Children’s Hospital, London, ON, Canada; McMaster University Faculty of Health Sciences, Hamilton, ON, Canada; Johns Hopkins University, Baltimore, MD.

Background: General pediatricians may be the first-line providers to care for children with kidney disease, however studies suggest they find nephrology to be a difficult subject. This study aimed to identify areas of lowest perceived competency and importance within nephrology for general pediatricians.

Methods: A web-based survey was distributed to general pediatricians through the Pediatricians of Ontario network to all Pediatrics Residency Program Directors in Canada and Canadian Pediatric Nephrologists in the Canadian Association of Paediatric Nephrologists. Pediatricians were asked to rate nephrology objectives of training on a 5-point Likert scale for perceived competence and importance. Program Directors and Nephrologists were asked for perceived importance of each objective for general pediatricians. Scores were equally weighted using Student’s t-test and mean scores were calculated. Knowledge Gap scores were calculated as the difference between perceived importance and competence scores.

Results: General Pediatricians, 60/350 (17%) responded to the survey. Domains scoring significantly below the mean in terms of competency (2.9/5) and importance (3.2/5), respectively, were kidney stones (2.5 and 2.6), AKI (2.5 and 2.4), CKD (1.9 and 2.1), Tubular disorders (1.8 and 2.0), and kidney transplant (1.6 and 1.7). Hypertension had the most significant knowledge gap score (0.8/5, 16%, p<0.05). Program Directors.
PO1371
Assessment of Faculty Developed e-Curriculum in Hemodialysis
Namrata Krishnan,1 2 Yale teaching and learning center 1Yale University School of Medicine, New Haven, CT; 2Veterans Affairs Medical Center, West haven, CT

Background: E-learning is gaining popularity in medical education and offers several advantages. We have developed a comprehensive, hands-on online e-curriculum in hemodialysis based on ACGME competency requirements. The curriculum includes two online modules on Hemodialysis kinetics/adequacy; and Hemodialysis access. In this study we assessed the experience among nephrology trainees, of using this e-Curriculum, and assess its effectiveness as a teaching tool.

Methods: This pilot study sample included 11 nephrology fellows (8 from Yale and 3 from other US nephrology programs). Design: A mixed methods approach using a triangulation model. Data collection: A Qualtrics survey was distributed to the participants after curriculum completion. This was followed by a 15 minute zoom interview of each individual participant. This study was approved by our local IRB.

Results: The study sample had an even distribution of participants across all levels of nephrology training, identified as visual learners. Irrespective of the learner type, animated videos were the most desired feature of the E-modules and helped visualization of abstract concepts. Concepts of flux vs. efficiency, convection vs. diffusion, Kt/V, physical examination of an AV fistula, and access recirculation were topics reviewed repetitively. Based on survey data, there was 100 % agreement among the learners that the websites were easy to navigate; the content represented common clinical scenarios and the interactive knowledge testing helped in concept retention and improving student engagement. Statistical analysis (paired t-tests) showed that there was significant improvement in knowledge by the learner in 6 core competencies after module completion (p<0.01). The advantages of an E-curriculum were reported to be simplified visualization of key concepts; excellent clinical application, time flexibility/repetitive review, standardization of content, learner centric approach; and a flipped classroom model. The disadvantages were the lack of community learning and the inability to ask questions immediately.

Conclusions: In conclusion, the hemodialysis E-curriculum was an effective educational platform for nephrology fellows. Although an E-curriculum allows standardized learning with a learner-centric approach, it can cause social isolation and reduced self-motivation. A blended learning approach, combining E-learning and traditional methods may be ideal.

PO1372
Implementation and Assessment of Virtual Standardized Patient Sessions to Teach Communication Skills to Nephrology Fellows During COVID-19
Racquel J. Holmes,1 Jonathan Fischer,1 Jared Lowe,1 Jane O. Schell,2 Samira S. Farouk,2 Matthew A. Sparks,1 Duke Nephrology 1Duke University, Durham, NC; 2University of Pittsburgh Medical Center, Pittsburgh, PA; 1Icahn School of Medicine at Mount Sinai, New York, NY.

Background: Standardized patients (SP) are routinely used in medical education teaching learners how to communicate in traditionally challenging environments like end-of-life discussions or delivery of a difficult diagnosis. Adherence to the need for social distancing during COVID-19 has eliminated in-person SP encounters and necessitated virtual sessions using a video conferencing software. We assessed the impact of virtual, SP-based communication skills workshops on a cohort of nephrology fellows.

Methods: Over two weeks, nephrology fellows were invited to participate in two 90-minute communications workshops with a SP conducted over Zoom. Workshops included a didactic portion and SP interviews simulating difficult conversations. Fellows observed each other and provided feedback during the interviews. A 10-question survey was then distributed to the participants to evaluate the training sessions and compare themselves to analogous in-person communication workshops.

Results: All invited fellows participated in at least one session and completed the survey (100%, 12/12). Five first-year fellows (42%, 5/12), 5 second-year fellows (42%, 5/12), and 2 third-year fellows (17%, 2/12) participated. 67% (8/12) of participants reported that they found the sessions useful. Of the fellows who had attended a prior in person simulation-based workshop (67%, 8/12) with standardized patients, 88% (7/8) rated the virtual session as good as or better than in-person role-playing. 83% (10/12) of participants reported that skills learned during the virtual session would be used in their clinical practice. 83% (10/12) felt observing their co-fellows was useful. Write-in comments indicated a barrier to using virtual role playing was a challenge in recognizing emotion and empathy.

Conclusions: Virtual training sessions with SP actors were rated highly by the fellows and provided an opportunity for them to practice communication skills to incorporate into current practice. The virtual workshops were easily implemented, well-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
Jessica M. Loizides,1 2 Joshua Fogel,1 Sofia Rubinstein,1 2 New York Institute of Technology College of Osteopathic Medicine, Old Westbury, NY; 3Nassau University Medical Center, East Meadow, NY; 2Brooklyn College Department of Business Management, Brooklyn, NY.

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 (IMH) of proper dose adjustment of commonly used rheumatology and allergy/immunology medications for patients with CKD.

Methods: We surveyed 353 IMH 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 (34.0%, 34.0%), ketotifen (82.2%, 92.2%), 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, 99.13, p<0.001), colchicine (OR:3.98, 95% CI:1.00, 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) than 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 IMH 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,1 Ellie Kelepouoris,2 1Medscape Education, New York, NY; 2Drexel University College of Medicine, Philadelphia, PA.

Background: As new therapies for Alport syndrome continue to progress through development, nephrologists require increased understanding of these therapies. The objective of this study was to determine if online education 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. 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, >0.26 considerable). The activity launched online on March 1, 2019, and data were collected through April 3, 2020.

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=0.26 (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= 0.297 (extensive educational impact), P=0.001) 63% demonstrated improved identification of adverse effects for emerging treatments for Alport syndrome (V=0.51 (extensive educational impact), P=0.001), 38% reported increased confidence in understanding role that chronic renal inflammation plays in AS Continued educational gaps: 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
PO1375
Online CME Effectively Improves Nephrologists' Knowledge, Competence, and Confidence Related to Hyperkalemia Management

Methods: The online CME curriculum consisted of 6 activities. Of these, 5 were video-based and used repeated post-assessment questions designed with McNemar’s test ($P < 0.05$ is considered significant) to assess educational effect. The last activity was a medical patient simulation that utilized tailored clinical guidance (CG), based on current evidence and expert recommendation, 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. The activities launched in 2019 and data were collected for up to 12 weeks.

Results: The education reached over 14,000 physicians, including over 3,200 nephrologists. Overall, knowledge improved by 29%, competence 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 competence related to effective use of potassium binders ($P<.001$) 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: The current observations demonstrate that by designing knowledge and competence 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 to 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 Vilor Company

PO1376
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 questions allowing them to make clinical decisions about treatment. Educational effect was assessed using a 4-question repeated pairs pre-post-assessment and McNemar’s chi-squared test questions allowing them to make clinical decisions about treatment. Educational effect was assessed using a 4-question repeated pairs pre-post-assessment and McNemar’s chi-squared test. P values are shown as a measure of significance; $P$ values $<0.5$ 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 ($P=0.05$; $V=0.179$) improved at using a loop diuretic when a low-potassium result of participation in the CME activity. Specific areas of improvements include: 8% of nephrologists ($P=0.05$; $V=0.179$) improved at using a loop diuretic when a low-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 (N=184) 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 euvoletic but had elevated potassium levels.

Conclusions: This study demonstrates the success of an online curriculum with multiple educational components at improving knowledge, competence, and confidence of nephrologists related to hyperkalemia management. Persistent gaps were identified for future educational targets.

Funding: Commercial Support - independent educational grant from AstraZeneca

PO1377
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 post-assessment questions designed with McNemar’s test ($P < 0.05$ is considered significant) to assess educational effect. The last activity was a medical patient simulation that utilized tailored clinical guidance (CG), based on current evidence and expert recommendation, 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. The activities launched in 2019 and data were collected for up to 12 weeks.

Results: The education reached over 14,000 physicians, including over 3,200 nephrologists. Overall, knowledge improved by 29%, competence 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 competence related to effective use of potassium binders ($P<.001$) 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: The current observations demonstrate that by designing knowledge and competence 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 to 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 Vilor Company

PO1378
An Analysis of Scienteometrics and Social Media in Nephrology
Neha G. Vaghiyani,1 Nishi Shah,2 Natsal Lal,3 Tejas Desai,3 Anna Vinnikova,1 Thyrocare Commonwealth University School of Medicine, Richmond, VA; 3NOD Analytics, Charlotte, NC.

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, IASJ 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.

Results: Articles were categorized as ‘highly cited or tweeted’ when they were ≥ 75th percentile of citations or tweets, and ‘less cited or tweeted’ at ≤ 25th percentile.

PO1379
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 life-limiting illnesses (e.g., End of Life Care Pathway-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 ACP materials, and (2) learn without patient wishes to kidney care within 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.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Results: Fifteen intervention participants ages 59-87 were interviewed (10 women, 5 men). The 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 that while the coaching activities of the coaches included problem-solving and prompting change in daily life, participants noted that empathy and problem-solving played 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 be better addressed with their nephrologists if or when the need arose. Future studies should further explore the interrelational of general ACP and CKD-specific care planning.

Funding: Private Foundation Support

PO1380
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, data collection, analysis, interpretation, and dissemination. Patients 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.

PO1381
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 confidence as well as prompting change in daily life.

Methods: The caregiver education was designed as 2 online, interactive activities. Both were comprised of text and visual images, 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 staged 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? Here are Some Tips for Managing Potassium In Your Diet Participants: 35, 889 Completers of all questions (included in outcomes analysis): 4,305 Demographics: 65% female; 63% white, non-Hispanic; 67% over the age of 54; 45% have hyperkalemia, 42% were interested in learning more about the condition and problem-solving; 79% reported increased confidence talking to their doctor about ways to lower their potassium levels Activity 2: Are Medicines That Lower Potassium Right for You? 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 providers about higher than ideal low-protein diet before the follow-up visit; 73% reported increased confidence talking to their doctor about medicines that can treat hyperkalemia

Conclusions: The metrics and outcomes gathered in this assessment are a strong indication 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 - Replysa, a Vifor Company

PO1382
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 providers can be used to develop a better understanding of patients’ diverse disease and treatment beliefs which may ultimately improve the caregiver-patient relationship.

Funding: Private Foundation Support

PO1383
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 We-Chat platform and Specialty 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 and diet to treat hyperkalemia (42% pre to 74% post) Intent-to-act: 69% plan to talk to their providers about higher than ideal low-protein diet before the follow-up visit; 73% reported increased confidence talking to their doctor about ways to lower their potassium levels Activity 2: Are Medicines That Lower Potassium Right for You? 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

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Conclusions: The metrics and outcomes gathered in this assessment are a strong indication 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 - Replysa, a Vifor Company
PO1384
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 eighty (57%) were male, 44 (23%) non-Hispanic Caucasian, 26 (12%) non-Hispanic African American, 26 (12%) other races, and 98 (53%) were Hispanic. Students 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 (2.3 (1.1) to 3.9 (1.6) 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

PO1385
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 we application REDCap to 880 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. Only 6.3% of residents identified a mentor in nephrology. Only 5.8% of residents selected nephrology. Only 6.3% of residents identified a mentor in 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 residency, 75% of respondents rotated in nephrology and the rotation took place during PGY1 for 68% of the respondents. 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

PO1386
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.

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PO1387
Changes in the Demographics and Research Focus of Renal Physician-Scientists in the United States
Delaney C. Abood, Susan M. Wall. Emory University School of Medicine, Atlanta, GA.

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.
(PIs) with active kidney-focused RO1s in 2005 and in 2020. We also compared changes in the demographics and research focus of more junior physician PIs by examining the K series grants over the same period that have focused on the kidney.

**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 PIs 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 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

**POI388**

“I Hear and I Forget. I See and I Remember. I Do and I Understand.” Incorporating Emergency Room-Based, High-Fidelity Medical Simulation into the Undergraduate Nephrology Course

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**Background:** Medical simulation develops clinical skills by implementing scenario in a real-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. Thematic analysis revealed that students evaluated the module as ‘interesting’, ‘useful’ and ‘informative’, but they found number of classes significantly insufficient. Students pointed out that due to the small emphasis placed on practical aspects in the existing curriculum e.g. routes of drug administration and conversion of doses, they could not fully benefit from simulation.

**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.

**POI390**

The Skeleton Key Group: Teaching Electrolyte Disorders Using Social Media Tools and Spaced Learning

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**Background:** Social media is being adopted by healthcare professionals as a platform for education. It’s ability to close geographic gaps and flex to busy schedules is increasing the demand for online educational platforms. The Skeleton Key Group (SKG) is a free open access medical education (FOAMed) platform focusing on electrolyte physiology and management. Group members collaborate to publish a monthly case report with learning objectives on the Renal Fellow Network (RFN) website. Content is supplemented by a visual abstract, tweetorials and follow up quizzes to ensure effective long-term learning and reach multiple learning styles.

**Methods:** An anonymous survey was conducted and disseminated on Twitter to gather information from users to evaluate if SKG teaching methods added to their education. Questions were designed as multiple-choice answers or qualitative responses on a 0-100 scale.

**Results:** There were a total of 130 responses from 32 different countries. The majority were nephrology fellows (33%), followed by internal medicine residents/interns (29%), attending physicians (23%), other specialty trainees (10%) and medical students (5%). On a scale of 1-100 (100 is considered highest quality), the mean score was 91±15.5 for the quality of our case reports. Overall, 95% of surveyors found our educational materials useful with tweetorials ranked highest (Fig 1). As training level progresses, a
larger percentage of readers found the tweetorial more useful compared to the case report. Around 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 COVID19 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 as 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 (Figs). 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-Revision 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 included: Other providers giving overly optimistic descriptions of the benefits of acute (54% seeing frequently, 64% 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 training during, 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., robust workflow, 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 nephrology fellows. The degree of burnout among pediatric nephrology 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 from February – 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 and faculty than pediatric residents and graduate physicians. Future studies should explore how to promote well-being through addressing key factors such as overall learning/environment, stress reduction, and building resilience.

POI1394

Protein Kinase A Catalytic-α and Catalytic-β Proteins Have Non-Redundant Functions
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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
Single-Cell RNA Sequencing Reveals Transcriptomes of DCT1, DCT2, Macula Densa, and Two Subtypes of Cortical Thick Ascending Limb Cells

Chi, Chen, Chung-Lin Chou, Mark A. Keppner. 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 tube (DCT) to the connecting tube (CNT). However, a complete understanding of the cellular composition and transcriptional profiles of the cells in this region remains 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 transcriptomes of microdissected renal tubule segments.

Results: Unbiased clustering and UMAP visualization revealed a single cluster of cells showing Slc12a3 expression without Prlwh, which we identified as DCT2 cells. These cells express ENaC subunits but little or no Hollid12 or Agnp2 mRNA. These DCT2 cells also express Cdh1, Slc1a2, Slc26a1, Ptg1, and Ptg3. In contrast, there were 6 tightly arranged clusters of cells expressing both Slc12a3 and Prlwh, which we identify as DCT1 cells. DCT1 heterogeneity appears to be associated with variable expression of Slc9a1, Cdh1, and Ckb among other mRNAs. An additional cluster (Slc12a3 Prlwh-) showed marked enrichment of cell cycle and cell proliferation associated mRNAs (e.g., Pena, Mki67, Cdki, and Top2a), which fits with the known plasticity of DCT cells. In addition, scRNA-seq identified three distinct CTAL (Slc12a1+) cell subtypes. One of these expressed Nos1, Apet1a, and Papag2, consistent with macula densa cells. The other two CTAL clusters were distinguished by Cldn10 and Pappa2, one and Cldn10 and Palla, 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 DCT. The new data have allowed the creation of a publicly accessible web resource for the support of future studies.

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Dietary Potassium Restriction Induces Nephrogenic Diabetes Insipidus

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Background: Dietary potassium deficiency is well-recognized to induce diabetes insipidus (DI) but the underlying mechanisms have not been established.

Methods: C57BL6J mice were randomized to control or diets with graded reductions in dietary K+ for 8 days. Kidney function tests were performed in metabolic cages, and tissues were harvested for western blotting and immunocytochemistry at the end of the experiment.

Results: We found that C57BL6J mice rapidly develop DI when potassium is eliminated from the diet, coinciding with the development of hypokalemia. Loss of free-water reabsorption, polyuria and polypdipsia was observed within four days, despite increased plasma copeptin, a vasopressin surrogate. In contrast to control mice, desmopressin treatment failed to increase urine osmolality and urine volume after dehydrating, further indicating diabetes insipidus (DI). Data indicate that dietary potassium restriction induces nephrogenic DI (NDI). Characterization of responses to graded reductions in dietary K+ diet revealed NDI was dependent on the development of hypokalemia. Females were more prone to develop hypokalemia, even in response to maintained potassium levels in dietary potassium and displayed more severe DI than males. Females also exhibited a much greater increase in AQP2 and phosphorylated s26AQP2 in response to dietary potassium deprivation.

Conclusions: These data together indicate i) hypokalemia-induced DI is nephrogenic, ii) a tight relationship links hypokalemia to renal concentrating ability, iii) females are more prone to develop hypokalemia and as a consequence, more prone to NDI.

Funding: NIDDK Support P01397

Tfp2a Integrates Cellular Patterning and Barrier Formation in the Renal Collecting Duct

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Background: The renal collecting duct plays important roles in fine-tuning urinary composition, electrolyte and water balance, blood pressure, as well as acid-base regulation. The patterning and molecular signatures of principal cells (PCs) and intercalated cells (ICs) of the collecting duct are tightly controlled by transcriptional processes and determine collecting duct physiological function and related clinical abnormalities. The transcription factor Tfp2a has previously been implicated in epithelial differentiation, in pronephros development in zebrafish, and in human congenital kidney defects. Using an integrated bioinformatics approach, we predicted that Tfp2a may critically control collecting duct functions. We tested our hypothesis using experimental model systems.

Results: We developed an in vitro model of collecting ducts. Additionally, mouse inner medullary collecting duct (IMCD3) cells were engineered to harbor CRISPR-Cas9-induced knockouts (KO) of Tfp2a. Deregulated genes were identified by mRNA sequencing. Patterns of principal and intercalated cells in mouse kidneys were analyzed by digital in situ hybridization. In vivo model was used in metabolic studies to analyze urinary concentration function.

Conclusions: More lacking Tfp2a in the collecting duct were viable and fertile but showed a defect of urinary concentrating ability. mRNA sequencing of Tfp2a-deficient kidneys revealed that Tfp2a and subsequent gene ontology analysis indicated an impact of Tfp2a on molecular processes including Notch signaling, focal adhesion formation and tight junction formation. Further experiments indicated abnormalities of PCs/CIC patterning in Tfp2a-deficient collecting ducts.

Funding: Our data suggest that Tfp2a controls transcriptional processes that integrate patterning and barrier formation in the collecting duct.

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 S/T269. As AQP2 is abundantly excreted in urine, the in vivo model was used in metabolic studies to analyze urinary concentration ability.

Results: More lacking Tfp2a in the collecting duct were viable and fertile but showed a defect of urinary concentrating ability. mRNA sequencing of Tfp2a-deficient kidneys revealed that Tfp2a and subsequent gene ontology analysis indicated an impact of Tfp2a on molecular processes including Notch signaling, focal adhesion formation and tight junction formation. Further experiments indicated abnormalities of PCs/CIC patterning in Tfp2a-deficient collecting ducts.

Conclusions: Our data suggest that Tfp2a controls transcriptional processes that integrate patterning and barrier formation in the collecting duct.

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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 S/T269. As AQP2 is abundantly excreted in urine, the in vivo model was used in metabolic studies to analyze urinary concentration ability.

Results: More lacking Tfp2a in the collecting duct were viable and fertile but showed a defect of urinary concentrating ability. mRNA sequencing of Tfp2a-deficient kidneys revealed that Tfp2a and subsequent gene ontology analysis indicated an impact of Tfp2a on molecular processes including Notch signaling, focal adhesion formation and tight junction formation. Further experiments indicated abnormalities of PCs/CIC patterning in Tfp2a-deficient collecting ducts.

Conclusions: Our data suggest that Tfp2a controls transcriptional processes that integrate patterning and barrier formation in the collecting duct.

Funding: Other NIH Support - ZIA- HL-001285 and ZIA- HL-006129
PO1399
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 transcription 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 1344 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-acylation ChIP-Seq, and RNA-polymerase II ChIP-Seq data to identify enhancer regions in the CTCF 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 transcription start site (TSS) that is predicted to bind Tcf1, Tcf3, and Tcf7 (p-value < 1 × 10^-16). By using a method that predicts function based on positional features, we predicted that the identified 517 bp region might be involved in the regulation of AQP2 expression. Then we asked how protein chaperones like heat shock protein H1 (Hsp1) as well as chaperonin GroEL (Hsp60) found that in addition to Hsp1, there are over 500 osmotically-induced genes that are regulated transcriptionally. The PRO-seq assay was used to identify where within enhancer regions high probability binding sites for TFs specifically identified to regulate Aqp2 gene transcription, viz. Nfia/Ref5/Neat3, Nktx1/Rela, and Grib1. In addition, enhancer regions identified by the ENCODE project, namely Cebpα, Ap-1 (Jun/Fos2), and E2F/E4, as well as sites for several TFs that are so far unannotated for 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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PO1400
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 osmolality remains unknown. To address this knowledge gap, we identified the pausing regions of 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.

Methods: We used the Precision nuclear Run-on and Sequencing assay 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 did not alter the VP-induced phosphorylation state of AQP2 at residues serine-256, threonine-254, and threonine-258 but did alter VP-induced phosphorylation at residues serine-238 and serine-240. In plasma membrane preparations of MKD cells subject to low and high FSS, AQP2-LW NK1 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 MKD 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 in microprepared 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.

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Underline represents presenting author.
PO1403

STCH Regulates NKCC2 Biogenesis by Both the Endoplasmic Reticulum-Associated Degradation and the Endoplasmic Reticulum-to-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.

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 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.

Funding: Government Support - Non-U.S.

PO1404

P2Y, Receptor Directly Mediates Collecting Duct Remodeling Induced by Acid Loading in Mice
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Background: Previously we reported that genetic deletion of P2Y2-R suppresses lithium(Li)-induced collecting duct (CD) remodeling. Since genetic depletion of P2Y2-R has a generalized ameliorating effect on Li-induced diabetes insipidus, here we evaluated the direct effect of P2Y2-R in CD remodeling using a model of acid loading.

Methods: Groups of WT or P2Y2-R knockout (KO) mice (B6D2; N = 3 or 4/group) were fed standard rodent chow and given tap water with/without addition of 0.28 M NaHCl for 9 days and humanely euthanized. AQP2 and [H]-ATPase double immunolabeling was used to identify the principal (PC) and intercalated (IC) cells of the medullary CD, respectively.

Results: As reported previously, KO mice developed more severe metabolic acidosis than WT after NH4Cl loading (not shown here). Furthermore, as shown in the pie charts, statistical analysis of the numbers of cells found a marked increase in the number of medullary ICs in NH4Cl-treated vs. untreated control (CT) mice in WT (28 ± 2 vs. 6 ± 1), but only a blunted response in P2Y2 KO mice (10 ± 1 vs. 4 ± 1, P = 0.001 WT vs. KO). These increases in ICs was associated with significant decreases in the proportion of PC cells in NH4Cl-treated vs. untreated CT mice in WT (72 ± 2 vs. 94 ± 1), and again a blunted response in P2Y2 KO mice (90 ± 1 vs. 96 ± 1, P = 0.001 WT vs. KO).

Conclusions: The data clearly show that P2Y2 receptor has a "direct effect" on CD remodeling in the kidney following acid-loading.

Funding: NIDDK Support, Veterans Affairs Support

PO1405

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 could 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 tubule cells 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.

Funding: Shoklo Malaria Research Institute, Mahidol University.

PO1406

Angiotensin II Receptor Blockade Alleviates Calcineurin Inhibitor Nephrotoxicity by Restoring p38 MAPK/NF-kB/COX-2 Signaling in Kidney Cortex
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Background: Immunosuppression based on calcineurin inhibitors (CNI) such as cyclosporine A (CsA) is the current standard for patients undergoing organ transplantation. Nephrotoxic side effects of CNI include reduction of renal cortical cyclooxygenase 2 (COX-2) expression along with pathophysiological alterations of glomerular filtration rate and sodium balance. The underlying molecular mechanisms are poorly understood. Since CNI stimulate the renin-angiotensin system (RAS), we hypothesized that the suppression of COX-2 is related to enhanced RAS activity.

Methods: To test this hypothesis, short- (3 days) and long-term effects (3 weeks) of CsA(25mg/kg’d), candesartan (5mg/kg’d), celecoxib (50 mg/kg’d) or their combinations

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were evaluated in Wistar rats to monitor COX-2 and RAS, as well as kidney morphology, with a histopathological examination. Cultured macula densa (MD) cells were treated with Ca2+-<ins>angiotensin II</ins> (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 CsA or siRNA increased COX-2 expression and protein expression by 3.8 MAPK and NF-kB. Coconcentrating the action of Ang II abolished these effects suggesting a dominant role for RAS. In rats, 3 days and 3 weeks CsA treatments led to increased renin biosynthesis, decreased cortical COX-2 expression, reduced creatinine clearance, and sodium retention due to activation of mineralocorticoid receptor (MR), NCC2, and NCC. The transcriptional repression of Cldn19 variant B is completely normalized by simultaneous administration of a RAS inhibitor candesartan for 3 days or 3 weeks, respectively. In contrast, administration of a selective COX-2 inhibitor, celecoxib, largely recapitated effects of CsA and significantly reduced the beneficial effects of the renin-angiotensin drug administration. 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 cortical COX-2 activity, thus overriding 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 Hyperparathyroidism with Hypercalcuria and Nephrocalcinosis (FHHCN) Bearing the Most Frequent Human CLDN16 Mutation

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Background: Mutations of claudin (CLDN) 16 and CLDN19 cause FHHCN, characterized by a 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 thin 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 recapitate the human disease, as it was complicated by neither nephrocalcinosis nor renal failure. Cldn 16 knock-down mice have a renal loss of Na and hypercalcemia. We hypothesized that a more frequent CLDN16 mutation (p.L151F) would be helpful to delineate the abnormalities caused by mutated Cltn16.

Methods: Clndn16<sup>L151F/L151F</sup> mice were generated by CRISPR Cas9-based mutagenesis. Cldn16<sup>L151</sup> and Cldn16<sup>L151F/L151F</sup> female mice were housed in metabolic cages at 3 months of age. Daily fluid and water intake, body parameters (Na, Cl, Ca, Mg, Pi, creatinine), were recorded. Blood and urine were collected. Claudin 16 and Cltn19 expression were analyzed by qRT-PCR.

Results: At 3 months weight, food and water intake, blood parameters (Na, Cl, Ca, Mg, Pi, creatinine) did not differ between Cldn16<sup>L151</sup> and Cldn16<sup>L151F/L151F</sup> mice. Cldn16<sup>L151</sup> 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 calcitriol was significantly increased in Cltn 16<sup>L151F</sup> mice. No nephrocalcinosis was seen at 12 months. Cldn 16 was almost never seen at TJ and Cldn 19 seems to be less expressed on Cldn19 expression.

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 cortical COX-2 activity, thus overriding 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.

PO1408

Sex Differences in Expression of Renal Urate Transporters

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Background: Elevated urate (UA) levels in the serum (hyperuricemia, HUA) contribute to the development of diseases, including kidney stones, chronic kidney disease, cardiovascular disease, metabolic syndrome, and gout. Men are 5x more likely to have HUA than women, yet this risk increases in women 4x after menopause. This suggests premenopausal women are protected against developing HUA, but the mechanisms have yet to be elucidated. These differences are echoed in our HUA mouse model, where injection of orthotopic or pathological UA transplanted into male of the most frequent (p.L151F) would be helpful to delineate the abnormalities caused by mutated Cltn16.

Methods: SiRNA-Seq was performed on male and female wild type (WT) and Q140K mice, followed by Deseq2 analysis to determine differentially expressed genes between both sexes of each genotype.

Results: Targets of interest included 12 transporter and 3 transcription factor (TF) genes associated with serum UA levels in humans in recent genome wide association studies. We found small (0.49–2.1-fold) but statistically significant changes in many of these genes. Specifically, female mice had lower expression of UA transporters SLC22A12, SLC22A14, and ABCA1. These genes have variants that associated with lower UA levels in human populations, consistent with female mice potentially more efficiently excreting surplus UA. Females also had significantly increased urinary excretion of calcitriol and ABCG2 transcripts, consistent with a possible mechanism of differentiation. The Q140K mice Deseq2 analysis reveals 273 alterations in male Q140K kidney gene expression as compared to WT, including 5 potentially compensatory SLC transporters. None of these changes were observed in female mice. These changes are the result of the elevation in SUA and not due to mutant ABCG2 protein.

Conclusions: Female sex may confer protection from developing HUA and related conditions. Further understanding this mechanism should lead to improved understanding of UA homeostasis and new insights into HUA treatment.

Funding: NIDDK Support

PO1409

SPAK Signaling Stimulates the Activity and Protein Expression of Large Conductance Ca<sup>2</sup> -Activated Potassium (BK) Channels

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Background: Sex differences in the renal UA handling between the sexes. We hypothesized that these differences in UA excretion may contribute to the development of diseases, including kidney stones, chronic kidney disease, cardiovascular disease, metabolic syndrome, and gout. Men are 5x more likely to have HUA than women, yet this risk increases in women 4x after menopause. This suggests premenopausal women are protected against developing HUA, but the mechanisms have yet to be elucidated. These differences are echoed in our HUA mouse model, where injection of orthotopic or pathological UA transplanted into male of the most frequent (p.L151F) would be helpful to delineate the abnormalities caused by mutated Cltn16.

Methods: Electrophysiology, cell culture, western blot, siRNA knockdown, and protein expression in kidney.

Results: We first determined the effects of SPAK gene deletion using SPAK KO mice on BK channel activity in the isolated, split-opened 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 SPAK expression on BK in HEK293 cells. Overexpression of SPAK markedly increased BK protein expression with concomitant increase in BK channel activity. Moreover, overexpression of SPAK activated BK channel activity in HEK293 cells. We found that SPAK knockdown decreased BK channel activity and protein expression in the CD165 BK channel and its protein expression via the ERK1/2 signaling pathway. It remains largely unknown whether SPAK kinase directly modulates the BK activity and protein expression in kidney.

Funding: NIDDK Support, Veterans Affairs Support

PO1410

High Dietary K+ Attenuates Salt-Nduced NCC and mTORC1 Activity in Dahl Salt-Sensitive Rats

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Background: Na+ reabsorption by renal Na<sup>-</sup>Ca<sup>2+</sup> 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 medullary target of ramiprilat 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 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 diet (LS) for 14 days. HS→HS+HK (4% NaCl) 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-(Ser240/244) to total S6, was used as mTORC1 activity marker.

Conclusions: In response to HCTZ, urina excretion was trending lower in HS+HK than HS alone, the baseline excretion was unaltered. Total NCC (nCC) and phosphorylated NCC (pNCC) abundance, a surrogate for NCC activity, were significantly lower in HS+HK than HS alone.

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Poster
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 new 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.

**Funding:** Other NIH Support - NHLBI (2 grants) and NIA (2 grants) to Richard D. Wainford

### POI1411

**Four Weeks of Dietary Potassium Restriction Causes Distal Convoluted Tubule Remodeling**

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**Background:** Previous studies have described a ‘renal salt switch’ within the distal nephron that turns on the thiazide-sensitive Na–Cl cotransporter (NCC) in the distal convoluted tubule (DCT) in response to low potassium intake and off the 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 may cause the DCT remodeling physically.

**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 identified that total and phosphorylated NCC were higher in mice on low potassium diet, compared to mice on control diet. By immunolabeling with pThr55-NCC antibody, we visualized the DCTs in optically cleared kidney slices. Three-dimensional morphometric analysis suggested that four-weeks of low potassium diet (46 ± 19 mm, n=6) significantly decreased DCT length by 13% compared to NK diet (49 ± 29 mm, n=5).

**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− 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− 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−, Cl− 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 Na− 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 inappetance and 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.

**Funding:** NIDDK Support

### POI1413

**Architecture of the Distal Neprhon Mineralocorticoid Receptor-Dependent Transcriptome Defined**

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**Background:** The mineralocorticoid receptor (MR, Nrsr2) 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 electrogenic 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-dependent genes.

**Methods:** MRKO/Pax rats vs. control rats, were used as a doxycycline (DOX)-inducible Nr3r2 gene KO model. After DOX treatment, four groups were prepared to distinguish between MR effects on mice on normal K+ diet (CT-NK) or 21 high 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 Nr3r2 gene confirmed complete disruption of Nr3r2 gene in the MR KO. All known aldosterone-response genes, including Spk1, Scnn1a, Nrg2, Per2, Tsc2d3, Zbtb16, Milp and App1al were significantly decreased in MR KO-LK compared to CT-HK. In addition, 5 DE genes (Spk1, Scnn1a, Nrg2, Fxydh and Hmx1) were more highly expressed in the NKO group compared with the control group (458 ± 14 m). Analysis of the whole kidney confirmed that total and phosphorylated NCC were higher in MR KO-LK vs. CT-HK (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.

**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.

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

### POI144

**Effect of Patriomer and Sodium Zirconium Cyclosilicate on Blood Pressure in a Rat CKD Model Induced by 5/6th Nephrectomy**

Lingyun Li, Ansgar Conrad, Alain Romero, David A. Bushinsky, Relypsy, Inc., a Vifor Pharma Group Company, Redwood City, CA; University of Rochester School of Medicine, Rochester, NY.

**Background:** Patriomer (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:** 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 (6 g/kg), for 24 hrs once weekly for 8 wks. Blood pressure data was collected for 24 hrs once weekly for 8 wks. 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 (135 ± 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 (24 ± 4.2 mmHg, P = 0.001). 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 ± 0.43 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 5/6th Nx exhibited significantly lower BP compared to vehicle-treated and SZC-treated rats. Additional analyses are warranted to determine GALNAc 3′-SMT’s effect on BP in this model of CKD.
PF-06869206 Is a Selective Inhibitor of Phosphate Transport: Evidence from In Vitro and In Vivo Studies
Linton Thomas, Jianxiang Xue, Jessica Dominguez Rieg, Timo Rieg. USF Health Morsani College of Medicine, Tampa, FL.

**Background:** The kidneys are key players in maintaining the body's phosphate (P) homeostasis, and patients with chronic kidney disease (CKD) develop hyperphosphatemia. Two renal transporters mediate the majority of P reabsorption, the Na+-phosphate cotransporters Npt2a and Npt2c, with Npt2a accounting for ~80% of P reabsorption. The aim of the current study was to determine the in vitro effects of a Npt2a-I (PF-06869206) in opossum kidney (OK) cells as well as its in vivo effects in Npt2a knockout (Npt2a-/-) mice.

**Methods:** To study the in vitro effects of Npt2a-I (0.1-100 μM/L) on P uptake, 14C phosphate was used as a tracer.

**Results:** In vitro, Npt2a-I dose-response (3-300 μM/L, 1% by oral gavage) effects on urinary P excretion were observed in metabolic cages for 3 hours in wild-type (WT) and Npt2a-/- mice. Effects on Plasma P, were studied before (baseline) and 2 hours after application of Npt2a-I (30 μM/L, 1% by oral gavage).

**Conclusions:** Our studies show that PF-06869206 is a competitive inhibitor of P transport in OK cells and the effect on urinary P excretion can be observed at plasma levels of Npt2a-I. Hexokinase IV is clearly the best kinase to identify if Npt2a is a useful treatment for hyperphosphatemia.

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

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**POI1415**

**PO1415**

**PF-06869206 Is a Selective Inhibitor of Phosphate Transport:** Evidence from In Vitro and In Vivo Studies
Linton Thomas, Jianxiang Xue, Jessica Dominguez Rieg, Timo Rieg. USF Health Morsani College of Medicine, Tampa, FL.

**Background:** The kidneys are key players in maintaining the body's phosphate (P) homeostasis, and patients with chronic kidney disease (CKD) develop hyperphosphatemia. Two renal transporters mediate the majority of P reabsorption, the Na+-phosphate cotransporters Npt2a and Npt2c, with Npt2a accounting for ~80% of P reabsorption. The aim of the current study was to determine the in vitro effects of a Npt2a-I (PF-06869206) in opossum kidney (OK) cells as well as its in vivo effects in Npt2a knockout (Npt2a-/-) mice.

**Methods:** To study the in vitro effects of Npt2a-I (0.1-100 μM/L) on P uptake, 14C phosphate was used as a tracer.

**Results:** In vitro, Npt2a-I dose-response (3-300 μM/L, 1% by oral gavage) effects on urinary P excretion were observed in metabolic cages for 3 hours in wild-type (WT) and Npt2a-/- mice. Effects on Plasma P, were studied before (baseline) and 2 hours after application of Npt2a-I (30 μM/L, 1% by oral gavage).

**Conclusions:** Our studies show that PF-06869206 is a competitive inhibitor of P transport in OK cells and the effect on urinary P excretion can be observed at plasma levels of Npt2a-I. Hexokinase IV is clearly the best kinase to identify if Npt2a is a useful treatment for hyperphosphatemia.

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

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**Critical Role of Threonine Residue in PDZ-1 Binding Motif of Type 2a Sodium-Phosphate Cotransporter (Npt2a)**
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**Background:** Npt2a brush border membrane (BBM) expression is the major determinant of proximal tubule phosphate reabsorption. Binding of the Npt2a carboxy terminus Class I PDZ binding motif (ST-x-x-x-COOH) to NHERF1 (sodium-hydrogen exchange regulatory factor 1), a PDZ protein, is critical for Npt2a BBM expression. We have shown that NHERF1 deficiency results in reduced binding of Npt2a to 14-3-3 epsilon in an IRES-containing bicistronic mammalian expression vector. We transiently transfected these cDNA constructs in NHERF1-deficient opossum kidney cells, assessed membrane expression by confocal microscopy, and Npt2a function by (32P) phosphate uptake.

**Results:** Npt2a (T635), Npt2a (E635), or Npt2a (A635) alone showed dense cytosolic expression and negligible 32P phosphate 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 plus 14-3-3 construct DNA construct exhibited apparent membrane localization, but none co-localized with 14-3-3 epsilon or exhibited significant 32P uptake.

**Conclusion:** We concluded that the Thr of the Class I PDZ binding motif of Npt2a is essential for interaction with NHERF1 and functional activity of the cotransporter. 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

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**POI1417**

**Metabolic Acidosis Exacerbates Pyelonephritis in Mice Prone to Vesicoureteral Reflux**
Jeffrey M. Parkinson, Janine L. Corley, George J. Schwartz. University of Rochester Medical Center, Rochester, NY.

**Background:** Acute pyelonephritis is a serious bacterial infection in children. The prevalence of acute pyelonephritis is due at least in part to gicusgericetal gulos (VUR). 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 on pyelonephritis was studied in C3H mouse strains prone to VUR.

**Methods:** MA was induced in female C3H mice via NH4Cl (2%/w/w) supplementation of food. Acid-base state was assessed by blood gas analysis using an iSTAT G3+ and urine pH with U-TEST. Urinary Tract Infection of mice (6-8 wks) with Uropathogenic E. Coli (UPEC strain CFT073) 0.5 X 10^11 cfu/50 μl was performed via the transurethral injection of bacterial blander and kidney 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 antibodLtLy6G (1A8). Cytokine (IL-1β, TNFα, IL-6) and chemokine (CXCL1, CXCL2, CXCL5) RNA 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±0.01, Ur pH: 6±0.05. MA concurrent with UPEC-UTI markedly increased kidney UPEC burden in innate immune competent HeN mice (HeN = 4E5 versus MA HeN= 1E6±1E6; p<0.02 MW-U-TEST), but not Th1-deficient HeF mice (HeF = 2E6±1E6 versus MA HeF = 5E5±1E5). MA markedly increased CD inflamed neutrophil infiltrates (HeN = 6E5; p<0.02 MW-U-TEST), but not Th1- or Th2-deficient HeF mice (HeF = 2E5±1E5; p≥0.02 for Bonferroni correction).

**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.

**POI1418**

**Oxidized Alkyl Phospholipids Stimulate Proximal Tubule Sodium Transport via PPARγ/ERK Pathway**
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**Background:** We previously reported thiazolinediones stimulated proximal tubule (PT) sodium transport via non-genomic PPARγ/ERK pathway. However, the contribution of endogenous PPARγ ligands to PT transport has been unknown. In this study, we investigated effects of 1-O-hexadecyl-2-azelaoyl-sn-glycero-3-phosphocholine (azPC), an endogenous lipid oxidation product (LOP) acting as a potent PPARγ 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 VAPase inhibitor, Belafoncim A. To examine the signaling pathway of azPC, we used a PPARγ antagonist (GW9662) and a MEK inhibitor (PD98059) and siRNA against PPARγ. The expression of PPARγ 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 stimulatory effects were completely suppressed by GW9662 or PD98059 without affecting the basal activities. siRNA against PPARγ 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 phosphorylation 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.

**POI1419**

**A Novel Distal Convoluted Tubule-Specific Tamoxifen-Inducible Cre-Recombinase Driven by the NaCl Cotransporter Gene**

**Ryan J. Cornelius,** Avika Sharma, Xiao-Tong Su, David H. Ellison, Andrew P. McMahon, James A. McCormick, Oregon Health & Science University, Portland, OR; 2VA Portland Health Care System, Portland, OR; 3Keck School of Medicine of the University of Southern California, Los Angeles, CA.

**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, allowing targeted gene modification in the DCT is the DCT-specific mouse with Cre-recombinase under control of the Pshgl 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 YFP, indicating minimal leakiness. After five days of tamoxifen injection, mice showed YFP expression in almost all NCC positive cells and there was complete overlap of YFP expression in NCC positive cells. Crossing to TdTomato mice revealed higher leakiness (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.

**NIDDK Support, Veterans Affairs Support, Private Foundation Support**

**POI1428**

**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 wall and shares a similar structure to the human 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 Amphotericin B also causes nephrogenic diabetes insipidus (NDI) by preventing insertion of vasopressin-a similar structure to the human 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.

**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 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 furocarnozole 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.

**POI1449**

**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 hyponatremia 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 (NCT04256499), 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 hyponatremia of other origin. Among the SIAD patients, 33(41%) had a fasting plasma sodium (PNa) ≥135mM (‘nephrogenic SIAD’), 47(59%) had ‘hyponatremic SIAD’. We found no differences in demographic data or medical history between these two groups. During WLT, ‘nephrogenic SIAD’ patients behaved specifically by exerting hyponatremia (while normal individuals did not), resembling ‘hyponatremic SIAD’ patients (Figure 1). While their fasting urine osmolality (U-Osm) was initially higher, ‘nephrogenic SIAD’ and ‘hyponatremic SIAD’ patients reached the same minimum U-Osm (389±257 vs. 350±203mOsm/kgH,O, p=0.76). Additionally, they reached a higher minimum value of PNa than ‘hyponatremic 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 ‘nephrogenic SIAD’.

**Conclusions:** We conclude that, without WLT, a diagnosis of SIAD could be missed in 40 to 65% of SIAD patients.

**POI1430**

**Reconsidering the Edelman Equation: Impact of Individual Total Body Cation Content and Body Weight**


**Background:** Treatment of hypo- and hyponatremia is guided by formulas that are a highly heterogeneous population. However, the Edelman equation does not account for the recently uncovered body compartment where Na+ can be temporarily stored and released without affecting TBW.

**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.
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\(^+/\))\(\times\)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\(^+/\))\(\times\)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\(^+/\))\(\times\)TBW was different for high and low weight categories (table). Sex or presence of edema did not alter the association. In piecewise regression, a significant change in slope was found in 149 mmol/L (Na\(^+/\))\(\times\)TBW (figure; 1.12 vs 0.56, \(p<0.01\)).

Conclusions: The coefficients of the Edelman equation are significantly affected by weight and body cation content. The less steep slope for the higher (Na\(^+/\))\(\times\)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

Hypotenatremia: It’s in the Eye of the Beholder
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Introduction: An 85 year old American female presented with 2 days history of worsening right eye pain, headache, scalp tenderness, and hypertensive 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, amlodipine, and pain with opioids. Over the course of the next 24 hours she began to have somnolence. Initial sodium (Na) on admission was 131 mmol/L, with prior normotremia. She was given a normal saline bolus followed by infusion due to concern for encephalopathy 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 117mmol/L requiring repeated doses of 3% Saline. Daily urine osmolality continued to decrease to 500s mosm/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 hypotenatremia 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 hypothalami.

PO1432

Acute Hemodialysis Prescription in Severe Hypotenatremia Patient
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Introduction: Severe hypotenatremia in end-stage renal disease with fluid overload give rise to clinical dilemma. Dialysis and ultrafiltration are needed to reduce uric acid and fluid overload, yet there is a danger of osmotic demyelination syndrome if blood sodium level rapidly increase above the permissible range.

Case Description: A 60 years old male patient was admitted with acute pulmonary oedema due to chronic kidney disease. He came with uremia 140 mg/dL, creatinin 20.3 mg/dl and had severe hypotenatremia 94 mEq/L. He underwent hemodialysis with low blood flow rate (50 ml/min) and low dialysate sodium (130 mEq/L). Second hemodialysis was done with blood flow rate 100 ml/min and dialysate sodium 130 mEq/L. With this approach, we succeeded in increasing sodium gradually, not exceeding the limit of 10 mEq/day.

Discussion: In order to avoid rapid increment of serum sodium level, the sodium in dialysate can be set as low as possible to 130 mEq/L. We aim to limit the increment of serum Na to 10 mEq/day. Since the patient’s total body water is approximately 36 L, an increase of 3 mEq/L/hour during 3-hour dialysis session would require a transfer of 108 mEq of Na per hour or total 324 mEq. We set a very slow blood flow rate, set dialysate rate to 800 ml/min and we assume that there is a 100% equilibration of Na between the patient’s blood and the dialysate, resulting in net transfer of 36 mEq Na (Na\(\text{dialysate} \cdot \text{Na}_\text{dialysate} \cdot \text{Na}_\text{serum}) / \text{total blood flow rate} \cdot \text{dialysate sodium} 130 mEq/L. Second hemodialysis was done with blood flow rate 100 ml/min and dialysate sodium 130 mEq/L. With this approach, we succeeded in increasing sodium gradually, not exceeding the limit of 10 mEq/day.

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POI1434
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. His 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 1L of D5LR and 1L of LR during labor. She had urinary retention following delivery and a Foley catheter immediately drained 2L of urine. Her initial postpartum sodium level was 123 mEq/L without associated symptoms. Urine osmolality was 64 mOsm/kg on admission. History revealed typical daily fluid consumption of 6L. Two days prior to admission, she abruptly increased fluid intake to 13L 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 5L. 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.

Discussion: Primary polydipsia served as the leading driver of acute hyponatremia in this mother and infant, appropriately associated with ADH suppression. Although well-known drivers of increased ADH secretion were present, such as urinary retention and labor pain, their effects were less significant, as evidenced by very dilute urine on presentation. She was not exposed to the antidiuretic effects of oxytocin, which is an additional consideration in the peripartum period. Higher plasma volume during pregnancy and chronic polydipsia increased the mother’s propensity to develop clinically significant hyponatremia in this case. This may have been detected earlier had serum sodium testing been included in routine prenatal care.

POI1435
Hyponatremia: A Real Headache
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Introduction: Pituitary apoplexy is a condition characterized by pituitary gland injury via either infarction or hemorrhage. This can result in endocrinologic dyscrasias. We describe a case of SIADH secondary to pituitary apoplexy.

Case Description: A 70 year old female 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 1L 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 of 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 nephropathy 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. Pituitary apoplexy should be considered in the differential diagnoses for SIADH in the setting of recent brain surgery or new red flag neurological symptoms.

POI1436
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) for a median follow-up of 8.8 years. We analyzed baseline and time-dependent hyponatremia (<136 mmol/L) and hypernatremia (>145 mmol/L) with all-cause mortality and risk of ESKD using Cox proportional hazard models and competing risks models.

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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 hyponatremic ephelathapathy 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 14,648 (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
Joy Ayyoub, Shahzard Zonoozi, Pooneh Alborzi. Penn Medicine, Philadelphia, PA.

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 toxicity.

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 cholesterol 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 subject 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
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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 lipoprotein-X, an abnormal lipoprotein observed only in patients with cholestasis.

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POI1441
Continuous Renal Replacement Therapy (CRRT) for Overcorrection of Hyponatremia After Left Ventricular Assistance Device (LVAD) Placement
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Introduction: Rapid correction of severe hyponatremia can result in osmotic demyelination syndrome, central pontine myelolysis and locked-in syndrome. Rapid correction is defined 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 very 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.

POI1442
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 hyperosmolality 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, ALT 6398 U/L, creatinine 44 mg/dL. NAc and IV bicarbonate were quickly initiated, and a short plasmapheresis treatment was started 12hours later, inducing moderate hypercalcaemia, hyponatremia (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. Hyperonc NaCl 23.4% (50 mmol) was added to a low-chloride IV fluid in 5 mL dialysate production (PrismaCalc2) to obtain Na of 150 mmol/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 serum sodium targeted. However, after numerous medical complications, the patient was electively 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 NaCl into the dialysate bag allows us to modify its tonicity to obtain neuroprotective hyponatremia. However, as shown in our case, complete sodium equilibration between dialysate and patient, even when using high-volume CVVHDF, is unlikely because of residual kidney function and concomitant hypo- and isotonic IV medications. To obtain and maintain therapeutic hyponatremia in these conditions, the CRRT dialysate tonicity should be slightly higher than the targeted serum sodium.

POI1443
Unraveling the Role of Serum Chloride Level as a Strong Predictor of Outcomes in Patients with Heart Failure: A Systematic Review and Meta-Analysis
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Background: The field of heart failure (HF) is conventionally sodium-centric. Low serum sodium concentration has long been recognized as an established marker of adverse outcomes and is commonly included in HF risk prediction models. Not only could the mechanisms leading to hyponatremia result in concurrent hypochloremia, but chloride also has distinct biological roles (e.g., modulating renin secretion) that are relevant in HF. We sought to explore the impact of hypochloremia on the outcomes of patients with a HF.

Methods: This is a PRISMA-guided systematic literature review and meta-analysis (registered in PROSPERO). We searched PubMed, Cochrane, and Embase databases from March 2010 to March 2020 for clinical trials exploring relationship between serum chloride and the outcomes of HF patients. A cumulative analysis of Hazard Ratios (HR) with 95% confidence intervals (CIs) was done using comprehensive meta-analysis software.

Results: A total of 9 studies with 15,979 patients were eligible for analysis; 5 had patients with systolic HF, 3 with both systolic and diastolic HF, and 1 with diastolic HF only. These studies reported HR for risk of mortality with change in serum chloride levels stratified by unit, standard deviation, or predefined groups, and adjusted for serum sodium and a variety of potential confounders. On cumulative analysis we found that serum chloride levels are inversely associated with risk of long-term mortality HR 0.92 (95% CI 0.77 - 0.96; p<0.01).

Conclusions: Based on the data from currently available studies, we identified low serum chloride level as a strong independent predictor of mortality in various phenotypes of HF. While it remains to be elucidated whether it represents a marker of disease severity or reflects an actual pathogenetic mechanism, our results suggest that inclusion of serum chloride in HF risk models is likely to improve their predictive value.
PO1445
Post-Discharge Outcomes Among Hyperkalemic Patients Treated with and Without Sodium Polystyrene Sulfonate in the Inpatient Setting
Jill Davis,1 Rubeen K. Israni,1 Erin Cook,2 Fan Mu,2 Keith Betts,2 Deborah A. Anzalone,3 Emma Billmeyer,2 Esteban J. Lemus Wirtz,2 Let Yin,2 Harold M. Szerlip,2 Gabriel I. Uwafio,3 Vivian A. Fonseca.3 AstraZeneca, Wilmington, DE; 2Bayou Interim Medical Center, Dallas, TX; 3Ochsner Medical Center, New Orleans, LA; 4Tulane University Medical Center; Tulane University School of Medicine, New Orleans, LA.

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 a 1 IP stay with HK (≥3 potassium [K] lab >5.0 mEq/L) were identified 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=5.6-6.0, 40.4% ≥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 average 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 users 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.

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PO1446
Serum Potassium Levels at Hospital Discharge and 1-Year Mortality Among Hospitalized Patients
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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, 3.0-3.4, 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 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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PO1447
Mitragyna speciosa (Kratom)-Induced Hyperkalaemia
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Introduction: Kratom is a non-controlled herbal supplement that has been used for its opioid-like effects. Case reports of different organ toxicities from Kratom have been reported in the literature. However, little is known regarding its effects on potassium (K+) homeostasis. We present here the first case-report of kratom-induced hyperkalaemia.

Case Description: A 61 yo male with a history of degenerative disc disease and hyperlipidemia, referred to nephrology clinic for unexplained hyperkalaemia for the past 2 months. He was asymptomatic. His only home medication was rosuvastatin. Serum K+ was elevated in four different occasions with 5.5 mmol/L being the highest (non-hemolyzed samples). He denied NSAID or antibiotic use, smoking, alcohol intake, illicit drug abuse, sickness, or high (K+) diet intake. No family history of renal diseases. Physical exam was unremarkable with a blood pressure of 140/90 mm Hg without orthostatic changes. Serum creatinine (Cr) was 0.8 mg/dL, eGFR=60 mL/min, plasma aldosterone was 3.6 ng/dL, rennin activity was 0.88, urine (K+) was 14 mmol/L and urine Cr was 16 mg/dL, (K+) fractional excretion was 15%, sodium of 141 mmol/L, CO2 33 mmol/L and the rest of the electrolytes were normal. TSH, CPK, AM cortisol, and WBC were within normal limits and he had no hematuria or proteinuria. Kidney ultrasound was normal. Upon re-interrogation, patient admitted taking daily Kratom for recreational purposes for the past 4 months as herbal supplement. A repeat blood chemistry 4 weeks after patient confirmed abstinence from Kratom, revealed normalization of (K+) down to 4.6 mmol/L.

Discussion: Mitragyna speciosa (Kratom) is a herbal supplement with potential abuse due to its opioid-like properties. Our patient had hyperkalaemia unexplained by low renal clearance, adrenal insufficiency, medication use, or other etiologies. A study in cultured heart cells revealed a blocking effect of the cardiac (K+) inward rectifier channels (Kir 2.1) by Mitragynine causing prolonged QT interval arrhythmia. Kir family does exist along the nephron with little known about Kir 2.1, or other Kir channels is yet to be further studied. This case-report serves to highlight the importance of the identification of lesser-known supplements with potential abuse that can cause life-threatening side-effects.

PO1448
The Relationship Between Comorbidities and Hyperkalaemia in Patients with CKD
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Background: Hyperkalaemia (HK) is common in patients with chronic kidney disease (CKD) due to the role the kidneys play in maintaining normal potassium (K+) homeostasis. The presence of comorbidities in patients with CKD may further increase HK risk. Therefore, this study explored the incidence of HK in CKD patients with different comorbidities.

Methods: A retrospective cohort study was conducted using primary and secondary care data from the UK Clinical Practice Research Datalink and linked Hospital Episode Statistics, respectively. Eligible patients had non-dialysis dependent CKD, with or without resistant hypertension (RHTN), heart failure (HF) or diabetes (type 1 or type 2) recorded between January 2003 – June 2018. Patients were grouped according to CKD severity (stage 3a, 3b, 4 and 5) and follow-up time was partitioned based on their current exposure status. The incidence rates of HK per 1,000 patient-years were assessed for each group and the data was further categorised according to HK-defining potassium K+ thresholds: ≥5.0, ≥5.5 and ≥6.0 mmol/L.

The Kaplan-Meier plot of one-year mortality based on discharge serum potassium levels

Poster
Results: In total, 229,350 patients with CKD stage 3+ contributed to follow-up, including 514, 250, 114 and 39 thousand patient years in the CKD only, RHTN, diabetics and HF cohorts, respectively. Declining renal function was consistently associated with increasing incidence of HK at all K- thresholds. Additionally, within the same CKD stage, comorbidities were also consistently associated with an increase in HK incidence. Patients in the diabetes cohort were consistently at the greatest risk of HK, with a significant ($\alpha = 0.05$) increase in risk of HK (defined at ≥5.0 mmol/L) compared with other comorbidity groups. Conversely, patients without any comorbidities were at the lowest risk of HK, regardless of CKD stage and HK threshold.

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

POI1449
Hyperkalaemia Secondary to Carabapenem Use
Sabine Karam. Saint George Hospital University Medical Center, Beirut, Lebanon.

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 etephane use.

Case Description: A 24-year-old gentleman with no past medical or surgical history presented with a known history of renal disease with end-stage renal disease on chronic haemodialysis. He underwent a CT scan that showed a perforated appendix with small abscesses. Upon admission, his creatinine level was 1.26 mg/dL and his potassium level was 4.24 mg/dL. He was initiated on intravenous fluids and etephane 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 mg/dL. He was switched to meropenem, however the hyperkalaemia persisted and resolved only when he was switched to ciprofloxacin.

Discussion: Carabapenem use is associated with severe hyperkalaemia and this complication seems to stem from a class-effect rather than the effect of a specific drug.

POI1450
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 relationships between CKD duration, serum potassium level (K-) and rates of 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 and MACE were estimated over follow-up from index date to event or end of follow-up (earliest of death, loss to follow-up or study end) based on 1,000 patient years. Published risk equations for ACM and MACE were refitted with adapted coefficient values to include CKD duration (≥5 and >5 years). Reference category for incidence rate values was K- level 4.5 to <5.0 mmol/L.

Results: Among 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). Mean eGFR at index was 49.7 mL/min/1.73m² (SD 11.6). Crude rates of ACM and MACE in patients with CKD duration ≥5 years were 60.8 and 1,000 patients year (95% confidence interval (CI) 60.3-61.3) and 102.6 (95% CI 102.0-103.3). Rates in patients with CKD duration >5 years were 76.3 (95% CI 75.4-77.2) and 127.4 (95% CI 126.2-128.5), respectively. Irrespective of duration of CKD, K- ≥4.5 or ≥5.0 mmol/L were associated with increased rate of MACE/ACM in comparison with 4.5 to <5.0 mmol/L.

Conclusions: CKD patients with K- outside the normal range are at increased risk of ACM and MACE of CKD duration. Improved management of K- may reduce adverse clinical outcomes in these patients.

Funding: Commercial Support - AstraZeneca

POI1451
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 comorbidities that are 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 - 4.4 mmol/L), and the median creatinine level at admission was 0.88 mg/dL (IQR 0.74 - 1.1 mg/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 RAASIs, 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.
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]) (Table). Clinical variables with high importance were identified (Figure).

Conclusions: The machine learning model successfully identified 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.

Calibration analyses for 3-year mortality

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<th>Sensitivity</th>
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<td>0.873</td>
</tr>
</tbody>
</table>

Top 20 important clinical variables for predicting 3-year mortality

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

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 72 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.

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 PEGM excretion by 5.9% (95% CI 1.2-10.6%). Potassium supplementation had no effect on ECV, plasma renin, or urinary PGE2 excretion. The linear regression model of 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).

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

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 diastolic; 20% kidney transplant recipients) and eight clinicians (n=4 nephrologists, n=2 cardiologists, n=2 endocrinologists) 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/flatulence, and cramping in hands and legs (all 36%). The most disliked treatment characteristic was the medication’s taste/texture; 58% of patients ranked it among the five most important treatment characteristics. Among most patients reported gastrointestinal-related side effects, 54% did not rank diarrhea and 46% did not rank 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 as the two most important characteristics. Medication preparation, medication storage, and consumption 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 showed that they take 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 approved 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 Polysulphonate (SPS), 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 replicate the real-world patient experience. Patient ratings, assessed on a 0-10 scale and emotional response using the AdSAM tool®, will be evaluated (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.

Funding: Appropriate Support - AstraZeneca
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

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 normalization of cardiac arrhythmia.

Case Description: A 69 y/o male presented with generalized weakness, oliguria 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 hypoperfusion. 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 patients with chronic kidney injury and cardiac diseases requiring AV nodal blocking medication, BRASH is still an underrecognized syndrome with only a handful of reported cases. Mild hyperkalemia without EKG changes make this diagnosis difficult, as such it is vital to recognize this syndrome from a multi-organ perspective - treatment with immediate correction of potassium via CRRT or hemodialysis can result in resolution without unnecessary transvenous pacing or pacemaker insertion.

PO1458
Laxative Use and Plasma Potassium Trajectory in Patients with Advanced CKD Transitioning to Dialysis
Keiichi Sumida,1 Ankur A. Dashputre,1 Praveen Kumar Potukuchi,1 Fridjof Thomas,1 Yoshitsugu Obi,2 Miklos Z. Molnar,1 Elan Streja,1 Kamyar Kalantar-Zadeh,3 Csaba P. Kovesdy,1,1 1The University of Tennessee Health Science Center, Memphis, TN; 2University of California Irvine, Irvine, CA.

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 for K+ slope in the mixed-effects models.

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 enhanced 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

PO1459
Effect of Lactated Ringer Solution Use on Serum Potassium in Advanced Kidney Disease
Arun Rajasekaran, Naveen K. Bade, Abolfazl Zarjou. UAB, The University of Alabama at Birmingham, Birmingham, AL.

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 [defined by estimated glomerular filtration rate (eGFR) of < 30 ml/min/1.73m2 - including patients with acute kidney injury (AKI)], chronic kidney disease (CKD), and end-stage kidney disease (ESKD) either on dialysis or post renal transplantation] admitted at the University of Alabama at Birmingham Hospital between 9/1/2017 to 9/1/2018 who received LR for resuscitation and its effect on serum K levels. We stratified patients based on renal function; accounted for concomitant medication use and frequently potentiate hyperkalemia, use of K supplements, blood transfusions immediately prior to LR use, presence of sepsis, and administration of tube feeds.

Results: Average age of patients was 59 years. 19 patients had AKI, 60 patients had AKD on CKD, 20 patients had known 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-hour 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 without hyperkalemia were within 24 hours post 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 excrete 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
Ankur A. Dashputre,1 Keiichi Sumida,1 Justin Ghatwood,1 Fridjof Thomas,1 Oguz Akbilgic,2 Praveen Kumar Potukuchi,1 Yoshitsugu Obi,1 Miklos Z. Molnar,1 Elan Streja,1 Kamyar Kalantar-Zadeh,3 Csaba P. Kovesdy,1,4 1The University of Tennessee Health Science Center, Memphis, TN; 2University of California Irvine, Irvine, CA; 3Merck & Co, Inc, Rahway, NJ; 4University of Alabama at Birmingham, Birmingham, AL.

Background: Patients with advanced CKD may experience immediate hospital/ emergency department (ED) visit due to dyskalemia-associated adverse events (e.g. arrhythmias). The association of dyskalemia 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 excrete K adequately. Further large scale clinical studies are warranted to confirm our findings.

Methods: From among 102,477 US Veterans transitioning to dialysis between 2007-2015, we identified 21,150 patients with pre-dialysis eGFR <30 ml/min/1.73m2 and a concurrent plasma potassium (K) measurement. We examined the association of hypokalemia [K <3.5], hyperkalemia [K ≥5.5] and normokalemia [3.5-5.5, reference] with hospital/ED visits within 2 days of plasma K measurement using logistic regressions adjusted for sociodemographics, smoking status, comorbidities, BMI, healthcare encounters, SBP, medications and eGFR.

Results: The mean age of the cohort was 67.3 years; 98% were male; 32% were African American. The mean eGFR and K were 22.3 ml/min/1.73m2 and 4.6 mEq/L, respectively, and 7% and 3.5% of patients were hyper- and hypokalemic, respectively.

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)

PO1460
Association Between Dyskalemias and Short-Term Hospital/Emergency Department Visits in Patients with Advanced CKD Transitioning to Dialysis
Ankur A. Dashputre,1 Keiichi Sumida,1 Justin Ghatwood,1 Fridjof Thomas,1 Oguz Akbilgic,2 Praveen Kumar Potukuchi,1 Yoshitsugu Obi,1 Miklos Z. Molnar,1 Elan Streja,1 Kamyar Kalantar-Zadeh,3 Csaba P. Kovesdy,1,4 1The University of Tennessee Health Science Center, Memphis, TN; 2University of California Irvine, Irvine, CA; 3Merck & Co, Inc, Rahway, NJ; 4University of Alabama at Birmingham, Birmingham, AL.

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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)
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 (ORs [95% CIs] 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

Association between dyskalemias and short-term hospital/emergency department visits in patients with advanced CKD

PO1461
Characteristics of CKD Patients with Hyperkalemia: A Report from the DISCOVER CKD Retrospective Cohort
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Background: Hyperkalemia (HK), defined as serum potassium (sK+) >5.0 mmol/L, is a potentially fatal condition most often observed in patients with chronic kidney disease (CKD), heart failure (HF) or diabetes and exacerbated by medications that inhibit the renin-angiotensin aldosterone system (RAAS). This real-world study describes characteristics of patients with HK in a large observational international study of CKD patients.

Methods: The DISCOVER CKD retrospective cohort was extracted using the US TrifectaX hospital-EMR and Japan Medical Data Vision (IMDV) databases. The study included patients aged ≥18 years (>20 IMDV) with a diagnostic CKD code (stage 3A to Stage 5 including renal replacement therapy [RRT]) or 2 estimated glomerular filtration rate (eGFR) measures <75 mL/min/1.73m2 at least 90 days apart between January 2008 and March 2020. The index date was last sK+ measurement ≥5.0 mmol/L. Descriptive analyses were used.

Results: Preliminarily, 16436 CKD patients with HK (43% female, mean±SD age 72.2±13.7 years) were identified. Common comorbidities included HF, hypertension and type 2 diabetes, which increased in prevalence with increasing HK severity. Table 1. Mean eGFR was 43.3±24 mL/min/1.73m2 and mean sK+ was 5.4±0.5 mmol/L. HK severity, RAAS and diuretic use increased as mean eGFR decreased.

Conclusions: HK was more common in patients with significant comorbidities where RAAS inhibitors have evidence-based indications. Future analyses will determine whether HK limits appropriate management of these comorbidities.

PO1462
Ambulatory Treatments for RAAS Inhibitor-Related Hyperkalemia and the 1-Year Risk of Recurrence
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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 ≥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. 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 SPS prescription (N=154) interventions. 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.
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. Nephrology was consulted for hyperkalemia, metabolic acidosis and secondary HLH. Despite medical management with intravenous bicarbonate, 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 dialysate 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 QRS interval on her ECG and episodes of ventricular tachycardia and zero potassium dialysate bath, lowered the potassium level. The patient continued to have excessive cytokine overproduction. Often, CRRT with higher DFR than recommended has been used in the past to achieve solute clearance. Our case was unique as the patient suffered from a cardiac arrest when her potassium was 6.9 meq/dl. Suspected malignancy 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). The associations of laxative use with dyskalemias remained statistically significant even after multivariable adjustment (adjusted ORs [95% CI] for hypo- and hyperkalemia, 1.08 [1.02-1.13] and 0.79 [0.76-0.83], respectively; Table). The associations of laxative use with dyskalemias were independent of other confounders; the associations of laxative use with dyskalemias remained statistically significant even after multivariable adjustment (adjusted ORs [95% CI] for hypo- and hyperkalemia, 1.08 [1.02-1.13] and 0.79 [0.76-0.83], respectively; Table).

Results: The mean (SD) age of the cohort was 68 (11) years; 98% were male; 32% were African American; and 76% were diabetic. In the crude model, laxative use (vs. non-use) was significantly associated with higher risk of hyperkalaemia (OR [95% CI], 1.19 [1.13-1.25]) and lower risk of hyperkalaemia (0.74 [0.71-0.78]) (Table). The associations of laxative use with dyskalemias remained statistically significant even after multivariable adjustment (adjusted ORs [95% CI] for hypo- and hyperkalaemia, 1.08 [1.02-1.13] and 0.79 [0.76-0.83], respectively; Table).

Conclusions: Laxative use was independently associated with higher and lower risk of hypo- and hyperkalaemia, respectively, during the last 1-year pre-ESRD period. Our findings suggest the potential role of constipation in potassium disarray and the need for careful consideration for the risk-benefit profiles of laxatives in potassium management in advanced CKD.

Funding: NIDDK Support

Adjusted odds ratios (95% CI) for dyskalaemia associated with time-varying laxative use (vs. non-use) during the last 1-year pre-ESRD period (n=34,697)

1Model was adjusted for demographics, smoking status, BMI, comorbidities, length of hospital stay, in-hospital AKI, number of outpatient medical visits, and time-varying medication use and eGFR

Laxative Use and Incidence of Dyskalemia 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 dyskalemias in advanced CKD.

Methods: In 34,697 US veterans who transitioned to ESRD from 2007-2015 and with ≥2 plasma potassium (K+) measurements during the last 1-year period before ESRD transition, we examined the association of time-varying laxative use with incidence of dyskalemia over the 1-year pre-ESRD period, using generalized estimating equations with adjustment for potential confounders. K+ levels were categorized as <3.5, 3.5-<5.5 (reference), and >5.5 meq/L at each K+ measurement and treated as a repeated measure.

Results: The mean (SD) age of the cohort was 68 (11) years; 98% were male; 32% were African American; and 76% were diabetic. In the crude model, laxative use (vs. non-use) was significantly associated with higher risk of hyperkalaemia (OR [95% CI], 1.19 [1.13-1.25]) and lower risk of hyperkalaemia (0.74 [0.71-0.78]) (Table). The associations of laxative use with dyskalemias remained statistically significant even after multivariable adjustment (adjusted ORs [95% CI] for hypo- and hyperkalaemia, 1.08 [1.02-1.13] and 0.79 [0.76-0.83], respectively; Table).

Conclusions: Laxative use was independently associated with higher and lower risk of hypo- and hyperkalaemia, respectively, during the last 1-year pre-ESRD period. Our findings suggest the potential role of constipation in potassium disarray and the need for careful consideration for the risk-benefit profiles of laxatives in potassium management in advanced CKD.

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1Model was adjusted for demographics, smoking status, BMI, comorbidities, length of hospital stay, in-hospital AKI, number of outpatient medical visits, and time-varying medication use and eGFR

Acquired Bartter-Like Syndrome: An Unusual Presentation of Disseminated Tuberculosis

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Introduction: Acquired Bartter-like syndrome is a rare renal tubular disorder described to occur in granulomatous disorders such as sarcoidosis, but, its propensity to occur in tuberculosis (TB) is less known.

Case Description: We report the case of a 33-year-old Filipino woman with a 2-week history of lower extremity weakness. She had normal blood pressure and mild weakness on manual muscle testing. Abdominal examination revealed an incidental left lower quadrant mass. Workup revealed hypokalaemia with urinary potassium wasting, hypercalciuria, hyponogonadism, hypochloremia, and metabolic alkalosis, all consistent with Bartter-like syndrome. Abdominal CT scan findings were suggestive of disseminated TB. Ultrasound guided aspiration of the psoas abscess and pigtail insertion were done. Abscess aerobic, anaerobic, and fungal cultures did not isolate any organisms. Histopathology did not reveal any malignant cells. Detection of acid fast bacilli by Zielh-Neelsen stain and culture confirmed the diagnosis. The patient was started on anti-TB therapy and was maintained on spironolactone, potassium and magnesium supplementation upon discharge. On follow up, electrolyte abnormalities resolved after four months of anti-TB therapy.

Discussion: TB may be a rare acquired cause of Bartter-like syndrome. Management involves treatment of the underlying cause, spironolactone and electrolyte supplementation.
POI1466
Curious Case of Bartter Syndrome-Like Phenotype Unmasked by Diuretics
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Introduction: SLC12A1 mutations have been associated with Bartter syndrome type 1. Here we present a case of severe hypokalemia with diuretics which when investigated led to discovery of a novel SLC12A1 mutation which might have predisposed the patient to Bartter syndrome like phenotype.

Case Description: 68 y/o f with no history of hypokalemia developed heart failure with preserved ejection fraction and was started on low dose loope diuretics which was gradually increased to1-1.5 mg daily Bumetanide. She developed severe hypokalemia with diuretics which worsened with increasing diuretic doses, needing enormous amounts of potassium supplements. She continued to have persistent hypokalemia (serum potassium 3.0-3.5 mmol/L) with significant urinary potassium excretion despite being on 260 mEq of oral potassium supplement/day, which improved mildly with addition of Amiloride. She also was hypotensive and was alkalotic secondary to diuresis. Given the significant kaliuresis leading to severe hypokalemia which was out of proportion to the dose of diuretics we did Genetic testing for presence of Bartter’s mutation. Genetic testing revealed a novel heterozygous variant mutation in SLC12A1 gene. It showed 1972 C>T transition in exon 16 of SLC12A1 gene. This change converts a codon for leucine (CTT) to a codon for phenylalanine (TTT).

Discussion: Bartter syndrome (BS) type 1 is an autosomal recessive disorder caused by loss of function mutations. Mutations in SLC12A1 gene leading to dysfunction of NKCC2 co-transporter is one of the known mutations associated with Bartter’s syndrome. Bartter syndrome type 2 involves mutations in the ATP2B1 gene leading to loss of function mutations. Mutations in SLC12A1 gene leading to dysfunction of the NKCC2 co-transporter is one of the known mutations associated with Bartter’s syndrome. Our patient is unique as she has a novel heterozygous variant mutation in SLC12A1 gene and this mutation has not been reported to be associated with bartter syndrome. We believe this mutation might cause mild bartter phenotype. Our patient probably has a mild subclinical Bartter like phenotype secondary to heterozygous variant of the mutation and developed severe hypokalemia when exposed to loop diuretics. Pursuing genetic testing for appropriately severe hypokalemia needing exorbitant amount of potassium supplementation in a patient due to loop diuretic is a worthy consideration. Further research into this variant is needed to confirm it’s pathogenicity.

POI1467
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 estradial for oligomenorrhea, acne and hirsutism. Blood pressure (BP) was 98/67mmhg and heart rate 88 bpm with orthostasis. She had male pattern hair loss and dense comedones on cheeks. Labs were significant for normal renal 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 hirsutism prompted investigation of congenital adrenal hyperplasia (CAH). Work-up found elevated levels of ACTH (146 pg/ml), DHEA-S (694 mcg/dl), 11-deoxycortisone (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-deoxycortisone, 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.
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 to the endocrinology department with a diagnosis of hypokalemia. Medica- tions included KCL 360 mEq/day, amlodipine, carvedilol, doxazosin, hydrozalcine, and losinopril. Labs showed hypokalemia (2.4 mmol/L) and metabolic alkalosis (HCO3 31 mmol/L). Urinary potassium losses were raised catecholamines. Adrenal hormone workup detected raised cortisol levels and ACTH levels. Renal potassium wasting was found.

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 ACT source, patient became normokalemic and was discharged with steroid replacement.

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

PO1470
Thyrotoxic Periodic Paralysis: A Stunning Diagnosis
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Introduction: Thyrotoxic periodic paralysis (TPP), acute hypokalemia and proximal muscle weakness in the setting of thyrotoxicosis, is primarily seen in Asian men with undiagnosed hyperthyroidism in the 2nd-4th decade, often with family history of paralysis and thyroid disease. We describe a case of a young male presenting with acute TPP.

Case Description: A 28-year-old white male with no medical history presented with acute onset diffuse weakness with inability to get out of bed, preceded the night prior by leg stiffness. He exercised 2 days prior. He reported marijuana use and a balanced diet. He denied recent travel, medication or supplements. His father had Hashimoto’s thyroiditis. Exam showed tachycardia (106 bpm) and hypertension (132/74 mmHg), and EKG revealed sinus tachycardia with QTc 629. Labs showed: K+ 1.7 mEq/L, HCO3- 25mmol/L, Cr 0.7 mg/dL, TSH <0.01, fT4 >6ng/dL, and T3 320ng/dL. Fractional excretion of K+ was 3.2%. He was treated with 120mEq KCl with repeat K+ of 5.6 mEq/L in 4 hours and symptom resolution. Elevated TSH receptor, anti-thyroglobulin, and thyroid stimulating antibodies with a homogenous radioactive iodine uptake scan [Fig 1] confirmed Grave’s disease. He was started on metoprolol and methimazole and discharged home without further episodes.

Discussion: TPP results from acute intracellular K+ shift due to Na/K-ATPase activation in myocytes from a hyperadrenergic state (increased number and sensitivity of β-receptors) and thyroid hormone stimulation. Muscle hyperpolarization and loss of excitability required for contraction results. Body K+ stores remain unchanged. Episodes are associated with high insulin or epinephrine states (e.g. mornings, exercise, high-carbohydrate meal). Paralysis, lasting minutes to days, is ascending, symmetrical, and proximal, chiefly affecting legs (bulbar or respiratory involvement is rare). Usually painless, it can be preceded by muscle aches or cramps. Sinus tachycardia is common and life-threatening arrhythmias can occur. Labs demonstrate normal acid-base status and low urinary K. CPK can be elevated. Low TSH, elevated free T4 and T3 confirm the diagnosis. Treatment involves cautious K replacement (due to risk of rebound hyperkalemia), non-selective β-blockers, and therapy for hyperthyroid state.
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 (13.2 mg/dL). Labs showed ↓PTH (9 pg/mL), ↓/↔25-VitD (35 ng/mL) & ↑↑1,25-VitD & 25-VitD. 25-VitD:24,25-VitD > 80 warrants genetic analysis. Azoles inhibit 1-hydroxylase & urinary calcium, ↓PTH,

Discussion: CYP24A1 gene encodes 24-hydroxylase which inactivates 25-VitD and 1,25-VitD to 24,25-VitD and 1,24,25-Vit D. 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 and ↓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. Antepartum 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 G1bIV 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 result he developed mild to moderate hypercalcemia (5.6-2.0 ng/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 mg/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 paraproteinemias. Given the absence of a clear explanation for his non-PTH mediated hypercalcemia, we present a case of hypercalcemia, possibly related to patiromer.

Discussion: Patiromer is a cation exchange resin approved by the FDA in 2015 for the treatment of hypercalcemia. It binds to 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, hypomagnesemia 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 14 mg/dL, acute kidney injury with a creatinine of 2.9 mg/dL from a baseline of 1.6 mg/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...
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 hypercalciuria. However, data related to the use of potassium-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 hypercalciuria 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 medication.

Results: A total of 15 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 hypercalciuria 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;9-96). 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/day pre vs 310.0 mg/day post, p=0.552). Daily urine calcium ranged from 11 mg to 165 mg. Three (20%) patients had a 24 hour urine collection with values greater than 12 mg and were started on thiazide. Amiloride was given to one patient due to intolerance of thiazide, one patient due to persistent hypercalciuria on thiazide, and one due to progression of stone disease.

Conclusions: In patients that have failed thiazides for treatment of hypercalciuria, switching to or adding amiloride did not result in lower urinary calcium levels.

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 serum phosphate levels were categorized based on the occurrence of hospital-acquired hypophosphatemia and hyperphosphatemia. We defined hypophosphatemia as phosphate level <0.5 mg/dL and hyperphosphatemia as phosphate level >4.2 mg/dL.

Results: Fifty-four percent of patients developed new serum phosphate derangements during their hospitalization. The incidence of hospital-acquired hypophosphatemia and hyperphosphatemia was 11% and 1%, respectively. Hyperphosphatemia was 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-value<0.001).

Discussion: Hospital-acquired serum phosphate derangements affect approximately half of hospitalized patients and are associated with increased in-hospital mortality rate.
Discussion: Hypermagnesemia is a rare event and occurs in the context of high dose Mg infusion (ie. eclampsia treatment) or Mg ingestion 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 fluids (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 while on AKI. 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.


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. 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 presented with slurred speech and weakness leading to a fall. She complained of chronic constipation and had taken an unknown amount of milk of magnesia with her docusate. Neurologic exam revealed slowed speech and symmetric muscle weakness. Labs revealed sodium 128 mmol/L, creatinine 1.03 (baseline 0.5) mg/dL, magnesium 10.0mg/dL, calcium 8.0mg/dL, and phosphate 6.5mg/dL. After imaging ruled out any intracranial pathology, the patient was diagnosed with hypermagnesemia, then started on IV fluids and loop diuretics. Her electrolytes and kidney function continued to correct with hydration, diuretic therapy, and stopping all magnesium-containing medications. It was discovered that she had ingested 52 grams of magnesium by drinking two 26oz bottles. Her weakness improved throughout the second day and returned to full muscle strength by the third. She was discharged with a magnesium level of 2.3mg/dL.

Conclusion: This 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 treatment 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 could become fatal (respiratory failure, heart block, cardiac arrest, and flaccid quadriplegia).

PO1480 Clinicopathological Characteristics and Long-Term Prognosis of Monoclonal Immunoglobulin Light Chain-Associated Fanconi Syndrome Jiaying Li, Xiaoxiao Shi, Peng Xia, Limeng Chen. Peking Union Medical College Hospital, Dongcheng-qu, China.

Background: Monoclonal immunoglobulin light chain associated Fanconi 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 gammopathy in Peking Union Medical College Hospital were included in this study. Clinicopathological data was retrospectively reviewed.

Results: At diagnosis, the mean age of the 26 Asian LC-FS patients was 54.7±26.4) ml/min/1.73m2, with 33% were notable for edema at the most recent visit. Indeed, overall the rate of edema increases as renal function declines. More recently, metabolic acidosis has been identified as a key risk factor for the progression of CKD in addition to being linked to increased risk of renal osteodystrophy and muscle wasting. Presently, there are no FDA indicated therapies for the treatment of chronic metabolic acidosis, though sodium bicarbonate is commonly used to try to maintain serum bicarbonate levels in the normal range (22 – 29Eq/L). We sought to understand how prevalent metabolic acidosis is in a real world setting.

Methods: Patient level data was collected online via a HIPAA-compliant form in November 2019 as part of an independent chart audit. A total of 1,008 patient records were submitted by 201 nephrologists. Records were selected based on the most recently seen non-dialysis patients in the outpatient setting with an eGFR<60mL/min/1.73m2.

Conclusions: Metformin is a first line medicine in the treatment of diabetes mellitus, but it rarely cause lactic acidosis, usually in patients with acute or chronic kidney disease stage III onwards. We report a case of lactic acidosis 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 neurologic deficits. Her creatinine was 4.4 mg/dl (with a baseline of 1.4), potassium 5.9 mmol/L, bicarbonate 3.3 mmol/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 acidemia 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 acidemia 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 (Salameh AI, 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 available metabolic acidosis laboratory values. The study population included patients ≥ 21 years of age with ≥ 2 abnormal metabolic acidosis values measured at ≥ 24 hours apart. The primary outcome assessed was all-cause mortality. Secondary outcomes included all-cause readmissions within 1 year. The analysis was adjusted for age, sex, race, pre-existing comorbidities, and baseline eGFR and ACR.

Results: 51,558 patients qualified for analysis; 17,350 with metabolic acidosis, 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 severe causing the lactic 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 glycolic metabolites.

Funding: None

PO1486

Anion Gap (AG) and Negative Osmotic Gap (OG) due to Remdesivir's (R) Exciipient

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Introduction: The FDA authorized R for COVID-19. Excess Na sulfobutyl ether (SBE) substituted β-cyclodextrin (CD) solubilizes R (PMID: 32376442). Minute accumulation of SBECD can cause an AG as its substitution in R contributes to mortality in patients with chronic kidney disease (CKD) is unknown. 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 available metabolic acidosis laboratory values. The study population included patients ≥ 21 years of age with ≥ 2 abnormal metabolic acidosis values measured at ≥ 24 hours apart. The primary outcome assessed was all-cause mortality. Secondary outcomes included all-cause readmissions within 1 year. The analysis was adjusted for age, sex, race, pre-existing comorbidities, and baseline eGFR and ACR.

Results: 51,558 patients qualified for analysis; 17,350 with metabolic acidosis, 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.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
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 (9.8%). Figure 1 shows the associations between anion gap in tertiles with cardiovascular related mortality. In analyses restricted to those with a history of cardiovascular disease the results were 116% increased risk for cardiovascular mortality [HR 2.16; 95% CI (1.37,3.4)].

Conclusions: Higher anion gap may be a risk factor for cardiovascular-related mortality in adults.

Figure 1. Risk of cardiovascular mortality according to anion gap as tertiles (method = weighted survey cox regression)

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 for 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 was decompensated 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 therapy was begun in an attempt to restore function of the PDH complex and restart the metabolism of pyruvate through the citric acid cycle, limiting further type B lactate production. Within hours, lactate levels fell with parallel rise in serum pH. The patient was extubated, alert, and taken off CRRT within 24 hours of beginning thiamine therapy.

Discussion: This patient developed a profound metabolic acidosis secondary to type B lactic acidosis via accelerated glycolysis from dextrose infusion. This case highlights the intricate regulation of dextrose metabolism as well as thiamine as a vital therapy in type B lactic acidosis. Thiamine therapy was key, presumably reinitiating aerobic respiration through the PDH complex and ultimately leading to cessation of lactate production. Given the critical role of thiamine in this case, it is plausible that thiamine could be crucial for other cases of metabolic acidosis, particularly those secondary to type B 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, FTSD and bipolar disorder. Her medications included ciprofloxacin, delirium tremens, lithium, trazodone, and risperidone. 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 nmol/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 lactic acid. 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. Teaching points 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 Chorrillo”

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 Chorrillo” 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.
Poster

PO1491

Starvation Ketoacidosis in a Patient with Muscular Dystrophy
Khaled Srour, Bilal Shahzad Azam Khan, James E. Novak. Henry Ford Hospital, Detroit, MI.

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, osteoarthritis 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 osmolality = 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 acids 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 in clinical routine.

Methods: AlcalUN (NCT03035812) is a multi-center, prospective, open-label study aiming to assess 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%) participants 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. 35%, p=0.001), while patients in the No-NaHCO₃ group (citrate) had more nephrolithiasis (95 vs. 28%, 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 similar distribution in both groups (71 vs. 75%, p=0.79). We found similar results after post-hoc propensity score matching.

Conclusions: Chronic oral alkalization with NaHCO₃ does not increase ECV more than citrate, even though it is used in 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 mmol/kg/d] NaHCO₃, n=48; and Higher-Dose [0.8 mmol/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 35±40 ml/min/1.73 m², serum tCO₂ 24±2 mmol/L. Median (IQR) urinary values at baseline were: KIM-1/Cr 185 (24, 767) mg/g Cr, NGAL/Cr 0.43 (0.36, 1.26) ng/mg, and NGAL/Cr 14.3 (6.44, 34.0) mg/kg. 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
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 bradycnepic, with oxygen supply FiO2 28%. He maintained gastric passive drainage for 5 days, around 3 to 3.5 L/day. Blood work showed Cr 4.15 mg/dL, urea 103.9 mg/dL, hyponatremia 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 mm/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. 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, and with low bicarbonate dialysis may be indicated.
POI499
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 pelvis 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 predominated 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 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

Results: Prior to HF induction, rNPT increased urine output (UOP) & 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). UOP, 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). UOP (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

POI1500
Accurate Estimation of Individual Sodium Intake with Repeated Spot Urine Sampling
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Background: In clinical practice, individual sodium (Na+) intake is estimated by measuring Na+ excretion in one 24-h urine collection (UC), whereas long-term Na+ balance studies indicate that 7 consecutive 24-h UCs may be needed. To reduce the burden of 24-h UF, single spot urine based alternatives have been suggested, but this approach has been shown to be very inaccurate. Whether the use of repeated spot UCs is an appropriate alternative for (multiple) 24-h UCs to estimate Na+ intake is unknown.

Methods: We performed a post-hoc analysis of a metabolic ward study in 8 healthy male adults who consumed a 7-d diet with a fixed amount of 200 mmol/d Na+. Urine was collected in 4 daily intervals (7-13h, 13-19h, 19-23h and 23-7h). After reaching steady state, we estimated Na+ intake by single and repeated 24-h UCs and repeated spot UCs, using the Kawasaki formula with measured 24-h urine creatinine excretion.

Results: After day 5, mean 24-h Na+ excretion matched intake, indicating that steady state was achieved (Fig 1A). Mean absolute differences (Δ) between measured Na+ intake and 3-d spot UC estimates were 18.8 (SD 14.6), 32.3 (SD 18.7), 74.6 (SD 30.0) and 28.2 (SD 19.8) mmol for interval 7-13h, 13-19h, 19-23h and 23-7h, respectively (Fig 1B). With the exception of samples collected between 19-23h, Na+ intake estimates by 3-d spot UCs did not significantly differ from Na+ intake estimates by single (Δ 29.8 mmol; SD 23.9) and three 24-h UCs (Δ 22.9 mmol; SD 11.4).

Conclusions: Bias in Na+ intake estimation did not significantly differ between repeated spot UCs and single and repeated 24-h UCs. Adequately powered studies need to confirm whether repeated spot UCs are an accurate and low burden alternative to 24-h UCs.

Funding: Private Foundation Support

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.

POI1501
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 baseline RAP using inferior vena cava (IVC) ultrasound is now common, though it is not without numerous pitfalls limiting its utility. For example, IVC changes in size in the IVC 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 with hypervolemia can direct management for diuresis/volume removal. These changes seen on doppler waveform aids in management for decongestive therapy.
Patients with CKD Closely with Hypertension and Target Organ Damage in Chinese

Abnormal Circadian Rhythm of Urinary Sodium Excretion Correlates

Results: A total of 1,099 Chinese CKD patients were recruited, 308 patients were excluded, and 791 patients were final 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

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 thenardite 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 (diuretic 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=0.002), 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=0.000). Moreover, weight loss was significantly positively correlated with decrease in LC (r=−0.612, P=0.000).

Conclusions: This study suggests that MEA 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

Background: The estimate of sodium excretion (NaE) is important for the management of hypertension, but 24 hours urine 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-hrs-UC for estimating NaE.

Methods: 4/subject 24-hrs-UC and the related 439 urine samples (1/voiding), were analyzed for uNa and uCr. uNaE (in mEq/Kg/day) was derived from the means of uNa/uCrR 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-uCrR 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 94.2%. 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-uCrR 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

Patients with CKD

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.
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.

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 model. Here we assess the degree of redox imbalance between NAD/NADH in mitochondrial phenotypes. Altered oxidoreductase activity is detected in an ADPKD model. Moreover, we use an in vitro model to express variations of PC1CTT that localize to different subcellular compartments and reveal an association between PC1CTT localization and Redox modulation. Finally, we show that expression of a PC1CTT variant with predominant nuclear as opposed to mitochondrial localization exacerbates the cystic phenotype in a Pkd1 KO mouse model.

Methods: We quantified the ratio between NAD+ and NADH in lysates from Pkd1+/- and Pkd1-/- mouse renal epithelial cells. We also assessed the NAD/NADH ratio in kidney lysates from ADPKD mouse models and WT controls. We generated 3 variations of PC1CTT with either an N-terminal HA-tag (2HA-PC1CTT), a C-terminal HA-tag (PC1CTT-HA) or no additional tag, and applied the assay to lysates from HEK cells transfected with these constructs. Finally, we expressed 2HA-PC1CTT in a Pkd1 KO mouse model and observed phenotypic differences.

Results: The NAD/NADH ratio was 80% higher in Pkd1+/- cells in comparison to Pkd1-/- cells. Kidney lysates from WT mice had double the NAD/NADH ratio compared 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 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.

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Cardiac Dysfunction in Pkd1-Deficient Mice Is Associated with Metabolic Rewiring
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Background: Myocardial abnormalities are associated with significant clinical burden in ADPKD but the underlying pathogenesis is still largely unclear.

Methods: We investigated the metabolic basis of the ADPKD-associated cardiac phenotype using a mouse hologemous for a Pkd1 hypomorphic allele that prevents PCD cleavage (Vv) with early cardiac dysfunction.
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Underline represents presenting author.
(10% K Bicarbonate/Citrate) dramatically accelerated cystogenesis despite augmented renal TRPV4 expression. TRPV4 activity (estimated as a GSK1016790A-dependent rise in [Ca^{2+}] in freshly isolated cyst monolayers from Pck453 rat kidneys) was approximately 2 fold larger in cyst cells from high K+ diet-treated compared to control. Basal [Ca^{2+}] and flow-induced [Ca^{2+}] levels were also higher on this condition. In contrast, TRPV4 activity was 2 fold larger in cysts on high K+ high alka diet.

**Conclusions:** We show a positive correlation between TRPV4 functional status and the time course of ARPKD progression in PCK 453 rats. Chronic alcali load renders TRPV4 to an inactive state, which contributes to exacerbated cystogenesis in Pck453 rats. Studies of TRPV4 of TRPV4+/- vs TRPV4-/- with high K+ high alka diet will be instrumental to attenuate the rate of PKD progression in clinical.

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**PO1513**

**Abstract Withdrawn**

**PO1514**

**Somatic Tubular Epithelial Cell Model of Type II Polycystic Kidney Disease Reveals Phenotypes of Altered Ciliary Length and Polycystin-1 Intracellular Complexes in Drosophila**

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**Background:** Autosomal dominant polycystic kidney disease (PKD) is a life-threatening inherited disease that affects around 12 million people worldwide, commonly due to loss-of-function mutations in PKD1 or (type II) PKD2, encoding polycystin-1 (PC1) and polycystin-2 (PC2), respectively. These form a receptor-channel complex in the primary ciliary whose molecular function remain uncertain, making it difficult to develop targeted therapeutic. Mice that lacks one of these proteins can exhibit PKD phenotypes, but are slow and complex, posing challenges for mechanistic analysis.

**Methods:** To establish a somatic cell model of PKD, we generated five clones of porcine proximal tubule cell line (LLCPK1) completely lacking PC2 using the CRISPR-Cas9 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. Cystic index was 21.0 ± 0.1% for the Pkd1 RC/RC kidneys, respectively. Pkd1 RC/RC mice also had elevated renal fibrosis and BUN levels at 9 months, consistent with a decline in renal function.

**Conclusions:** This study demonstrates that heterozygous loss of Pkd2 accelerated the onset of cystogenesis in Pkd1 RC/RC mice, supporting the hypothesis that 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 RC/RC, Pkd2 mice makes it a promising model for evaluating therapeutic interventions.

**Funding:** NIDDK Support

**PO1516**

**FPC, TFAP2B, and MCM3 Function in a Species-Specific Regulome That Modulates Myc/MYC Expression: Implications for ARPKD**

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**Background:** Mutations in PKHD1 cause human ARPKD (MIM 263200), but mouse Pkd1 mutants have limited or no renal cystic disease. We previously showed that MYC is elevated in mice with human ARPKD kidneys but not in mouse Pkd1 mutant mice, and that mouse FPC-C-terminal domain (FPC-CTD) activates MYC (ASN 2018). Trudel (2019) has reported that Myc is a central driver in Pkd1-induced pathogenesis. Relevant to the current study, mice express three TFAP2B isoforms while humans express only one, VTAP2B. Here, we describe a species-specific regulatory framework (regulome) in which FPC-CTD, TFAP2B, and MCM3 regulate Myc/MYC expression in renal collecting duct (CD) cells.

**Methods:** Human and mouse CD cells line, Myc-tagged TFAP2B, Tpap2b, and Tpap2b Cry2-ha tagged human and mouse FPC-CTD constructs, and Cyp1, Pkd1 and MHC-PMY promoter constructs were used to perform dual luciferase and co-IP assays.

**Results:** In mouse cells, TFAP2B & 2 positively regulated expression of Pkd1 and Cyp while Myc was positively regulated by TFAP2B but negatively regulated by TFAP2B. In Pkd2 mice, TFAP2B negative regulation of Myc was epistatic over FPC-CTD activation. MCM3, previously identified as a FPC-CTD binding partner, positively regulated Myc promoter activity. Human MYC was activated by FPC-CTD and negatively regulated by TFAP2B.

**Conclusions:** We show that in both mouse and human, FPC-CTD and TFAP2B regulate Myc/MYC expression. Notably, mouse TFAP2B isoforms differentially regulate Myc expression, while humans lack a MYC activating isoform. Based on our data, we propose a model in which a regulome that includes FPC-CTD, TFAP2B, and MCM3 modulates Myc/MYC expression in CD cells in a species-specific fashion. Species-specific renal phenotypes could be attributable to differences in constituent proteins, isoform diversity, and epistatic interactions within the proposed regulome. We speculate that this model may explain the differential effects of PKHD1/Pkd1 deficiency on renal cystogenesis and provide initial clues for putative renoprotective mechanisms in Pkd1 mutant mice.

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

**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 missense 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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Underline represents presenting author.
Cystic Kidney Diseases: Mechanisms, Genetics, and Treatment

Posters

**POI158**

**Cystin Deficiency in Cystic Kidney Disease**

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**Background:** The severity of tuberous sclerosis complex (TSC) manifestations seem to be 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 CRISPR/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.

**Results:** To characterize the EVs, we used tunable resistive pulse sensing, dynamic light scattering, transition electron microscopy and immunoblot analysis.

**Conclusions:** The size of the EVs, we used tunable resistive pulse sensing and dynamic light scattering. The parental cell line had an average size of 123.5 ± 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 ± 2.1 mV and -19.8 ± 2.7 mV respectively. The isolated nanosized vesicle had excellent purity as assayed using transmission electron microscopy.

Both cell lines had a heterogeneous population of EVs based on size, and more than 90% of the EVs were larger than 500 nm. Quantitative PCR analysis showed the downregulation of miR-212a-3p and miR-99a-5p in EVs derived from Tsc1 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.

**Funding:** Other U.S. Government Support

**POI152**

**Tsc2 Mutation Induces Renal Tubular Cell Nonautonomous Disease**

**John J. Bissler,** 1,2 Prashant Kumar, 1 Ying Yao, 1 Fahad Al-Zadjali, 1 The University of Tennessee Health Science Center, Memphis, TN; St. Jude Children’s Research Hospital, Memphis, TN.

**Background:** Tuberous sclerosis complex is associated with both renal tumors and cysts in most affected patients. The renal cystic disease is poorly understood and has no approved treatment. Using a new principal cell-targeted murine model of the Tsc2 gene deletion, we found that the renal cystic epithelium was mostly composed of type 1 renal proximal tubular epithelial cells.

**Methods:** We used lineage tracing experiments to understand the tubular cell fate, and dynamic light scattering, tunable resistive pulse sensing, transition electron microscopy and western blot analysis to characterize the extracellular vesicles. We used microarray analysis to characterize the expression of the extracellular vesicles on target tubule cells.

**Results:** Using lineage tracing experiments, we find that while principal cells are involved and undergo clonal expansion, they contribute a surprisingly small number of cells to the cyst. We identify that cystic kidneys contain more interstitial extracellular vesicles than noncystic kidneys, excrete fewer extracellular vesicles in the urine, and contain fewer extracellular vesicles in the cyst fluid. We demonstrate that the loss of the Tsc2 gene in the cells producing the extracellular vesicles greatly changes the effect of extracellular vesicles on renal tubular epithelium, such that they develop increased secretory and proliferative pathway activity. mTORC1 activity is not the only controller of extracellular vesicles production, but mTORC1 inhibition does reduce the extracellular vesicle production and greatly changes the effect of extracellular vesicles from treated cells. This may be, at least in part, why mTORC1 inhibitors have a beneficial effect in patients.

**Conclusions:** Taken together, these results contribute to the mechanistic understanding of how genetically intact cells contribute to the disease phenotype.

**Funding:** Other U.S. Government Support

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**Underline represents presenting author.**

486
Whole-Exome Sequencing in 97 Families with Renal Ciliopathies Reveals a Causative Mutation in a Known Kidney Disease Gene in 62% and Identifies Potential Novel Causative Genes

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Background: Nephronophthisis-related ciliopathies (NPHP-RC) represent the most frequent genetic cause of end-stage renal disease in the first three decades of life. Affected children present with increased echogenicity and/or cysts on renal ultrasound. As mutations in 96 recessive genes have been identified as disease-causing (Kidney Int 95:914, 2019), whole exome sequencing (WES) represents the best approach for the identification of the causative mutation (Nephrol Dial Transplant 31:1802, 2016). In a previous study of consanguineous or familial cases of NPHP, we identified causative mutations in 63% of all patients (Kidney Int 89:468, 2016) by WES.

Methods: To reveal the percentage of causative mutations in NPHP-RC and to identify potential novel disease genes, we evaluated WES data from 97 families with childhood-onset NPHP-RC for causative mutations in 178 monogenic chronic kidney disease genes. Clinical inclusion criteria were increased renal echogenicity or identification of ≥2 renal cysts on renal ultrasound.

Results: In 60 out of 97 families (62%), we identified a mutation in a known monogenic kidney disease gene as causative for the phenotype. Out of these, 47 families harboured mutations in one of the known ciliopathy genes. 13 families were diagnosed for a disease that phenocopies NPHP-RC. Amongst these, CAKUT represented the most frequent phenocopy disease (7/13 families), followed by Alport syndrome, metabolic diseases and nephrocalcinosis (2/13 families each). In 10 families, in which a mutation in known disease genes was excluded, we identified a biallelic mutation in a potential novel causative gene candidate.

Conclusions: By whole exome sequencing we identified a disease-causing mutation in 62% of families with a diagnosis of NPHP based on renal ultrasound 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 Cr≥175 μmol/l, 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 of PKD could either have milder undiagnosed PKD, or non-pathogenic mutations. The genetic complexity of PKD1 and 2, and the difficulty of ascertainment 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-yr 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 Institute 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 yrs; range 20-95) vs. PKD2 (16%) (47 yrs; range 20-95 yrs, p=0.0001) and had a slightly lower blood pressure, body mass index, and baseline estimated glomerular filtration rate (eGFR; 70.2±16.2 vs. 75.4±16.2 ml/min/1.73 m², p=0.01). 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 and is commonly treated with growth hormone (GH). Autosomal dominant polycystic kidney disease (ADPKD) is a multisystem disorder that has bilateral renal cysts and is an important cause of end stage renal disease (ESRD).

Case Description: A 5-1/2 yr old girl with TS with 45 X, 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 aneurysms. 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 treatment was stopped. After 6 months off GH therapy, renal enlargement was uncontrolled with enlargement of her cysts. Patient got 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 normal 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 therapy and 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 deficits.

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 D, 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 I-60). Medullary and/or corticomedullary junctional 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 1-5). The mean size of the smallest and largest cyst were 3.6 ± 2.2 mm (range 2-8) and 11.9 ± 6.9 mm (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.
more dense collagen, and collagen hybridizing peptide labeling showed more denatured collagen in pkd2 zebrafish kidney. Preliminary data from Pkd10.3−/− mice show similar patterns of collagen density and denaturation.

**Conclusions:** To our knowledge, this is the first report of any phenotype in pkd2 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

Increased collagen density in kidney of pkd2 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)**

**Janina Paula F.C. Prince, M. Singh, S. Nasr, T. Chebib.**

**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) thinning 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 and 19.6 (± 24) mm respectively. The number of cysts (≥ 5 mm) in 34% of cystic patients (cystic) and 20% and 19.6 (± 24) mm respectively. The number of cysts (≥ 5 mm) in 34% of cystic patients 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 serum creatinine (1.1 vs 1.7 mg/dL) at the end of follow-up, and MCD was the only risk factor for the progression of CKD (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 = 0.00) at the end of follow-up, and MCD was the only risk factor for the progression of CKD (p = 0.004). 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 = 0.00) at the end of follow-up, and MCD was the only risk factor for the progression of CKD (p = 0.004). 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 = 0.00) at the end of follow-up, and MCD was the only risk factor for the progression of CKD (p = 0.004). 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 = 0.00) at the end of follow-up, and MCD was the only risk factor for the progression of CKD (p = 0.004). 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 = 0.00) at the end of follow-up, and MCD was the only risk factor for the progression of CKD (p = 0.004). 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 = 0.00) at the end of follow-up, and MCD was the only risk factor for the progression of CKD (p = 0.004). 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 = 0.00) at the end of follow-up, and MCD was the only risk factor for the progression of CKD (p = 0.004). 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 = 0.00) at the end of follow-up, and MCD was the only risk factor for the progression of CKD (p = 0.004). 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 = 0.00) at the end of follow-up, and MCD was the only risk factor for the progression of CKD (p = 0.004). 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 = 0.00) at the end of follow-up, and MCD was the only risk factor for the progression of CKD (p = 0.004).

**Conclusions:** MCD is frequently observed in TBMD patients and is a risk factor for the progression of CKD.

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

**Underline represents presenting author.**
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 abnormal liver 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-estimated 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 the UKBB, P=2×10^-6). The penetrance of diabetes was 30% and average eGFR was 71 (45% with eGFR<60) compared to 91 (40%) in UKBB population. Their liver function is comparatively different. Gamma GT 110 v 37.4 (32%), polyuria (30%), renal pain (25%), blood creatinine increase (23%) and nocturia (22%); the rates were similar between the 2 subgroups. One incidence of hepatic enzyme increase with one of hemodialysis and one death (unrelated to TOL) was only observed in Subgroup 2.

Conclusions: HNF1B deletions and duplications can be detected in a large unselected dataset. Deletions are more pathogenic than duplications. However, HNF1B duplications do not have an effect in phenotype, 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. HNF1β mutations are rare, associated with multisystemic disease and heterogeneous kidney involvement. HNF1β-associated kidney disease may not manifest until adulthood. We present a case of an older female with chronic kidney disease and heterogeneous kidney involvement. HNF1β-deleted 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 hypogammaglobulinemia. 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 hypogammaglobulinemia 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 leading to diagnosis later in life. Our patient’s constellation of medical problems including glucose intolerance, mild hyperparathyroidism, hypogammaglobulinemia, unilateral ovary agenesis and genitourinary (GU) tract abnormalities are all features of HNF1β-associated kidney disease. This diagnosis should not be overlooked in patients with GU abnormalities, electrolytes disturbances and/or signs of tubulointerstitial kidney disease. Additionally, these patients should be monitored for progressive kidney disease and undergoing periodic screening for renal cell carcinoma.

PO1534
A Post Hoc Analysis of Tolvaptan (TOL) Efficacy and Safety in Slowing Rate of Renal Function Decline in Subjects with Very Late-Stage Autosomal Dominant Polycystic Kidney Disease (ADPKD)
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Background: ADPKD is a progressive disease that causes end-stage renal disease in ~50% of the affected individuals by age 60. TOL, a selective vasopressin V2-receptor antagonist, has been shown to slow the progression of renal function decline in ADPKD subjects with an eGFR of 25 mL/min/1.73m2 or higher. The efficacy and safety of TOL in subjects with lower eGFR remain understudied. This post-hoc analysis evaluated the efficacy and safety of TOL in subjects with stage 4 CKD (eGFR of <30 mL/min/1.73m2).

Methods: This is a retrospective analysis of a subgroup of ADPKD subjects who enrolled in the TOL open-label extension (OLE) trial (NCT02251275). Included subjects had a baseline eGFR of <30 mL/min/1.73m2, received ≥1 TOL dose, and were randomized to the placebo group in the REPRISE trial (NCT02160145). Two subgroups of subjects were analyzed, one with baseline eGFR of 25-30 (Subgroup 1) and one <25 (Subgroup 2). The variables evaluated included demographics, adverse event (AE) profile, and intra-subject comparison of change in annualized eGFR decline during the OLE trial to that during placebo use in the REPRISE trial. Annualized eGFR change slopes in the treatment period were calculated using eGFR values between Month 1 and 12 visits to compensate for the acute hemodynamic effect of tolvaptan. Comparison was made by linear mixed model.

Results: Of 1,803 subjects enrolled, 159 (8.8%; 76 in Subgroup 1 and 83 in Subgroup 2) met the selection criteria. Annualized eGFR change slopes for all subjects (n=148) were -5.28 in the REPRISE trial and -3.16 in the OLE trial with a treatment effect of 2.11 (95% CI: -0.05, 4.26, p=0.066). The treatment effects were 1.99 and 2.17 for Subgroups 1 and 2, respectively (p=0.0001 for both subgroups). The 5 most common AEs were thirst (32%), polyuria (30%), renal pain (25%), blood creatinine increase (23%) and nocturia (22%); the rates were similar between the 2 subgroups. One incidence of hepatic enzyme increase, one of hemodialysis and one death (unrelated to TOL) was only observed in Subgroup 2.

Conclusions: This post-hoc analysis demonstrated that TOL significantly decreases the rate of eGFR decline in ADPKD subjects with stage 4 CKD, including those with an eGFR of <25 mL/min/1.73m2.
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 various years. 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 1 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. Patients stratified by Mayo classification (Class 1A-1E). Analyses included the comparison of the annual changes of eGFR at eGFR (mL/min/1.73m²/year) and total kidney volume (ATKV (>2cm³/year)) between pre and post-treatment, and AeGFR or ATKV 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 (CKD5-3B). Duration of treatment was 3.3±1.3 years. eGFR of tolvaptan group were lower and hATKV of tolvaptan group were higher compared to those of control group at baseline (eGFR: 53.7±22.8 vs 65.7±30.0, p=0.06. hATKV: 1198±157 vs 829±799.5 mL/min, p<0.0001). There was no significant difference in AeGFR between treatment (53.9±2.86 vs 53.8±2.86) or control group (53.8±2.86 vs 53.8±2.86). However, in tolvaptan group AeGFR improved compared to pre-treatment (-2.95±2.86 vs -4.33±5.72, p=0.027) and this improvement lasted at least for 36 months in 50 patients. ATKV of tolvaptan group was lower than that of control (21.99±30.3 vs 30.43±6.05 vs 5.10±4.06±1.6, p<0.01) and this trend was also found in Mayo class 1B-1D. ATKV also decreased compared to pre-treatment (2.19±0.33 vs 4.06 vs 4.67±0.57-6.76, p<0.01).

Conclusions: Tolvaptan dramatically reduced ATKV, while there was no beneficial effect for AeGFR compared to control. However tolvaaptan improved AeGFR compared to that of pre-treatment. The discrepancy between our results and previous reports might arise from the fact that our cohort mainly comprised advanced CKD stage patients or limited sample size. Further long-term observation is required 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 only approved treatment in Canada for slowing renal function decline and kidney enlargement in ADPKD patients. As per Health Canada Mitigation Strategy (REMS), which is a mandatory program for patients prescribed tolvaptan, tolvaptan treatment pattern analysis and to report on treatment persistence and liver transaminases elevation rate through the HSMDP.

Methods: Descriptive analyses were conducted on the following baseline measures: demographics, hereditary kidney disease. Tolvaptan (Jynarque®), the first and only approved treatment in the 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.

Results: 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 Dataverse (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, hereditary kidney disease, and disease characteristics. All measures were identified within the 6-month period prior to the index date in the Symphony Health IDV.

Conclusion: This is the first real-world study to describe characteristics of ADPKD patients initiating treatment with tolvaptan in the US.

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 (Jynarque®), 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 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 Dataverse (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, hereditary kidney disease, and disease characteristics. All measures were identified within the 6-month period prior to the index date in the Symphony Health IDV.

Results: Analysis was conducted for 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%) participants, 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 characteristics of ADPKD patients initiating treatment with 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.

PO1539

Early-World Descriptive Findings on Tolvaptan-Treated Patients with Autosomal Dominant Polycystic Kidney Disease in the United States Mylene Sanon,2 Sunning Tao,1 Irene Cosmatos,1 Gretchen S. Dieck,1 Michele L. Julian,1 Timothy Wilt,2 Kristin Pareja,2 Alvin Estilo,2 Carol I. Matthews.1 United BioSource LLC, Blue Bell, PA; 2Otsuka Pharmaceutical Development and Commercialization Inc, Princeton, NJ.

Background: Tolvaptan is the first and only 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, which is the most severe adverse event potentially associated with tolvaptan. 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 HSMDP.

Methods: A retrospective analysis of patients with ADPKD enrolled in C-MAJOR was conducted. All patients treated with tolvaptan for more than 1 year were included for analyses. Patients who initiated tolvaptan from June 2014 to March 2020 in Hokkaido University Hospital. 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. Patients stratified by Mayo classification (Class 1A-1E). Analyses included the comparison of the annual changes of eGFR at eGFR (mL/min/1.73m²/year) and total kidney volume (ATKV (>2cm³/year)) between pre and post-treatment, and AeGFR or ATKV between tolvaptan-treated and control.

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, 50.4%), the majority were white (n=2,153, 79.6%). Of those with known ethnicity (n=2,190, 94.0%), 759 (35.1%) 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 persistence was 325.9 days (SD: 173.2).

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 which is consistent with the patient population included in the treatment pattern analysis remained on tolvaptan close to 1 year.

Funding: Commercial Support - Otsuka Pharmaceutical Development & Commercialization Inc.
**PO1540**

**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 modeled 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).

**Conclusions:** 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 Pharmaceuticals Development & Commercialization, Inc.

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**PO1542**

**Urinary Lithogenic Risk Profile in ADPKD Patients Treated with Tolvaptan**

Matteo Baraschi,1 Nassar Dhayat,2 Pietro Manuel Fuster.3

**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.

**Methods:** 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, the urinary 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 urine relative supersaturation ratios for calcium oxalate (-0.56; -0.82 to -0.3, p < 0.001), brushite (-0.33; -0.54 to -0.11, p = 0.004) and uric acid (-0.02; -0.38 to 0.37, p < 0.001) and with increased urine citrate in mmol/mmol creatinine per day (0.25; 0.050-0.46, p = 0.02) and calcium in mmol/mmol creatinine per day (0.31; 0.090-0.53, p = 0.006) excretion. In addition, Tolvaptan treatment was associated with decreased net acid excretion in meq/mmol creatinine per day (-0.54; -0.90 to -0.17, p = 0.004) and increased net gastrointestinal alkaline absorption in meq/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.

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**PO1543**

**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 ADPKD 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.

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**PO1541**

**Global Real-World Evidence of Tolvaptan in Patients with Autosomal Dominant Polycystic Kidney Disease (ADPKD)**

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**Background:** ADPKD is a rare, hereditary, systemic kidney disease characterized by progressive renal damage. Patients frequently develop end stage kidney disease, requiring dialysis or transplantation. Treatment options are limited, and research in ADPKD is ongoing to improve outcomes. The vasopressin V2 receptor antagonist tolvaptan has been shown to slow ADPKD progression, and office blood pressure. 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, WINCENT®. 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(hTKV) 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 1.9 years in pre-prescription period and 2.8 years in post-prescription period respectively. Median age was 55 years old and 31 cases were female. Median hTLV and hHTKV 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 preTLV and had higher rate of taking ursodeoxycholic acid. Logistic regression analysis showed older age (OR 2.60[1.36-5.72],p<0.01) and higher preTLV (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 elder 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 vasopressin 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, intractable 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 tests. Improved pain control has allowed resumption of more normal daily activities and

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 develop from 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 CXCR4+/c-kit+/ureteric bud (UB) cell progenitors and further UB branching. The UB gives rise to renal collecting ducts and the lower urinary tract. We observed the development of UB-like cytorarchitecture 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 (AOP2, CALB1, MUC1) including principal (AOP3) and intercalated cells (AQP5). Moreover, we identified cilia formation on the inner surface of the luminal cavity of CD tubules forming a urinary tract model. We have shown that collecting duct cells can differentiate into kidney organoids from pluripotent stem cells. Cell Stem Cell; 21: 730-746


Funding: Commercial Support - Goldfinch Bio

PO1547

Fluidic Model of ARPKD Using Vascularized Kidney Organoids Identifies HIF-1 as a Potential Therapeutic Target
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Background: We have recently reported a method to generate vascularized kidney organoids from fluidic chips. Vascularized kidney organoids derived from PKHD1-/- mutants demonstrated clinically relevant phenotypes that recapitulate cystogenesis in distal nephrons unlike static models with forskolin which induces cysts in proximal tubules. Here, we utilized this new PKD model to elucidate pathomechanisms and identify potential therapeutic targets for ARPKD patients.

Methods: PKHD1-/-hiPSCs were generated by CRISPR/Cas9 genome editing and differentiated into kidney organoids by following our reported protocol. Cystogenesis was stimulated by either fluidic flow on fluidic chips or forskolin in static culture. Cystic phenotypic change quantification was performed by immunostaining. Gene expression was evaluated by 3D-gene microarray, and signal pathways were assessed by Metacore. Based on signal pathway results, candidate compounds were tested, and phenotypic improvement was evaluated by measuring tubular/cyst diameters using whole-mount immunostaining.

Results: Fluidic flow altered 407 signal pathways in PKHD1-/- organoids when compared to PKD1+/+/- organoids while 63 pathways were changed by forskolin in conventional static culture. In those pathways, 32 were involved in both flow- and forskolin-induced signal changes. In the common 32 pathways, HIF-1 pathway was top ranked with lowest p value of 3.71x10^-15, suggested as a potential pathomechanism of ARPKD. To validate the result, we treated vascularized kidney organoids with HIF-1 inhibitor from day 16, the earliest stage of nephron differentiation. The distal nephron diameter was increased from 36.2 ± 7.7 μm (n=96) to 54.8 ± 21.8 μm (n=59) by fluidic flow (p=8.65x10^-21), which mimics normal kidney development. Using pharmacological approaches, we were able to induce cysts formation in response to forskolin and choler toxin treatment, thus, simulating the abnormal CD response to excess cAMP in PKD or normal rodent embryonic kidneys [2].


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Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only  Underline represents presenting author.
PO1549

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 Pkd1<sup>+/−</sup> (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, Atg5, Atg16l1), decreased Rab9a and increased mTORC1 (p56, 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 Pkd1<sup>+/−</sup> (RC) mice.

Methods: Proteins were determined by immunoblot analysis. Male RC 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, an autophagy inducer. In 150 day old RC hearts, there was an increase in p-S6, p-Akt, p-Beclin, an autophagy regulator and activating molecule in Beclin-1-regulated autophagy (AMBR1A). There was suppressed autophagic flux (lack of an increase in LC3-II, a marker of autophagosomes, with the lysosomal inhibitor bafilomycin-Baf), 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.

Funding: Veterans Affairs Support, Other U.S. Government Support

PO1550

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<sup>−/−</sup> mice with erastin, a ferroptosis inducer, and Ferrostatin-1, a ferroptosis inhibitor.

Results: We found that the levels of free radical-induced oxidation and 4-HNE, a bioproduct of lipid peroxidation, were increased in Pkd1<sup>−/−</sup> 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<sup>−/−</sup> 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 Pkd1<sup>−/−</sup> mice (all p<0.01).

PO1551

Cux1 Regulates Cilia Length in Polycystic Kidney Disease

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Background: Renal cyst development in ADPKD results from mutations in the PKD1 or PKD2 genes, which encode the proteins polycystin1 (PC1) and polycystin2 (PC2). PC1 and PC2 proteins are localized to primary cilia where they are proposed to form a receptor channel complex that detects flow transmitting a calcium-mediated signal. Primary cilia are critical to the pathogenesis of ADPKD, which is one of the many ciliopathies that exhibit renal cystic disease. Cux1, a murine homolog 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),
PO1552
Low-Dose Repeated Cisplatin-Induced Renal Injury Promotes Cyst Formation in Both Ciliostatic and PC2 Mutant Mouse Models
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Background: Multiple renal cystic diseases, including PKD, are caused by dysfunction of the primary cilia 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 antitumor drug used widely in treatment of varieties of malignancies that displays severe nephrotoxicity 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 treatment of C57Bl6J (BW; IP once a week for 4 weeks) on adult-induced conditional Ihh88 and PC2 mutant mice. We preformed IF staining for the injury marker kim1 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 PC2 mutant and at 9 weeks in Ihh88 mutant after the final dose.

Results: Low-dose repeated cisplatin treatment resulted in increased kim1 expression, mainly in the cortex, compared to vehicle treatment group in both Ihh88 mutant and PC2 mutant mice as 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 Ihh88 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.

Funding: NIDDK Support

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 cilia genes polycystic kidney disease PKD1 and PKD2. Recent studies show that ADPKD is associated with abnormal bone health with increased bone formation and low bone serum alkaline phosphatase, even when kidney 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. Additionally, circulating bone ALP levels were decreased in ADPKD osteoblasts, which is consistent with the lowered circulating bone ALP levels.

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

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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 will 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 fumarate 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 progressing mouse model of ADPKD (Pkd1RC/RC) 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 chemistry 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-blot, immunofluorescence, and assay kits.

Results: At 30 days, Pkd1RC/RC mice presented increased CI and TKV/BW. However, serum creatinine and fibrotic markers were not different compared to controls. Pkd1RC/RC 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 (R²=0.693, p<0.05) and inversely with fibrotic markers (R²=0.672, p<0.05).

Conclusions: Our study shows longitudinal changes in the Nrf2 response in Pkd1RC/RC 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.

Funding: NIDDK Support

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 macropages, cytokines and accelerates cystogenesis in Pkd1-knockout mice. We hypothesized that Pkd1-knockout mice fed a high protein diet, similarly increases kidney macrophages and accelerates cyst growth.

Methods: We used adult tamoxifen inducible Pkd1fl/+ 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 buffer saline (intraoperatively 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 macropages by ICS.

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+). Mice fed a HP diet had 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 chemokines production 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 growth.

Funding: NIDDK Support, Private Foundation Support

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PO1559

Probenecid Inhibits Cyst Development in Pkd1<sup>RC/RC</sup> Mice

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Background: ADPKD cysts contain high levels of ATP that contribute to cyst enlargement. Among other effects, ATP excess leads to a reduced reabsorption in cyst-lining epithelium and cyst fluid accumulation. We demonstrated that Probenecid, a known inhibitor of the sodium-1 transport, slows cystogenesis in Pkd1<sup>RC/RC</sup> mouse kidneys. We now report the effect of Probenecid in the mouse model of Pkd1<sup>RC/RC</sup> mice.

Methods: Probenecid, a hypomorphic model of Pkd1<sup>RC/RC</sup>, aged with osmotic minipumps were implanted to deliver Probenecid for 42 days. After treatment, 30 cm<sup>3</sup>/min/100g at 12 months age. 42 days long Probenecid treatment of Probenecid on Na<sup>+</sup> reabsorption was tested on mpkCCD cells seeded onto permeable chamber. ATP excess leads to a reduced reabsorption in cyst-lining epithelium and cyst fluid accumulation. We demonstrated that Probenecid, a known inhibitor of the sodium-1 transport, slows cystogenesis in Pkd1<sup>RC/RC</sup> mouse kidneys. We now report the effect of Probenecid in the mouse model of Pkd1<sup>RC/RC</sup> mice.

Results: After treatment, 10 months old mice were subjected to glomerular filtration rate (GFR) measurements and kidneys were collected for histomorphological studies. Effect of Probenecid on GFR showed that GFR was reduced significantly as compared to control, 0.94±0.08 ml/min/100g at 12 months age. Probenecid treatment of Probenecid on Na<sup>+</sup> reabsorption was tested on mpkCCD cells seeded onto permeable chamber supports with open-circuit current measurements.

Conclusions: Probenecid inhibits cyst development in Pkd1<sup>RC/RC</sup> mice and supports with open-circuit current measurements. Probenecid demonstrates therapeutic potential against ADPKD cyst progression in a Pkd1<sup>RC/RC</sup> mouse model by reducing cyst size, renal hypertrophy and supporting GFR and reabsorption from the cyst space. Support: ASN Carl W. Gottschalk Award.

Funding: National Institute of Diabetes, Digestive and Kidney Diseases (NIDDK) Support

PO1560

Pharmacological Inhibition of β-Catenin-Activated Transcription Slows Cystogenesis in a Postnatal Mouse Model of ADPKD

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Background: The Wnt signaling pathway has an important role in nephron development and elevated expression of β-catenin, a master regulator of the Wnt signaling pathway, has been shown to correlate with cystogenesis in autosomal dominant polycystic kidney disease (ADPKD). Here we provide evidence that pharmacological inhibition of β-catenin-mediated suppression of cystogenesis is achievable in vivo and in vitro through the use of a novel β-catenin inhibitor.

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 Wnt 7a and higher levels of β-catenin in cystic kidneys of CAGG-CreER<sup>+</sup>/Pkd1<sup>fl/fl</sup> mice. In addition, fibronectin, a known transcriptional target of β-catenin was significantly overexpressed in murine kidney culture derived from human ADPKD kidneys. JCK cells exhibited decreased mitochondrial number, defective mitochondrial morphology and function, and increased expression of CAMP and cyst dynamics as compared to normal kidney. 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.

Conclusions: Small-molecule activators of β-catenin in postnatal murine kidneys inhibit cystogenesis. We tested CAGG-CreER<sup>+</sup>/Pkd1<sup>fl/fl</sup> mice with a small molecule, ICQ-001, that blocks the interaction of β-catenin with CBP. We detected significant reduced cyst formation as measured by reduced kidney/body weight ratio (0.047±0.004 vs 0.022±0.001) and the cyst area per kidney area (37.8±3.1 vs 13.7±3.1) and also observed a significant reduction in fibronectin after ICQ-001 treatment. Interestingly, cysts that may have formed prior to the start of the treatment remained large suggesting that ICQ-001 may primarily act on inhibiting cyst initiation, rather than inhibiting the enlargement of pre-existing cysts. Importantly, ICQ-001 treatment did not affect the growth of the mice.

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PO1561

Glucosylceramide Synthase Inhibition Preserves Mitochondrial Function and Reduces Reactive Oxygen Damage in the Jck Mouse Model of Poly cystic Kidney Disease

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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 (Genes671611) 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 Oxylight system (Millipore).

Results: Reductions in electron transport chain and mitochondrial membrane potentials as well as mitochondrial DNA were observed in control 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. Reductions in mitochondrial dysfunction in Jck mice following GCSi treatment correlates with preserved mitochondrial function.

Funding: Commercial Support - Sanofi-Genzyme

PO1562

Oral Delivery of Nanoparticles for Renal Disease

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Background: Nanomaterials are promising for drug delivery, but few have been successful for oral delivery, the optimal route for chronic diseases like polycystic kidney disease (PKD). Drug candidates that slow cyst growth require high dosages leading to side effects like hepatotoxicity. To limit this, we previously developed kidney targeting micelles (KM) and found they accumulated in the kidneys. To augment this system for oral delivery, herein, we load KM and metformin (met), a diabetes drug with PKD promise, into chitosan nanocapsules (CS-NC) to overcome the barriers of the gastrointestinal (GI) tract. We hypothesize that CS-NC will deliver met via the GI tract and show efficacy in PKD mice models. Furthermore, we characterize KM loaded into CS-NC to serve as a platform for future oral delivery of targeted therapeutics.

Methods: CS-NC were synthesized via ionic gelation. To confirm KM loading into CS-NC, dynamic light scattering (DLS) was performed for the following: KM loaded into CS-NC, CS-NC, mixed with CS-NC, CS-NC, or KM. To assess the oral delivery performance, we orally gavaged 300 mg/kg met loaded in CS-NC or free met to Pkd1<sup>fl/fl</sup>, Pkd1<sup>fl/fl</sup>Rc/Rc mice. On P22, kidneys were excised to assess kidney morphology.

Results: We observed increased expression of Wnt 7a and higher levels of β-catenin in cystic kidneys of CAGG-CreER<sup>+</sup>/Pkd1<sup>fl/fl</sup> mice. In addition, fibronectin, a known transcriptional target of β-catenin was significantly overexpressed in murine kidney culture derived from human ADPKD kidneys. JCK cells exhibited decreased mitochondrial number, defective mitochondrial morphology, and increased expression of CAMP and cyst dynamics as compared to normal kidney. 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.

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. Reductions in mitochondrial dysfunction in Jck mice following GCSi treatment correlates with preserved mitochondrial function.

Funding: National Institute of Diabetes, Digestive and Kidney Diseases (NIDDK) Support

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PO1563

Long-Term Effect of Novel Morphometric 3D Capsule Device to Constrain Growth in Polycystic Kidney: Comparison Between Wild-Type, Cy/+ , and PCK Rat Models

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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 cease 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. 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. 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 6.0g 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.

Funding: Government Support - Non-U.S.

PO1564

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 (4k16 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 3D 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

PO1565

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 microcysts. 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 relaxation 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 T1 and T2 maps, which 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±91 ms; T2: 71±6 ms) and medulla (T1: 1529±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 assess therapeutic efficacy in clinical trials.

Funding: NIDDK Support, Commercial Support - Siemens Healthineers
PO1566

Human Factors Impact on the Development of Software as a Medical Device (SaMD): A Case Study Using the System Usability Scale (SUS)

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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 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 renal function. Accurate prognostic tools may help predict outcomes and optimize clinical management to slow the loss of renal function.

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 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 a global SUS score was calculated, a total of 79 participants contributed to the global SUS scores: 37 nephrologists, 28 radiologists and 14 nephrologist/radiologist support staff.

Results: APM System received the following SUS scores in studies one through four: 72, 78, 80, and 80. The SUS score increased an 8 point from the first study to the fourth study. 4 New functions (e.g. Consultation workflow) introduced.

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.

PO1568

Correlation of Baseline Urinary Metabolic Biomarkers with ADPKD Severity in the TAME-PKD Study

Cystic Kidney Diseases: Emerging Concepts, Biomarkers, and Clinical Trials

Poster

Thursday, June 2019, 62 patients who met the conditions of no tolvaptan use, GFR ≥ 60.1 ml/min/L, the median TKV was 1137 mL, and the median urine NAG index (NAG-to-Cr ratio) was 4.64 U/mg Cr. In the reduced renal function group (30aCrGFR < 60 mL/min, n=32), we observed a correlation between NAG index and RKVP in single-regression analyses (R² = 0.330, p < 0.003), but not with 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, patients who met the conditions of no tolvaptan use, GFR<60, 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 68.47 mL/min/1.73m², the median TKV was 1137 mL, and the median urine NAG index (NAG-to-Cr ratio) was 4.64 U/mg Cr. In the reduced renal function group (30aCrGFR < 60 mL/min, n=32), we observed a correlation between NAG index and RKVP in single-regression analyses (R² = 0.330, p < 0.003), but not with eGFR, 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, 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 and multiple regression analyses, the predict RKVP by NAG index (U/mg Cr) and eGFR<60 mL/min, n=32, using the estimated equations will be shown.

Conclusions: To varying degrees, proteinuria, lactate, PKM2 and PDK1 urinary concentrations correlated with RKVP 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

PO1569

Urine NAG Is an Effective Clinical Parameter to Presume Disease Activity of Autosomal Dominant Polycystic Kidney Disease

Poster

Thursday, June 2019

Background: Patients with ADPKD are mixed with those who progress to ESRD and those who maintain stable, 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, patients who met the conditions of no tolvaptan use, GFR≥60, 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 68.47 mL/min/1.73m², the median TKV was 1137 mL, and the median urine NAG index (NAG-to-Cr ratio) was 4.64 U/mg Cr. In the reduced renal function group (30aCrGFR < 60 mL/min, n=32), we observed a correlation between NAG index and RKVP in single-regression analyses (R² = 0.330, p < 0.003), but not with eGFR, 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, 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 and multiple regression analyses, the predict RKVP by NAG index (U/mg Cr) and eGFR<60 mL/min, n=32, using the estimated equations will be shown.

Conclusions: To varying degrees, proteinuria, lactate, PKM2 and PDK1 urinary concentrations correlated with RKVP 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
Conclusions: In ADPKD patients with renal dysfunction (CKD stages3), it was confirmed that NAG index may be useful as a predictor of the disease activity associated with RKVP and, if it is 6.0 U/mgG or greater, may be presumed to be associated with higher disease activity.

PO1570

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 376 individuals with 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-vertexing 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 mutation class, overweight/obesity was 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: 1.28 [1.07, 1.55]; radicular pain: overweight: 2.28 [1.13, 4.60], obese OR: 2.68 [1.25, 5.76]. Longitudinally (n=823), overweight: 1.66 [1.02, 2.68], obese OR: 1.77 [1.03, 3.03]; radicular pain: overweight ± 2/yr, p= 0.04) and a faster median rate of eGFR decline (-2.2 vs -2.0 ml/min/1.73m²). Back, abdominal, and radicular pain were reported more frequently in individuals with overweight/obesity (p<0.05).

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. Thus, the purpose of the study is to evaluate and classify polycystic liver progression in patients with ADPKD based on participant’s age, sex, height-adjusted liver cystic volume (htLCV) and height-adjusted liver volume (htLV) measurements.

Methods: We used 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 class 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=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 fitted (BMI: A: 317; B:48.15; C: 49.51; D: 127.16; 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

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO1573
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 (e-GFR) 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 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 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 subgroup, the median age of the affected parent that reached end stage renal disease was 55 (range 28-87) years. Hypertension was diagnosed in 89% at a mean age of 37.2 ± 10.5 years. Hepatic cysts were present in 70.3% 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 e-GFR was associated with younger age at the time of PKD diagnosis (p < 0.002), younger age at hypertension diagnosis (p < 0.08) and greater values of TKV (p < 0.001), height adjusted TKV (p < 0.001) and Body Mass Index (BMI) (p = 0.02).

Conclusions: 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 were independently associated with low eGFR.

PO1574
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 Imaging Consensus (MCIC) score of early stage ADPKD patients is limited to End Stage Renal Disease (ESRD) were calculated. Patients eligible for tolvaptan treatment (MCIC 1C,1D,1E, age <55 years old and estimated-GFR (e-GFR) ≥25ml/min/1.73m2) were identified. Individual medical history, clinical and laboratory data were examined for associations with renal and imaging parameters using linear regression models.

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 1A, 20% as 1B, 34% as 1C, 25% as 1D and 16% as 1E, MCIC. In multivariable analysis, patients' age (p<0.01), male sex (p=0.001), parent's age at time of ESRD (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 (19.81) 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 ESRD 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 10ml/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, 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.

PO1575
Design, Development, and Characteristics of a National Patient Registry in ADPKD

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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/pkdcure). Participants are registered and consented through the online system and asked to complete a series of modules quarterly. The PKD 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 72% are female, 4% 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% reported a genetic test for PKD, and 89% reported having cysts observed 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 high-quality 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

PO1576
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 are sparse of those 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

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 greater engagement of 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 34 patients per year. After 2015, with eGFR 15-30ml/min registration increased from 43 to 117, 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 Safety and Impact on TKV Growth and eGFR Slope 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 Classification IIC–IIE) 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 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] slope 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] is 65.5 mL/min/1.73 m2. Overall, 55.1%, 30.7% and 14.2% are of Mayo Imaging Class 1C, 1D and 1E, respectively.

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

PO1578

STAGED-PKD: Patient Enrichment and Model-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 and 30% reduction in eGFR slope 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 changes 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 treatment arms. There was no significant effect of niacinamide on acetylated/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 between niacinamide and placebo. Ht-TKV increased slightly from 1049 to 1082 ml/m^2 (p=0.71) with small eGFR decline from 83.6 to 81 ml/min/1.73 m^2 (p=0.084) in niacinamide treated patients (combined study 1+2). Furthermore, there was no statistical 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 exacerbation of 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 sunitinib activity over 12 months of treatment, and there was no signal to suggest a beneficial effect on any efficacy measure.

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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
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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 a unique ability to activate transcription of key antioxidants, suppress inflammation, and reduce proliferation. We are conducting an ongoing randomized, 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 117±16 ml/min/1.73 m^2. FMD_d was 9.3±0.5%, aPWV was 516±107 cm/sec, and median (IQR) ht-TKV was 333 (234, 475) ml/min. In the sub-group of young adults who received a supraphysiologic infusion of ascorbic acid to inhibit vascular oxidative stress (n=24), FMD_d 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 - Verdeur 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
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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 tolvaptan reported the lowest treatment satisfaction. No consistent changes were observed for ADPKD-IS 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.

Figure 1. Change from Baseline in PROs

Funding: Commercial Support - Otsuka Pharmaceutical Europe Ltd.
Methods: ESRD patients treated with dialysis or transplant with at least one ADPKD diagnosis code and a reported ESRD 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 estimated.

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 (129.6 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

*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

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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 decrease, 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 4358 non-PKD patients. The incidence rates of 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 herpetic 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 analyses 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 Four-Score 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 proved useful in the diagnosis of renal and hepatic cyst infection (CyI) in patients with autosomal dominant polycystic kidney disease (ADPKD). However, the definition of CyI by [18F]FDG by uptake in case of CyI based on a visual 4-point scale.

Methods: All ADPKD patients who were hospitalized between January 2007 and March 2019 for suspected CyI and who underwent an [18F]FDG PET/CT scan were retrospectively identified. CyI was defined based on 5 concomitant criteria: (i) fever ≥38°C; (ii) abdominal pain; (iii) peak plasma C-reactive protein level ≥70 mg/L; (iv) no other cause of inflammation; and (v) favorable outcomes after antibiotics for ≥21 days.

First, all [18F]FDG PET/CT images were qualitatively interpreted by 2 blinded board-certified nuclear medicine physicians in nuclear medicine. CyI 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.

Results: A total of sixty [18F]FDG PET/CT scans with a mean age of 50.7 ± 18.0 years of patients with ADPKD were 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 suspected 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

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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, while median [interquartile range] was 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

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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 morphology in a Czech ADPKD patients.

Methods: Thirty ADPKD cases were enrolled and analyzed by the 3DMD Face System. Morphometric analyses were performed using the Morphoex3s 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 retraction of the eyebrows area, midface-zygomatic prominence and retraction of the lateral buccal region. Most of the ADPKD cases have thin upper lip (red part of lip) in opposition to a prominent lower lip.

Conclusions: The preliminary results of this pilot study suggest that there could be a distinct 3D facial gestalt in ADPKD. ADPKD is an ideal candidate for “phenotype-driven variant prioritization”, where molecular genetic analysis could be linked to 3D morphometry. In ADPKD families, where molecular genetics failed to identify a causative variant, 3D morphometry could be used as a predictive marker of the risk of disease in non-affected parents. Supported by Charles University Grant Agency, project number 44120.

Funding: Government Support - Non-U.S.
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 F-actin bundling activity and higher spatial correlation of F-actin alignment in podocytes. When subjected to mechanical stress in organ-on-a-chip culture devices, phosphomimetic 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-b.

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/FH 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 cubulin. How loss of Clc-5 leads to reduced receptor expression remains unknown. Previous gene expression studies in Clc5 KO mice suggest there are alterations in cholesterol and lipid metabolism. Elevated cholesterol levels have been demonstrated to alter the organization of the endothelial 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 endothelial pathway. Additionally, we assessed PT function, megalin/cubilin expression, and protein distribution in cultured CRISPR/Cas9-generated Clc-5 KO cells.

Results: KD or KO of Clc-5 resulted in significantly decreased endothelial 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-depleted cells. We confirmed LMW proteinuria in the KO mouse. Heterozygous females also have 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/cubulin 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, epidemiologic 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 gene editing. By applying super-resolution STED microscopy and functional measurements, we characterized the phenotype of Podc229Q mice. Additionally, we evaluated the podocin229Q protein stability in human cultured podocytes.

Results: Although Podc229Q mice do not develop overt glomerular disease, super-resolution microscopy and morphometric analyses revealed ultrastructural alterations that have recently been linked to disease predisposition. Ultrastructural alterations were even more prominent in homozygous Podc229Q mice eventually 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 were decreased in Podc229Q mice as compared to WT. However, cultured podocytes expressing the variant. Mechanistically, increased proetional 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 Neprhin Injury due to Albumin Knockout in the Heavily Nephrotic, Polymerization-Defective GBM Laminin B2-Del44 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 anabuminic rats exhibit little or no increase in renal injury following multiple insults, Alport mice lacking albumin were previously shown to have surgically increased lifespan with delayed injury to glomeruli and nephrin epithelium.

Methods: We mated CRISPR-mediated, albumin-knockout mice with laminin B2-Del44 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 12 months for analyses. Plasma was analyzed for BUN. Glomeruli were analyzed by electron microscopy to determine foot process effacement. Nephren projection was analyzed by immunofluorescent microscopy to determine status of injury markers.

Results: Alport mice express a significant increase in albumin-Del44 double mutant mice exhibited a significantly increased proteinuria as well as increased glomerular injury, which is suggestive of glomerular injury.

Conclusions: Collectively, our data suggest that podocin R231Q may contribute to genetic predisposition in adult patients.
was decreased at younger ages. Neophren 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

**POI591**

**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.

**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 potassium level was (2.68±0.13mmol/L, serum magnesium level was (0.58±0.13mmol/L, ninty-four patients(88.68%) had hypernagnesemia, seventy-nine patients(81.44%,79/97) had hypercalciuria. 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.T660M (22.86%),c.965-1_976delGCGGA CATTGTTGmACCCAAAATT(T6.19%),p.D486N(i.76%), p.I535K(r.76%). Triple mutations was identified in 8 patients, compound heterozygous mutations were identified in 70 patients, homoyzgous mutations were identified in 18 patients, whereas 10 patients had only one heterozygous mutation. The 5 large genomic rearrangements were exon deletion, including E7,E8 deletion, E8,E23 deletion, E20-E24 deletion, E8 deletion,E4-E6 deletion. The sensitivity of genetic testing was 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.

**POI592**

**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 SLS 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 homoyzgous mutations without consanguinity history.

**Results:** Fifty-nine patients(56.67%) were female, the age was (34.87±15.36) years, serum potassium was (2.68±0.13)mmol/L, serum magnesium level was (0.58±0.13)mmol/L, ninty-four patients(88.68%) had hypernagnesemia, seventy-nine patients(81.44%,79/97) had hypercalciuria. 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.T660M (22.86%),c.965-1_976delGCGGA CATTGTTGmACCCAAAATT(T6.19%),p.D486N(i.76%), p.I535K(r.76%). Triple mutations was identified in 8 patients, compound heterozygous mutations were identified in 70 patients, homoyzgous mutations were identified in 18 patients, whereas 10 patients had only one heterozygous mutation. The 5 large genomic rearrangements were exon deletion, including E7,E8 deletion, E8,E23 deletion, E20-E24 deletion, E8 deletion,E4-E6 deletion. The sensitivity of genetic testing was 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.

**POI593**

**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 (NCT0228460, 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[EC/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.

**Schematic diagram of mutations in 106 ChineseGS patients**
Results: Venglustat therapy led to a significant reduction from baseline in Vv(Inc/Endo) of 0.62 (21.1%; p<0.001) after 6 months and 0.19 (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 1H NMR 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 β-glucuronidase 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

PO1590

Atypical Histological Abnormalities in Patients with Nephronophthisis Diagnosed with NPHP1 Deletion

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Introduction: Nephronophthisis (NPHP) is a chronic tubular interstitial disorder that exhibits autosomal recessive genetic forms, causing progressive renal failure in children. It is rare to show urinary abnormalities, edema and hypertension in patients with NPHP. Thus, it is often detected only when the renal failure becomes advanced. NPHP is divided into three types leading to the age of end-stage renal failure, i.e., infant type (around five years old), juvenile type (around 13-14 years old), and adolescent type (around 19 years old). In present study, we report a case of NPHP diagnosed at twenty-six years old who was detected renal dysfunction by annual medical check-up.

Case Description: A 26-year-old woman has not been recognized any growth disorder, and has never been pointed out any urinary abnormality in a school checkup. She was detected renal dysfunction (ser C2-2.3mg/dL) by annual medical check-up at 26 years old. Urine test indicated low specific gravity urine, but not proteinuria and microscopic hematuria. However, urinary β2-MG was high (0.055g/L), and renal biopsy was performed for definitive diagnosis. Histological findings showed no significant findings in glomeruli. However, moderate fibrosis was observed in the interstitial area, and moderate atrophy was observed in the tubules. There was no significant finding in the immunofluorescence analysis, 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 caused by NPHP, interstitial disease is dominantly in distal tubule, it is necessary to discriminate NPHP even in the adult case.

PO1597

Biobank of Urinary Cells and Human Kidney Organoids Reveals Nephropathic Cystinosis Phenotypes and Gene Therapy Strategy

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Background: Cystinosis is a rare disorder caused by mutations in CTNS encoding a cystine transporter, leading to renal Fanconi syndrome and kidney failure. Cysteamine treatment slows the disease, but does not prevent these outcomes and animal models fail to exhibit Fanconi syndrome. Stem cell models of kidney organoids exhibit structure with segmental, nephron-like segments, providing an in vitro platform to study nephropathic cystinosis. As a monogenic disorder, gene therapy is an attractive therapeutic approach which can be optimized in kidney organoids. However, cystinosis patients are rare, and iPS cells representing this population are needed.

Methods: Cells from the urine of 16 patients with cystinosis and control subjects were reprogrammed into iPS cells via Sendai virus. CRISPR gene editing was applied to non-cystinotic iPS cells generating 8 CTNS’lines with isogenic controls. Patient-derived and CRISPR-derived CTNS mutant and control iPS cell cohorts were differentiated into kidney organoids and propagated in suspension culture to assess cystinotic phenotype. Organoids were transduced at different stages of differentiation with lenti and aden-associated viruses with fluorescent reporters to assess efficacy of gene transfer.

Results: Patient-derived and CRISPR-derived stem cells exhibited >100 fold increased intracellular cystine content and vacuole-like structures, compared to controls. Both patient and CRISPR iPSCs differentiated into kidney organoids with proximal and distal tubules and podocyte segments. However, cystinotic organoids developed lobular cyst-like structures in suspension culture, while control organoids developed cystinotic organoids with cyst-like structures in suspension culture, while control organoids developed cystinotic organoids with cyst-like structures in suspension culture, while control organoids developed cystinotic organoids. Cysteamine treatment lentiviral delivery and AAV transduction successfully entered kidney organoid structures and co-localized with nephron markers when transduced at early stage of differentiation.

Conclusions: We have established a biobank of urinary and iPS cells representing over 20 cystinotic phenotypes, with phenotypes in both patient- and CRISPR-derived CTNS mutant lines that show improvement with cysteamine. Viral transduction of kidney organoids can be timed to produce high levels of entry. This biobank provides a comprehensive resource for patient-specific development of more efficacious therapeutics for cystinopathic nephropathy, including gene therapy.

Funding: Other NIH Support - Somatic Cell and Genome Editing Consortium, Private Foundation Support

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 calcium is reabsorbed via paracellular transport through tight junctions along the human nephron epithelium where Claudins 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 Sanger sequencing by standard methods. 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 claudin 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=59/50) 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, CLDN16K292E, CLDN17 A94V, and CLDN19 H122D. Nine rare variants include CLDN4 A91T, CLDN9 A113T, CLDN10 4555, CLDN20 M209V, CLDN23 A90T, and CLDN24 V97L. CLDN4 A82T, CLDN8 A94V, CLDN11 S157F, and CLDN17 A94V are predicted to be deleterious. HEK293 cells were transiently transfected with CLDN4 A82T 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. Other CLDN variants are under evaluation.

Conclusions: The role of Claudin variants in the formation of kidney stones needs further investigation. Claudins determine the selectivity and permeability of different nephron segments. Claudin variants may contribute to the formation of kidney stones if they alter the paracellular renal transport of calcium.

Funding: Private Foundation Support

PO1595

Elucidation of Molecular Pathogenesis of Lowe Syndrome and Dent Disease Type 2

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Background: Lowe syndrome and Dent disease-2(Dent-2) are two X-linked kidney diseases caused by OCRL gene anomalies. 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 regulating intracellular calcium. The molecular mechanism by which deficiencies in OCRL gene anomalies lead to the disease phenotype by the gene product 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, 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 Exon5 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 harboring truncating mutation in exon 4 and 7, and Lowe syndrome model harboring truncating mutation in exon 16 and exon 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. 5-phosphatase activity of Dent-2 models was 59-85% of that of wild type model, whereas that of Lowe syndrome 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.

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Underline represents presenting author.

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 COL4A5 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 and 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 age 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 COL4A4 and COL4A5 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, hypercalciuria, 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, hypercalciuria, and nephrocalcinosis, pointing to OxF treated 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 EMBOSIS Matcher showed RPL36A protein amino acid sequence (Length: 106; Mass (Da): 12,441) is 99.1% like RPL36A 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 RPL36A 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.


PO1601
Focal Segmental Glomerulosclerosis with Glomerular Basement Membrane Abnormalities Caused by Compound Heterozygous Myosin 1E Gene Mutations
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Introduction: Nephrotic syndrome due to focal segmental glomerulosclerosis (FSGS) in children is often associated with genetic mutations in podocyte structural proteins. This clinical case report highlights a pediatric patient with nephrotic syndrome and FSGS found to have two genetic mutations in myosin 1E gene (MYO1E) encoding the motor domain of the protein. While both of these mutations have previously been identified as variants of unknown significance individually, we report a case of compound heterozygous mutations resulting in FSGS.

Case Description: An 11-year old white male presented with proteinuria and hematuria. Family history of kidney disease included a paternal cousin with hematuria that spontaneously resolved. The patient had no history of recurrent urinary tract infections, kidney stones or excessive NSAID usage. Kidney biopsy revealed FSGS with basket-weaving, splitting and segmental thickening of glomerular basement membranes (GBM) on electron microscopy. Genetic testing was negative for Alport mutations but identified two variants in MYO1E gene (Table). Parental testing revealed each had one variant inherited by the patient, resulting in compound heterozygous mutation in the patient.

Discussion: Both missense mutations in this patient encode the motor domain of myosin 1E protein (residue 19-692), essential for podocyte motility and structural integrity. Hereditary mutations at other locations encoding the motor domain of MYO1E have been described and associated with FSGS. Functional studies showed that MYO1E motor domain variants led to protein mis-localization and disruption to the podocyte structural integrity (Mele et al. NEJM, 2011). MYO1E depletion in mice causes GBM abnormalities similar to lesions in this patient (Chase et al. Am J Physiol Renal Physiol, 2012). While each individual mutation inherited by the patient is not known to be pathogenic, we hypothesize that the combination of non-conservative mutations in the patient resulted in abnormal myosin-1E protein function that caused GBM abnormalities and FSGS.

Genetic diagnostic testing results for proband and parents
PO1602
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 sequelae of chronic kidney diseases, such as diabetic nephropathy. Single cell RNA sequencing has allowed for an unprecedented understanding of the kidney’s transcriptionic 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: 10.1101/2020.12.23.912717), to a dataset of 36,560 single nucleus transcriptomes 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 cellular metabolic interest, as the most highly downregulated. Downstream of 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: Overall, the combination of an enhanced resolution of single nucleus transcriptomics with a systems-level analysis of metabolic networks in the kidney, has 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 understanding of 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 mutations in the genes COL4A3, COL4A4, and COL4A5 is unknown. We have 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 factors for CKD progression.

Methods: We generated endothelial aTomato reporter AS mice and isolated GEC at 4 month of age by FACS. We studied aEd specificity in GEC by flow cytometry, WB, and by monophon and confocal microscopy, and their transcriptome by RNA-seq analysis. Transcriptomes were compared to WT-GEC. The combination of single nucleus transcriptomics with a systems-level analysis of metabolic networks in the kidney, has 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 understanding of metabolic perturbations in human disease.

Funding: NIDDK Support

PO1604
NPHS1 Variants Can Cause Persistent Asymptomatic Proteinuria: Genetic and Clinical Characteristics of Patients with NPHS1 Variants in Japan
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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 exome 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 CNS and 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>C p.(V822M) and c.2515del were variably hotspot 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 (aQuickE) Study: Fabry Disease Prevalence Amongst Patients with CKD
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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 glycosphingolipids (GBLs) and GBL-related proteinuria. Fabry disease severity varies 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. To this end, we report the prevalence of FD amongst those with CKD.

Methods: A prospective cross-sectional study of FD prevalence amongst CKD patients in public Queensland nephrology services was undertaken across 7 sites Oct 2018-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 recommended for patients with positive DBS screening. All biochemical and genetic testing was undertaken in an accredited genetic laboratory.

Results: 6 unrelated cases (0.20%) of FD were identified. 3 were patients with a previously identified diagnosis of FD (100% sensitivity). 3 were patients with a new diagnosis of FD as a result of study participation. Of these 6 identified cases, 5 were male and 1 was female. The mean age at diagnosis was 48 years (range 18-72) and 0.3% of all male and 0.08% of all female participants respectively. 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, 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 primarily using DBS, as a primary screening method for FD in adult populations. Further, our results confirm that 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
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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/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 data.

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, a majority of alterations, such as transporter activity and responses to stimuli, remained disregulated or remerged despite ERT. Inferring an ERT-resistant genetic module on this basis identified targets suitable for drug repurposing (Figure 1).

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.

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PO1607
Circular RNA-Based Biomarker Profile of Patients with Fabry Disease
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Background: Fabry disease is a rare X-linked lysosomal storage disease, caused by mutations in the α-galactosidase A gene. Deficient activity of α-galactosidase A leads to glycolipid accumulation in multiple organs. Circular RNAs represent strong regulators of gene expression. Their circular structure ensures high stability in blood. We hypothesized, that blood-based circular RNA profiles improve phenotypic assignment and therapeutic monitoring of Fabry Disease.

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_0006853, 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

PO1608
Outcome of Primary Hyperoxaluria Type 3: Clinics, Diagnostics, and Follow-Up
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Background: Primary hyperoxaluria type 3 (PH3) is said to be the most benign form of PH and the risk of chronic kidney disease (CKD) and even end stage renal disease (ESRD) is reported to be low. We collected clinical, diagnostic and follow up data from our PH3 patients to evaluate the true disease characteristics.

Methods: We retrospectively screened the Oxalate Registry for data of PH3 patients known to the German Hyperoxaluria Center and analyzed them for clinical and laboratory parameters.

Results: From the 90 PH3 patients enrolled in the OxalateRegistry, 45 had all laboratory analysis done at the Hyperoxaluria Center (3-45 years of age, 43 males). Genetically confirmed diagnosis revealed 21 different biallelic mutations in HOGA1. The main symptom was recurrent urolithiasis, most prominently found in the first 3 years of life (>25% of patients). Nephrocalcinosis was seen in 7 patients. Mean follow up for all patients was 7.76 (0.25-34) years, median age at first symptom was 0.06 (0.17-10) and median age at diagnosis (based on genetics) was 4.57 (0.25-16.86) years. Not all patients experienced clinical remission: 3/6 patients > 20 years of age have ongoing kidney stone development. A high amount of stone removal procedures during the first years of life, but also later in life was observed. Urinary oxalate (Uox) excretion was significantly and continuously elevated over time. There was no significant difference in Uox between PH1 (1.37 mmol/1.73m2/24h), PH2 (1.40 mmol/1.73m2/24h) and PH3 (1.13 mmol/1.73m2/24h) with the exception of a lower Uox in PH1 patients sensitive to B6 medication (0.84 mmol/1.73m2/24h) vs. PH3 patients (p=0.05). A decline in kidney function was seen in 3 patients with a significant change in eGFR over a period of 15 years (134 to 68.1 ml/min/1.73m2), which we would relate several lithotripsy procedures (n=16), but also ongoing hyperoxaluria.

Conclusions: Our analysis from a subgroup of European PH3 patients provides additional information on clinical outcome. PH3 patients seem to have the highest kidney stone burden during the first years of life, but they do not stop producing stones. Some PH3 patients progress to CKD and lose kidney function over time. Uox is comparable to non B6 responsive PH1 and also to PH2 patients.

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PO1609
Patient Journey in Alport Syndrome
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Background: Patients with Alport Syndrome(AS) experience difficulties in diagnosis. Misdiagnosis remains frequent even after detailed clinical and pathological assessment. Qualitative interviews were conducted with patients diagnosed with AS and caregivers, to better understand the patient experience.

Methods: Thirty-nine Interviews (16 male and 23 females <18 years) from the United States, United Kingdom, France, Japan, and Germany were conducted with patients and caregivers. Respondents were recruited by each country's Alport advocacy groups. Responses were summarized and presented quantitatively and qualitatively.

Results: Thirty-nine participants (20 patients, 4 caregivers, 15 respondents being patients themselves and caregivers) completed the interview; and shared their experience as patients or that of the patients they care for (interviews reflect 32 firsthand patient experiences, and 7 patient experiences from caregivers; mean age=34). Thirty-four patients experienced their first symptoms as children (mean=9 years). Seventy-nine percent experienced hematuria before diagnosis. Despite early signs, diagnosis was delayed.
Males recorded hearing loss more than females (2/3 vs. 1/3 respectively) and at earlier ages (median age of males in 20-30s consulted a nephrologist earlier than females (median age: 12 vs. 28) and were diagnosed ~15 years earlier than females (median age=16, female=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 (n=143, 70%), with subsequent genetic testing performed by a panel of genes (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 undiagnosed (n=5) eligible 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 future outcomes, transplant is seen as inevitable future outcome. The same population included patients with dialysis (n=7) and transplant (n=5) experience. Participants perceived transplant as an improvement of renal symptoms compared to dialysis.

Funding: Commercial Support - Sanofi Genzyme

PO1610

Multidisciplinary Renal Genetics Clinics: Family Perspectives and Preferences

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Background: Multidisciplinary genetics clinics (MGCs) 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 MGC 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 as the two most important reasons for patients. Patients gave an average of 144.3% for having further information about the disease. 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 MGCs 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: Autosomal recessive renal tubular dysgenesis (ARRTD) caused by inactivation mutations in AGT, REN, ACE, and AGTR is a very rare but fatal disorder with incomplete knowledge about pathogenesis and a lack of therapeutic options.

Methods: We report six Taiwanese with ARRTD from six unrelated families diagnosed by renal histology. Clinical features, prevalence of carrier heterozygosity, and potential rescue therapy were examined.

Results: All patients exhibited antenatal oligohydramnios, postnatal anuria, pulmonary hypoplasia, and profound hypotension refractory to interventions. AGT (Angiotensinogen) protein levels were diminished in the liver along with reduced serum AGT, angiotensin I (Ang I) and II (Ang II) levels. Neonatal demise occurred in all but one. All carried the same homozygous E3, E4 del:287bp deletion/9bp insertion in AGT. The allelic frequency of this heterozygous AGT mutation was approximately 1.2% (6/500), suggesting that ARRTD may not be exceedingly rare in Taiwan. This mutation results in skipping of exons encoding the serpin domain of AGT, which is important for renin interaction and the generation of truncated protein (1-295 amino acids). In silico modeling revealed a diminished interaction between mutant AGT and renin, and proximity ligation assay demonstrated a significant decrease in the amount of this truncated protein.

Conclusions: This AGT mutation leads to the diminished interaction with renin and decreased Ang I and II generation. Hydrocortisone may potentially rescue the cases of ARRTD caused by this truncated AGT.

PO1612

KIDNEYCODE: A Genetic Testing Program for Patients with CKD

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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 KIDNEYCODE, 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, JNF1A, IN2, LMX1B, MYO1E, NPHS1, NPHS2, NX2, 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 FSGS are eligible. Family members of those with known or suspected AS or FSGS are also eligible.

Results: Of 455 test results, a genetic variant was reported in 278 patients. Of those, 206 patients had 219 variants in COLA43, 4, or 5 genes [112 Pathogenic/ Likely Pathogenic (P/LP), 107 Variants of Uncertain Significance (VUS)], 87 patients had 95 variants (32 associated with Fabry disease has become more important with the introduction of novel therapy (migalastat, which may not be compatible with numerous pathogenic mutations). The sensitivity of this genetic screen for the diagnosis of Fabry disease has become more important with the introduction of novel therapy (migalastat, which may not be compatible with numerous pathogenic mutations). The sensitivity of this genetic screen for the diagnosis of Fabry disease has become more important with the introduction of novel therapy (migalastat, which may not be compatible with numerous pathogenic mutations). The sensitivity of this genetic screen for the diagnosis of Fabry disease has become more important with the introduction of novel therapy (migalastat, which may not be compatible with numerous pathogenic mutations). The sensitivity of this genetic screen for the diagnosis of Fabry disease has become more important with the introduction of novel therapy (migalastat, which may not be compatible with numerous pathogenic mutations). The sensitivity of this genetic screen for the diagnosis of Fabry disease has become more important with the introduction of novel therapy (migalastat, which may not be compatible with numerous pathogenic mutations).

Conclusions: Initial results with the KIDNEYCODE 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 neurology. We proceeded with genetic testing to identify mutation of galactosidase A (GLA gene) and kidney biopsy (image 1). Genetic testing revealed a novel mutation variant c.328G>C (p.Gly274Arg) deemed to be heterogeneous 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 COLA4 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 COLA4 mutation. Her husband (II:2, in his 50’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 COLA4A3 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 COLA4 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 50’s) and presumed to be due to DKD for I:3 (died in his 80’s).

Discussion: ACTN4 and COLA4 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 alpha-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. BioRXiv: 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 kidneys cells (PA8*pd63) and not urothelium (PA8*pd63). Tubuloids contained proximal tubule, loop of Henle, distal tubule and collecting duct epithelium. Patient tubuloids showed hallmark cystine accumulation (1.25 ± 0.12 vs. 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.

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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 Frasier Syndrome, Denys-Drash 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 and exome 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 hypertension (onset 2 years prior to proteinuria); paternal 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 genitourinary tract malformations. We review the association of WT1 with nephropathy and postulate a potential interaction with XY 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.
PO1617
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 “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 (reducing 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 CGA (INF2/NPHS2/TRPC6/NPHS1), and 11.1% in other genes (DLC1/SMARCAL1/UMOD). Family history of kidney disease was present in 75% (n=15/20) of the patients in Group 1a, 16.7% (n=1/6) in Group 1b, and 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 nephotic 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. Clinicopathologic characteristics of the patients

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Clinopathologic characteristics of the patients</th>
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<tbody>
<tr>
<td><strong>Negative control</strong></td>
<td>Group 1</td>
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<tr>
<td><strong>Negative control</strong></td>
<td>(n=51)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>36 (7.7)</td>
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<tr>
<td>% of patients with family history</td>
<td>41.2% (21/51)</td>
</tr>
<tr>
<td>% of patients with proteinuria</td>
<td>71.8% (37/51)</td>
</tr>
<tr>
<td>% of patients with hematuria</td>
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<tr>
<td>% of patients with hypertension</td>
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<td>% of patients with edema</td>
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<td>% of patients with hypercholesterolemia</td>
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<tr>
<td>% of patients with diabetes</td>
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<td>% of patients with family history of other renal disease</td>
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<td>% of patients with family history of other renal disease</td>
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PO1618
A Rare Case of Nephrotic Syndrome Associated with Dent Disease

Introduction: Dent’s disease is a rare X-linked condition caused by a mutation in the CLCN5 or OCLR gene, which impair the megalin-cubulin receptor-mediated endocytosis in kidney’s proximal tubules. Thus, it may manifest as nephrotic-range proteinuria, hypoalbuminemia and edema formation are the key features of nephrotic syndrome (NS) and is often associated with progressive tubulointerstitial kidney disease. The presence of renal calcifications and no proliferation of mesangial cells. Electron microscopy showed renal medulla with calcium deposition in the renal medulla. Our case supports and reinforces the possibility of a single organ-limited mitochondrial disease develop CKD. Importantly, examples of mitochondrially inherited tubulointerstitial kidney disease in subjects with no other systemic 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). Urine analysis 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 (tRNAphe) 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. Importantly, 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 excess 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 oxalate 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 - Chinox 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; 56.0%). 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 10.3% of patients, respectively. In terms of HRU during follow-up an acute 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 our current and future patients’ experience 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 - Aylima Pharmaceuticals

PO1622
Recurrent SLC12A3 Mutations in Taiwanese Families with Gitelman Syndrome: A Rapid Detection for the Higher Prevalence
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Background: Recurrent mutations in SLC12A3 gene responsible for autosomal recessive Gitelman syndrome (GS) are reported to be common with uncertain prevalence. Recurrent 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 thirty independent families with genetically-confirmed GS referred from different regions of Taiwan were consecutively enrolled to define recurrent SLC12A3 hotspots and determine their prevalence. Using Taqman MGB probe-based real time primer chain reaction (RT-PCR), hotspots-based mutation detection plate was designed and optimized to recognize all hotspots. We validated this mutation 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 family 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 mutations of 12 newly-diagnosed GS patients within 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 - Aylima Pharmaceuticals

PO1623
AVR-RD-01, an Investigational Lentiviral Gene Therapy for Fabry Disease, Reduces Gb3 Substrate in Endothelial Cells of Renal Peritubular Capillaries
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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 protein/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, alpha-galactosidase A (AGA), which leads to pathological accumulation of substrates and metabolites, including globotriaosylceramide (Gb3) and globotriaosylsphingosine (lysogb3-Gb3). Significant morbidity and early mortality result from damage to kidneys, heart, and brain. Herein we report: 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 complementary 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 (lysogb3-Gb3) in plasma, now sustained up to 32 months. A Phase 2 clinical trial in 8-12 treatment-naive males (16-50 years) with classic FD investigates 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 BLISS methodology. At 24 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 lysogb3-Gb3, including an 87% reduction in plasma lysogb3-Gb3 at 48 weeks versus BL. Adverse events were as expected with the particular conditioning regimen and subsequent gene therapy.

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 of drug, blood chemistry findings (6), pain (2), dysuria (1), nasal congestion (1), edema (1), and erectile dysfunction (1). Three AEs were uncoded at this time. None of the participants 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 at the specified 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 nephritis that leads to end-stage kidney failure by 40 years of age in most affected males. Although kidney transplantation is well tolerated in X-linked Alport syndrome, donors should be carefully selected since the proband’s mother is usually the gene carrier.

Case Description: The patient was a 38-year-old man. Microhematuria had been present since during his early childhood and had been diagnosed with Alport syndrome based on the results of a kidney biopsy at 5 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 no renal urinalysis 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. However, there was no apparent genetic mutation in COL4A5 of his mother, indicating 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.

PO1627
Clinical and Economic Impact of Primary Hyperoxaluria: A Retrospective Claims Analysis
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Background: Primary hyperoxaluria (PH; types 1, 2, and 3) are rare genetic disorders resulting in the overproduction of oxalate in the liver and that manifest in renal complications. This study sought to quantify the healthcare resource utilization (HCRU), costs, and clinical characteristics of PH patients.

Methods: This retrospective study analyzed claims data from IQVIA PharMetrics® Plus (1/2014-12/2019). PH cohort inclusion was an ICD-10 code for PH (E72.53) and any evidence of secondary hyperoxaluria (SH). A random sample 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=525; median $1,079; mean $5,041) 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 (table 1) and care settings, including inpatient/outpatient settings (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 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

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO1628
Identification of Genetic Drivers of Age-Related Renal Histopathology
Susan M. Sheehan, Ron Korstanje. The Jackson Laboratory, Bar Harbor, ME.

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 in image analysis and machine learning to develop a high-throughput pipeline that uses machine learning on scanned slides, which allows us to automatically segment glomeruli and quantitatively measure matrix expansion (MMX) 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 $\Delta w\tilde{al}a13$ and $C\tilde{E}2$ 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 age.

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 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 for discovery and replication.

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-ZNF780 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 Diseases of the Kidney
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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 podocyte expression is regulated by WT1 (Leefevre 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 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 overlapped with 36 mouse candidate lists (1), 7-4 with the WT1-regulated candidate list (2). Of note, 3 genes (STNPO, SEMA3G, ITGB8) were shared by all 3 lists. We found a homogenous STNPO mutation (c.2540C>T, p.P847L) in a 4yo patient with NS. We show that loss-of-function of STNPO decreases CDC42 activity and reduces podocyte migration rate, both required by overexpression of wild type cDNA, but not by cDNA representing the patient mutation.

Conclusions: By overlapping 2 candidate gene sets with a set of 120 genes resulting from WES analysis in 1,382 NS families with NS, we identified STNPO as a potential novel monogenic cause of NS.

Funding: NIDDK Support

PO1631
An International Cohort Study of Mutations in REN 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 heterozygous 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 protein degradation and translocation of prorenin to the endoplasmic reticulum (ER), prosegment mutations led to abnormal deposition of renin and prorenin in the ER Golgi intermediate compartment (ERGIC), and mutations in mature renin led to deposition of prorenin and renin in the ER. Signal and prosegment patients were more severely affected, often presenting at <10 years (see Table 1) with anemia, hyperkalemia, and acute and chronic kidney disease. While eGFR was approximately 50 ml/min in children <10 years, eGFR remained stable until age 20, with mean age of end-stage kidney disease (ESKD) >50 in this cohort. The mean hemoglobin level in children was not by cDNA representing the patient mutation.

Conclusions: By overlapping 2 candidate gene sets with a set of 120 genes resulting from WES analysis in 1,382 NS families with NS, we identified STNPO as a potential novel monogenic cause of NS.

Funding: NIDDK Support
bicarbonate values increased in 9 patients taking fludrocortisone (4.7±0.55 mEq/L vs. 4.3±0.65 mEq/L, p<0.05) and 3.5 mEq/L vs. 25±9.23 mEq/L, p=0.003). Patients with mutations in mature renin presented with 20g with gut and chronic kidney disease.

**Conclusions:** There are 3 subtypes of heterozygous REN mutations that are pathophysiologically and clinically distinct.

**Funding:** Private Foundation Support

**Patient Characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean (SD)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>60 (29.82)</td>
<td>15-108</td>
</tr>
<tr>
<td>Age at presentation (in months)</td>
<td>30.1 (11.05)</td>
<td>0-120</td>
</tr>
<tr>
<td>Serum UA (mg/dl)</td>
<td>6.7 (3.5)</td>
<td>3.5-12</td>
</tr>
<tr>
<td>FEUA</td>
<td>120 (57)</td>
<td>70-180</td>
</tr>
</tbody>
</table>

**SLC22A12** also resulted in hypouricemia, EIAKI and nephrolithiasis. 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 DNA dataset. However, genes involved in the pathogenesis of branchiootooetal (BOR) syndrome (ET1, SIX1, SIX2, SIX3) clustered in nephron progenitor cells (NPCs) in both datasets. We therefore prioritize two lists of independent candidate genes derived from WES in 1,380 patients and ii) the 100 highest expressed genes may represent novel CAKUT candidate genes.

**Conclusions:** Utilizing two independent non-overlapping candidate lists, we established 10 potential novel candidate genes for human SRNS.

**Funding:** Other NIH Support - R01 - DK088767

**References:**

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**Funding:** Other NIH Support - R01 - DK088767

**References:**

Czeisler et al (2018). 86 novel CAKUT candidate genes were generated by Whole Exome Sequencing (WES).
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 25% using whole exome sequencing (Warpekoj CASSN 13.5:2018) 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 genes known 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 phenoalleles of SRNS, e.g. CO4LA3. 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; Warpekoj 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.

Funding: Other NIH Support - R01DK76683-14.

Recovery from Dialysis in Responsive Primary Hyperoxaluria Type 1
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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 three 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 (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 m^2 (range 23-52), POC was 8.8 mmol/L (4.6-11.3), and U/Ox was 0.93 mmol/24 hours (0.47-1.03). Kidney function was maintained during a median of 3.2 yrs (range 1.3-3.8) of follow-up.

Discussion: Our findings challenge the conventional wisdom that ESKD in PH1 is always irreversible. Rather, in selected PH1 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

The Distribution of APOL1 Risk Variants and Their Association with CKD in Rural East Africa: The SEARCH–CKD Study
Anthony N. Muiru,1 Assurah W. Elly,1 Jane Kabami,2 Mucunguzi Atukunda,3 Wendy Chan,1 Jennifer Puck,4 Edwin Charlebois,1 Diane Havlir,1 Moses Kannya,2 Michelle M. Estrella,1 Chi-yuan Hu,5 University of California San Francisco, San Francisco, CA; 2Kenya Medical Research Institute, Nairobi, Kenya; 3Infectious Diseases Research Collaboration, Kampala, Uganda.

Background: APOL1 protein level (APOL1) high-risk genotypes (G1/G1, G1/G2 or G2/G2) are well-known CKD risk factors that arose in sub-Saharan Africa. The G1 and G2 allele frequencies may be as high as 45% and 24%, respectively in some West African countries, but few studies have examined the association of high-risk genotypes and CKD in Eastern Africa.

Methods: We conducted a study of CKD prevalence among a population-based sample of 3,686 participants (PMCT055898) nested within an HIV trial in rural Uganda and Kenya. We collected dried blood spots (DBS) on filter cards for subsequent genetic studies. After DNA extraction, we genotyped APOL1 risk variants and used multivariable logistic regression models to assess the association of APOL1 high-risk genotypes with prevalent CKD defined as a serum creatinine-based eGFR <60 mL/min/1.73 m^2 or proteinuria (urine dipstick ≥1+).

Results: We successfully obtained DBS from 90% of all individuals approached for the study. We have extracted DNA and genotyped 492 (~10%) samples (convenient selection). Un-weighted CKD prevalence among these individuals was 7.7% (95% CI: 5.2-11.2%). The overall allele frequencies for APOL1 G1 and G2 variants were 6.1% and 5.8%, respectively and varied by region (Figure 1). Only 2.2% of individuals had APOL1 high-risk genotypes. The adjusted odd ratio for association of APOL1 high-risk genotypes with CKD was 1.5 (95% CI 0.15-15) in this limited sample.

Conclusions: Our study is one of the largest studies to define the prevalence of APOL1 risk variant frequencies and evaluate the association of APOL1 high risk genotype with CKD in rural East Africa. Our preliminary results show a relatively low prevalence of APOL1 risk variants—supporting the distinctive west-east Africa cline in APOL1 distribution previously reported. Further genotyping will permit more precise estimation of the association of APOL1 and CKD.

Funding: NIDDK Support.

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,G2,60G0,G0G1,G1G0 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.

Funding: Other NIH Support - Common Fund (NIH Director’s New Innovator Award), Private Foundation Support.
was found to have MH. The results suggested that both the transplant candidate and her daughter presented with 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 molecule causing abnormalities in the GBM. The presence of 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) 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 low-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 modifers 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 performed VAAST (p=9.4E-04), 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 re prioritization 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.
Results: In 30 of 211 (14%) families, we detected mutations in one of the 44 genes for isolated CANKT or in one of the 179 syndromic CANKT genes. In particular syndrome cases, reverse phenotyping was helpful to increase certainty of the deletoriusness of a genetic variant. In the remainder, we performed a targeted analysis for novel candidate genes. In 40 families of this subset, we identified likely deleterious mutations in 36 genes not previously reported to cause CANKT.

Conclusions: In a large, international cohort we detected causative mutations in 14% of families with a diagnosis of CANKT. We show that when combined with homozygosity mapping and segregation analysis, WES is useful in identifying potential candidate genes in consanguineous families or families with multiple affected.

PO1644
Extremely Rare Variants in Four Complement Genes Contribute to Genetic Susceptibility to Atypical Hemolytic and Uremic Syndrome

Background: The study of complement genetics has dramatically changed the landscape of atypical hemolytic uremic syndrome (aHUS) and has paved the way for highly tailored therapy. However, the assessment of the contribution of each identified variant to aHUS pathogenesis still remains a challenge. In this study we aimed to analyze the enrichment of rare variants in 6 aHUS-associated genes, including C3, CFH, CFI, CD46/MCP, CFB and THBD, in comparison with a reference population.

Methods: We analyzed the distribution of rare variants in 433 adult patients with a diagnosis of aHUS without co-existing condition of systemic lupus erythematosus (SLE) as a control group and 1440 European individuals from the 1000 Genomes project (N=503), focusing on the 6 genes of interest. We analyzed the enrichment of genetic variants in the aHUS cohort compared to the reference population.

Results: A total of 168 variants in complement complex genes, with a minor allele frequency (MAF) <1%, involved 247 alleles, were identified in 224 patients (51.7%). 115 of the identified variants were not reported in the population database gnomAD, including 75 variants detected in CFI gene (65%). Variants with a MAF of <0.01% in the C3 and MCP genes and variants with a MAF <0.1% in the CFH and CFI genes were enriched in the aHUS population as compared to controls. In contrast, rare variants in CFB and THBD genes were not significantly enriched in the aHUS population. We identified 18 variants overrepresented in patients, including the CFCHFHR1 hybrid genes. Among those variants, we observed functional deficiency in the encoded protein in the C3 variant p.Lys155Gln associated with risk of advanced age-related macular degeneration was not significantly increased in the aHUS population. Finally, multiple rare variants in a single individual were more frequently present in aHUS patients compared to controls.

Conclusions: We showed the enrichment of extremely rare variants limited to CFI, CFI, CD46/MCP and C3 genes. The study confirms that a variant with a MAF <0.01% should not be considered at risk for developing aHUS. Our study indicates that targeting these variants resulting with functional deficiency in the encoded protein the C3 variant p.Lys155Gln associated with risk of advanced age-related macular degeneration was not significantly increased in the aHUS population. Finally, multiple rare variants in a single individual were more frequently present in aHUS patients compared to controls.

PO1645
Whole-Exome Sequencing Identifies Likely Causative Variants in Four Candidate Genes in 16 Families With Spina Bifida

Background: Spina bifida (SB) is the most common central nervous system malformation compatible with life and the second leading cause of birth defects. The following lines of evidence support the hypothesis that SB may be caused by multiple monogenic genes: i) congenital nature, ii) familial occurrence, and iii) existence of monozygotic twins. However, only few monogenic genes have been described so far. The majority of the candidate genes from these models has been studied in human SB.

Methods: We evaluated the literature and generated a list of 95 candidate genes from four categories: i) known genes from human (isolated SB), ii) 11 genes from human syndromic SB, iii) 35 genes considered risk factors for human SB, and iv) 42 genes from mouse models. We evaluated whole exome sequencing (WES) data obtained from 16 individuals with SB who were enrolled at Boston Children’s Hospital from 06/2019 to 11/2019.

Results: In 4 of 16 families (25%), we identified 4 likely deleterious heterozygous (het) mutations in each one potential SB candidate gene. All variants are very rare with a frequency of less than 0.01% in a control database of 125,000 healthy control individuals (gnomAD). Specifically, in family B4110 with myelomeningocele, we identified a C6LS1 (p.Glu652Gly) variant. In family B4113 with myelomeningocele, we identified a single nucleotide variant in the GTF2H11 gene (p.Lys155Gln) associated with risk of advanced age-related macular degeneration was not significantly increased in the aHUS population.

Conclusions: We identified two novel APOL1-gene interactions, highlighting that secondary genes may modify the effect of APOL1 on kidney function, which may uncover underlying biological mechanisms and be useful for prevention.

PO1647
Results from the Ongoing Phase 2 Open-Label Extension Study of Lumasiran, an Investigational RNAi Therapeutic, in Patients with Primary Hyperoxaluria Type 1 (PH1)

Background: PH1 is a rare genetic disorder characterized by hepatic overproduction of oxalate, leading to recurrent kidney stones, nephrocalcinosis, progressive renal failure, and multiorgan damage from systemic oxalosis. There are no approved pharmacologic therapies for PH1. Lumasiran is a subcutaneously-administered investigational RNAi therapeutic that decreases hepatic oxalate production by targeting glycolate oxidase. We designed this phase 2 open-label extension (OLE) study to explore long-term safety and efficacy following the completion of the phase 2a, 12-month, open-label (OL) study (NCT03127663).

Methods: Phase 2 OLE includes patients with PH1, ages 6 years old, urinary oxalate (UOX) <0.7mmol/1.73m2/day, and eGFR >45mL/min/1.73m2 who completed the Phase 2a study. Patients received lumasiran 1mg/kg monthly, 3mg/kg monthly or 3mg/kg quarterly, and all transitioned to 3mg/kg quarterly. Endpoints include safety and efficacy assessments.

Results: This trial enrolled all 20 patients from the Phase 1/2 study. At baseline of the parent study, patients had a mean age 14.9 years (range: 6-43), mean baseline UOX of 0.7mmol/1.73m2/day, and eGFR >45mL/min/1.73m2 who completed the Phase 2a study. Patients received lumasiran 1mg/kg monthly, 3mg/kg monthly or 3mg/kg quarterly, and all transitioned to 3mg/kg quarterly. Endpoints include safety and efficacy assessments.

Conclusions: Through whole exome sequencing, we detected likely deleterious mutations in 5 affected individuals with a diagnosis of SB. We show that composing a list of 95 candidate genes based on established mouse models and genes known to be related to SB in human facilitates the detection of monogenic causes for SB. We are expanding this study to a larger cohort.

PO1641
APOL1 by Second-Generation Interaction on eGFR Among African Americans Without Diabetes: The Million Veteran Program

Background: Two high-risk variants in the Apolipoprotein L1 (APOL1) gene are associated with eGFR and a substantial increase in risk of end-stage renal disease (ESRD) among African Americans without diabetes. Not all individuals with high-risk variants develop kidney disease, suggesting that unidentified genetic factors may modify the effects of APOL1.

Methods: We tested interactions between the APOL1 haplotype and single nucleotide polymorphisms (SNPs) from 22 independent loci associated with eGFR among 55,004 African Americans without diabetes in the Million Veteran Program. We used linear regression to investigate multiplicative APOL1*SNP interactions on eGFR at enrollment, adjusting for age, sex, body mass index and the first 5 principal components of ancestry, with Bonferroni-correction for multiple testing (alpha=0.05/22=0.002).

Results: We detected significant interactions between APOL1 high-risk variants and SNPs at two loci (GATM/SPATA5L1 rs662024678, p-interaction = 0.0012) and UBE2Q2 (rs74024050, p-interaction = 0.0014) (Table). SPATA5L1 is a protein-coding gene with elevated expression in the kidney and previous associations with familial juvenile hyperuricemic nephropathy. UBE2Q2 is also a protein-coding gene with gene expression in the distal kidney tubule of a murine model.

Conclusions: Our results identify two novel APOL1-gene interactions, highlighting that secondary genes may modify the effect of APOL1 on kidney function, which may uncover underlying biological mechanisms and be useful for prevention.

Funding: NIDDK Support, Veterans Affairs Support
2.24 mmol/1.73m²/day (range: 0.94, 5.18). As of January 2020, patients were dosed in OLE for a median of 15 months (range: 11–22). Adverse events were reported in 19/20 (95%) patients; all were mild or moderate and the majority were assessed as unrelated to study drug. There were no discontinuations or drug-related serious adverse events. The median reduction in 24h UOx relative to Phase 1/2 baseline was 74.5% (N=17) and 17/18 patients achieved normal or near normal levels of UOx. Plasma oxalate levels also decreased (mean max reduction 55.2%, N=19). Plasma and urinary glycolate increased and later stabilized, consistent with the effect of lumasiran on glycolate oxidase.

Conclusions: Lumasiran had an acceptable safety profile. Continued therapy with lumasiran maintained reduction of UOx to levels near or below the upper limit of normal, consistent with the Phase 1/2 study. These data further enable ongoing Phase 3 studies to evaluate lumasiran in patients with PH1 of all ages and at all stages of renal impairment.

Funding: Commercial Support – Alnylam Pharmaceuticals

PO1649

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^-4). The most significant SNP was rs12606116 (18p11.32) with P=6.75x10^-10. The rest SNPs were rs11826924 (11p15.2, INSC), rs10151371 and rs17124022 (14q31.3, GPR65), rs14055744 (5q31.1, CD274), rs203339 and rs433091 (12q24.23, CIT), rs7157731 (14q32.2, WDR25), rs2372192 (3p14.1, MAGI1). Gene-based analysis results showed 11 suggestive SNPs in 11 loci (P<0.05): GPR139 (16p12.3, TH), TH (11p15.5), SEMA6D (15q21.1), EPHA5 (4q34.1, CD274), rs203339 and rs433091 (12q24.23, CIT), rs7157731 (14q32.2, WDR25), rs2372192 (3p14.1, MAGI1). Gene-based analysis results showed 11 suggestive SNPs in 11 loci (P<0.05): GPR139 (16p12.3, TH), TH (11p15.5), SEMA6D (15q21.1), EPHA5 (4q34.1, CD274), rs203339 and rs433091 (12q24.23, CIT), rs7157731 (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 and moderately associated with LN which may advance our understanding of the genetic basis of LN.

Funding: Government Support - Non-U.S.

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 psoriatic arthritis, 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 PKD1, 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.
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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Genetics, UMC Groningen, Groningen, Netherlands; 6Department of
Immunology, UMC Utrecht, Utrecht, Netherlands.

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 ‘genes
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
care at 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,
and 70 patients were performed a whole exome sequencing based 379 gene panel analysis.

Results: Genetic analysis yielded a diagnosis in 51%. Exonatoplated to the 273 patients,
who did not all fit the inclusion criteria, the diagnostic yield was still 21%. Retrospectively,
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 ES KD of
ages up to 50 varied from 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 ES KD 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 American Europeans. Genetic variants influencing kidney function have been 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, SPATA5/GATM on chromosome 15 (p-value = 3.78E-12). Two novel loci were detected. One in SLC30A4 (rs2653718 p-value = 4.51x10⁻⁸) a protein-coding gene for zinc transmembrane transporter, and one on LINC00972 (rs12889732 p-value = 2.68x10⁻⁸). Other previously reported signals in the European American population for kidney phenotypes were also found with genome-wide significance: UMOD/PDILT (rs7114135 p-value = 1.13x10⁻⁸), PRKAG2 (rs10224210 p-value = 1.99x10⁻⁸), UORC3 (rs720359 p-value = 2.22x10⁻⁸), SLC2A4 (rs318236 p-value = 1.29x10⁻⁸) and ALMS1 (rs1271588 p-value = 4.14x10⁻⁸). Several additional important CKD loci were associated with kidney function at p-values below the genome-wide threshold including: APOL1 (rs5092573 p-value = 2.98x10⁻⁸), TPRKB (rs33805651 p-value = 5.49x10⁻⁸), SHROOM3 (rs50259470 p-value = 3.63x10⁻⁸). Five of the variants that reached genome-wide significance were in 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 Hispanic populations.

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 thinning has diagnostic importance in patients with X-linked Alport syndrome (XLAS) but little prior research has been done to evaluate temporal macular thinning 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 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

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

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 variants were detected in two families. The patient 1 and 2 were siblings. They presented with proteinuria at 6 months old. She was subsequently found to have compound heterozygous mutation for LAMA5 gene (c.9232C>G, p.Arg3078Ter), and the other was splice site mutation (c.1282+1G>A). The patient 3 presented with proteinuria at 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.302G>T, p.Arg101Ter).(ELOF270Fe), c.1282+1G>C. We performed immunohistochemistry analysis of laminin e5 and her renal pathology showed completely negative staining pattern.

Box and whisker plots of TTI by group and sex

LAMA5 Gene Mutations in Japanese Cases with Infantile Nephrotic Syndrome

Gene expression of the Kidneys: Non-Cystic - 2
Poster
PO1655
Variation in Phenotype in Utah Families with Autosomal Recesssive Alport Syndrome
Laith Al-Rabadi, Edwin Lin, Lydia Sauer, Alex Vitale, Paul Bernstein, Martin C. Gregory. University of Utah Health, Salt Lake City, UT.

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.2083G>A, p.Gly695Arg) but differ in the second mutation (c.4981C>G, p.Arg1661Cys and c.4471T>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 Phenotypes
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Background: Congenital Anomalies of the Kidney and Urinary Tract (CAKUT) affect 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 hypothesized that identification of rare homozygous 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 this purpose.

Results: We completed variant calling for 2 singleton 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 revealed rare heterozygote 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 - T-32 Training Grant

PO1657
Perspective 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. Comprehensive genetic testing in CKD patients with a suspected genetic cause or predisposition is important for accurate diagnosis. However, the uptake of genetic testing among nephrologists is still low despite the increasing prevalence of genetic testing and advances in genetic counselors. Genetic testing in clinical practice to elicit feedback on the use of genetic testing in clinical nephrology care. The questions focused on perceived utility and potential barriers to ordering genetic testing.

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 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.


Funding: Commercial Support - Natera, Inc.

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 (AKI) induced by folic acid in a murine model. In this database we evaluated if 625 genes described as responsible for hereditary nephropathies have any independent contribution in the pathogenesis of acquired nephropathies.

Results: Among 23051 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 dataset. 260 (41.6%) of these 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 association receptosome”, “activation of immune response” 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 the genes in acute kidney injury (SCLC3A3, FN1), which supports the relevance of the transcriptomic results.

Conclusions: Several genes responsible for familiar nephropathies are differentially expressed in acquired nephropathies, suggesting that they could play a role in its

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

Underline represents presenting author.
pathogenesis, through complement activation, protein activation of immune response and the regulation of the RNA processing. The identification of those genes showing a more significant change will allow us to select biomarkers 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, ubiquinone) cause primary COQ8B deficiency resulting in various clinical phenotypes. COQ8B (also known 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). A 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 (the 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 (45%) had chronic kidney disease and twelve patients had end-stage renal disease (25%). 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. Severe proteinuria was present in medullary nephrocalcinosis in all 7 patients, notably all Koreans. Outcomes related to COQ8B replacement was reported in 14 cases and half of them reported partial or complete remission. Effect of calciumin inhibitors were reported in 7 cases which showed partial remission in 4 cases. Two patients had COQ8B-associated FSGS is a rare, hereditary nephropathy which can greatly benefit from early diagnosis and COQ8B supplementation. Ablent mitochondrial accumulation in the cytoplasm of the podocytes and increased medullary edechergency may add to diagnostic suspicion. So far, all patients with COQ8B mutation reported in South Korea had medullary nephrocalcinosis.

**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 3, PH3 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 age. 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 (5 years apart from each other). Here, in 1 patient eGFR significantly declined from 34 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, as long-term follow-up data is still missing, we nevertheless suspect PH3 not being as benign as currently being reported.

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

**PO1662**

**A Delayed Diagnosis of Gordon Syndrome: Better Late Than Never!**

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**Introduction:** Gordon syndrome, also known as Pseudohypoaldosteronism Type II (PHA-II) or Familial Hyperkalemic Hypertension (FHH), is a rare Mendelian syndrome causing hypertension(HTN), hyperkalemia and non-anion gap metabolic acidosis. Genes responsible are the with-no-lysine kinase 1 and 4 (WNK1/WNK4), kelch-like 3 (KLHL3) and culin 3 (CUL3). WNK1/WNK4 are expressed in the DCT, collecting tubule and collecting duct. WNK4 reduces cell surface expression of the thiazide sensitive Na-Ci co-transporter (NCC) and the potassium channel, ROMK. WNK1 prevents WK4 from interacting with NCC. KLHL3 and CUL3 are part of a ubiquitin ligase complex that targets WNK4 for degradation. While FHH from WNK1, WNK4 and CUL3 have an autosomal dominant (AD) mode of inheritance, disease from KLHL3 can be autosomal recessive (AR) or AD. AR disease presents at an earlier age with severe hypertension and hyperkalemia.

**Case Description:** A 56-year-old Caucasian male with history of recurrent atrial fibrillation with multiple cardioversions was referred to renal clinic for evaluation of chronic hyperkalemia. Upon presentation, he had been on furosemide 40mg and sodium polystyrene sulfonate (SLS) 30mg daily for the last 6 years for K+ values as high as 7 mEq/L.

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

Underline represents presenting author.

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Burden of Alport Syndrome in the United States: A Retrospective Study

**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, 2000 to March 31, 2018, with at least 1 year of activity prior to the AS diagnosis. 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. All patients had 12 months of activity prior to the AS diagnosis.

**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

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A Case with Somatic and Germline Mosaicism in COL4A5 Detected by Multiplex Ligation-Dependent Probe Amplification in X-Linked Alport Syndrome

**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 detected, and then kidney biopsy was performed. The pathological findings showed diffuse thin basement membrane and partial basket-weave capillaries. His hematuria was detected at 3 months of age, and gross hematuria was occasionally exhibited. His hematuria at the age of 2, proteinuria was first detected by MLPA. This information was important for the genetic counseling of the patient.

**Discussion:** Previous XLAS cases with somatic mosaicism in COL4A5 had SNVs, and these 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 are rarely diagnosed with XLAS with somatic mosaicism.

**Results:** We have identified 23 mutations, 13 being novel and 10 previously reported. 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)”. We 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 (95%), proteinuria (91%), 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.

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

**Underline represents presenting author.**
POI666

Clinomics Implementation in the Mayo Clinic Nephrology Practice

Table 1: Results of Genetic Analysis by Disease Group

POI667

CD11b Activation Suppresses Pro-Inflammatory suPAR in Myeloid Cells and Reduces Lupus Nephritis in Mice

Background: Lupus nephritis (LN) is a debilitating glomerular disease and a comorbidity of systemic lupus erythematosus (SLE). CD11b, the alpha-chain of integrin CD11b/CD18, 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. suPAR is produced by myeloid cells upon pro-inflammatory stimulation. suPAR is downstream of CD11b activation and is a circulating risk factor for glomerular diseases. suPAR is downstream of CD11b activation and is a circulating risk factor for glomerular diseases. suPAR is produced by myeloid cells upon pro-inflammatory

Results: In silico predictions, disease database classifications and functional characterization were performed.

Discussion: In silico predictions and functional characterization classified all 9 definitely pathogenic COLA43/A4/AS variants in the FSGS cohort correctly. In silico predictions classified the majority (93-97%) of definitely pathogenic COLA43/A4/AS variants in ClinVAR, ARUP, and LOVD. However, a significant proportion of benign variants were predicted as pathogenic. Thirty-five percent of COLA43/A4/AS missense variants obtained from gnomAD were also predicted deleterious. In silico predictions tended to overestimate the effects of COLA4 variants of uncertain significance (VUS) when compared to functional characterization.

POI668

Drug-Induced Thrombotic Microangiopathy as a “Second-Hit” Phenomenon

Introduction: Thrombotic Microangiopathy (TMA) syndrome is a diverse group of inherited or acquired diseases characterized by microvascular thrombosis and endothelial damage. TMA includes diseases such as thrombotic thrombocytopenic purpura, strokes due to medullary 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. We hereby 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 uncontrollable hypertension. He had a positive urine toxicology admittance to marijuana, amphetamines (crystal meth), and heroin use. Labs revealed severe anemia and thrombocytopenia. C3 and C4 were reduced and low in some cases of atypical HUS. The patient was treated with apheresis and dialysis dependent on discharge. Unfortunately, he was then lost to follow up.

Discussion: Thrombotic Microangiopathy (TMA) syndrome is a diverse group of inherited or acquired diseases characterized by microvascular thrombosis and endothelial damage. TMA includes diseases such as thrombotic thrombocytopenic purpura, strokes due to medullary 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. We hereby present a case of drug induced TMA in a patient with an underlying pathogenic mutation for aHUS.

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 COLA43/A4/AS have been reported to account for a significant proportion of chronic kidney disease. Here we evaluate the performance of in silico programs for type IV collagen variants.

Methods: Rare COLA43/A4/AS 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 COLA43/A4/AS variants in the FSGS cohort correctly. In silico predictions classified the majority (93-97%) of definitely pathogenic COLA43/A4/AS variants in ClinVAR, ARUP, and LOVD. However, a significant proportion of benign variants were predicted as pathogenic. Thirty-five percent of COLA43/A4/AS missense variants obtained from gnomAD were also predicted deleterious. In silico predictions tended to overestimate the effects of COLA4a variants of uncertain significance (VUS) when compared to functional characterization.
Conclusions: Our results demonstrate that in silico programs are sensitive but not specific, leading to many putative or uncertain 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.

Funding: Private Foundation Support, Government Support - Non-U.S.

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 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=679); 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%, representing coincidental diagnoses or phenocopies.

Conclusions: Our results reveal the importance of ES in the diagnosis of NS and its complications, with implications in risk stratification and clinical management. We showed that one every 4 cases carried a genetic variant that has potential to help clinicians optimize precision medicine approaches at the single-patient level. Our results enable designing cost-effective panels to maximize yield in routine clinical practice.

Funding: Other U.S. Government Support

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 nephropensorphysis (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 hydrourereteronephrosis and right grade 5 vesicoureteral reflux (VUR) carried a heterozygous frameshift variant (c.2028_2031del; p.Asn676fs*27). Individual A3460 with left renal agenesis harbored a heterozygous missense variant (c.970C>T; p.His324Ty). 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 echogenicity and corticomedullary cysts, carried a heterozygous missense variant (c.2252T>G; p.Leu751Arg). 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.

PO1672

Recessive Mutations in SEMA3G as a Potential Novel Cause of Nephrotic Syndrome

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Background: Steroid resistant nephrotic syndrome (SRNS) is the second leading cause of chronic kidney disease in the first three decades of life. The identification of monogenic causes of SRNS has revealed ~60 single-gene etiologies. While in 12-30% of patients with SRNS a causative mutation may be detected, many remain without a molecular diagnosis (Sadowski JASN 26:1279, 2015). These genes are predominantly expressed in glomerular podocytes and the encoded proteins merge onto molecular complexes and pathways that are essential to podocyte development or homeostasis.

Methods: To identify novel monogenic causes of NS, we performed whole exome sequencing (WES) in an international cohort of 1,382 NS patients.

Results: We identified homozygous mutations in SEMA3G in 3 unrelated children with nephrotic syndrome, 1 nonsense mutation (c.1079C>T; p.Arg360*), 1 essential splice site mutation (c.460-2A>G, predicted to lead to skipping of exon 5 and thus causing a frame-shift and truncation of the protein) and 1 missense mutation (c.2225G>A, p.Arg742Gln). SEMA3G is a secreted protein that has been implicated in cell migration and axon guidance, and shown to protect podocytes from inflammatory kidney disease in a mouse model (Ishibashi Sci Rep 6:25955, 2016). We evaluated publicly available kidney single-cell RNA sequencing datasets and found SEMA3G to be predominantly expressed in podocytes (Karaiskos JASN 29:2060, 2018). We then performed co-immunofluorescence staining in adult rat kidney sections for SemA3g and established markers of podocytes (neprhin), endothelial cells (CD31), and mesangial cells (oSMa). The SemA3g signal was strongest in podocyte foot processes as indicated by partial overlap with nephrin but lack of overlap with CD31, or oSMa signal.

Conclusions: We, here, identified recessive mutations in SEMA3G as a potential novel cause of nephrotic syndrome in children.

Funding: NIDDK Support, Government Support - Non-U.S.
PO1673

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 1,998 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 status while controlling for cluster membership.

Results: Collapsing analyses were conducted on all cases together and on pediatric, adult, African, Asian, and steroid-sensitive subgroups. We detected a significant enrichment of QVs in known FSGS genes WT1, INF2, and NPHS2; additional signals in other FSGS genes (e.g. PAX2, COL4A3, COL4A5, CD2AP); and two novel ones that did not reach study-wide significance due to the limited sample size and phenotype heterogeneity. In several models and subgroups, the majority of the top 10 genes was formed by known FSGS genes, confirming the robustness of our novel approach.

Conclusions: We show that our new collapsing approach decreases inflation when samples with different ancestries are analyzed together, while preserving the underlying disease signals. We are currently more than doubling our case cohort, which should increase the power to detect significant signals in known FSGS genes, clarify the suggestive signal in two new genes, and allow well-powered sub-phenotype analyses.

Funding: Commercial Support - AstraZeneca

PO1675

Alpha Lipoic 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.

PO1674

eNOS/NO Signaling Attenuates Progression of Age-Related Kidney Diseases via Suppression of Inflammammasome


Background: Ageing affects the function of the immune system and leads to immunosenescence, which is characterized by defective immune responses and increased systemic inflammation (also termed inflamaging). Inflamaging is maladaptive and results from multiple mechanisms, including aberrant inflammasome activation. The ASC is an essential component of inflammasome. Endothelial dysfunction is also a common pathophysiology of aging-related organ damage. Nitric oxide (NO) produced by endothelial nitric oxide synthase (eNOS) is an important mediator in the maintenance of vascular homeostasis. We’ve reported that the eNOS-NO pathway attenuates the progression of kidney injury via suppression of inflammasomes. However, the relationship between the eNOS-NO pathway and inflamaging in the kidney remains unclear. To determine if the eNOS-NO pathway attenuates kidney damage via the regulation of inflammasome in ageing kidney, we used eNOS-deficient mice (eNOSKO) and eNOS-ASC double-knockout mice (eNOS-ASC-DKO).

Methods: Wild-type mice (WT) and eNOSKO were used to determine the role of the eNOS-NO pathway in ageing kidneys. WT and eNOSKO were sacrificed at 18 months of age to harvest kidney tissue. The localization of inflammasome activation in the kidney was evaluated with immunohistochemical analyses. To determine the role of inflammasomes in ageing kidneys, we generated eNOS-ASC-DKO. The mRNA expression of inflammasome components were determined in isolated glomeruli.

Results: The glomerular injury was more exacerbated in eNOSKO-18M than in WT-18M. In the immunohistochemical, the expression of ASC coexisted with the macrophages detected by F4/80 staining in eNOSKO-18M. These data suggested that the inflammasome activation was located in the macrophages. In the isolated glomeruli, mRNA of inflammasome components were higher in eNOSKO-18M than in WT-18M. The glomerular damage were ameliorated in eNOS-ASC-DKO-18M compared to eNOSKO-18M. In summary, in eNOSKO, inflammasomes were activated in macrophages, and interstitial fibrosis was exacerbated. However, in eNOS-ASC-DKO-18M mice, the tubulointerstitial damage was attenuated.

Conclusions: Endothelial NOS/NO signaling ameliorates kidney damage in the aging process via the modulation of inflamaging associated with inflammasome-activation.
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-inflammatory defense. We observe higher kidney mitochondrial SIRT3 (mSIRT3) in females vs. males. mSIRT3 declines with age but sex differences persist. 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 mSIRT3 expression vs. age-matched females is associated with higher baseline ROS generation, and development of tubular cytoplasmic vacuoles by 6-mo and fibrosis by 14-mo. Aging-related changes are attenuated in SIRT3 Tg 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 injury 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 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 mSIRT3, and caused kidney injury (decreased CrCl and increased tubular vacuolization). T increased kidney mSIRT3 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.

Funding: Veterans Affairs Support, Private Foundation Support

Efficient Follow-Up and Its Effects on Questionnaire Responses in the EQUAL Study in the United Kingdom
Emer R. Gates,1 Barnaby D. Hole,1,2 Samantha J. Hayward,1,2 Fergus J. Caskey,1,2 EQUAL Investigators ’North Bristol NHS Trust, Westbury on Trym, United Kingdom; ’University of Bristol, Bristol, United Kingdom.

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 <20/mL/min). 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 88.2% (98/111) to 59.0% (65/110) for patients who completed 1.5 years of TFU. 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, before falling to baseline at the first EFU.

Conclusions: In this prospective study of older people with advanced CKD, response rates fell and error rates rose during TFU. On introducing a shorter postal questionnaire, response and error rates improved to levels resembling early TFU. 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.
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 over 40 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. eGFR was calculated by a nephrologist with CKD (estimated glomerular filtration rate (GFR) = 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/1.73m²/year.

Results: Of 101 patients, 55.4% (n = 56) were male. Thirty eight percent presented CKD complications, 37.6% had anemia and 18.7% needed hypothyroid-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 (13.1 ± 9.6 years versus 8.4 ± 6.6 years) in the progressive CKD group.

Conclusions: In over 80 years, average rate of progression of CKD was 2.0 mL/min/1.73 m²/year, which, associated with the reduced life expectancy of patients in this age group, allows us to state that the vast majority will not reach CKD stage 5.

Using the Difference in Estimated Glomerular Filtration Rate by Cystatin C vs. by Serum Creatinine (eGFRdiff) to Assess Muscle Mass and Frailty in Older Adults
O. Alison Potok,1 Joachim H. Is,1 Michael Shlipak,2* Nisha Bansal,3 Ronit Katz,4 Stephen B. Kritchevsky,1 Dena E. Ritkin,1,4 University of California San Diego, La Jolla, CA; 2University of Washington, Seattle, WA; 3Wake Forest University School of Medicine, Winston-Salem, NC; 4San Francisco VA Medical Center, San Francisco, CA; 5University of California San Francisco, San Francisco, CA; 6VA San Diego Healthcare System, San Diego, CA.

Background: Preliminary work has shown that the difference in estimated glomerular filtration rate by cystatin C vs by creatinine (eGFRdiff) is associated with frailty and mortality. As creatinine is influenced by muscle mass, more so than creatinine, we aim to determine whether muscle mass explains the relationship between eGFRdiff and frailty.

Methods: In the Health Aging Body Composition study, 2980 (97% of HABC) had baseline GFR calculated using CKD-EPI equations (cystatin-based [eGFR Cys] and creatinine-based [eGFR Cr], respectively), and eGFRdiff was defined as eGFR Cys - eGFR Cr. Total thigh muscle area was evaluated on computed tomography. Frailty was scored on a continuous scale based [eGFR Cys] and creatinine-based [eGFR Cr].

Results: Mean age was 74 (± 7) years, eGFR Cys was 72 (± 15) mL/min/1.73 m². Compared to participants with minimal difference in eGFR (within 10 mL/min/1.73 m²), those in the positive eGFRdiff group (≥ 10 mL/min/1.73 m²) were less likely to have fallen in the past year (19% vs. 21%), had stronger grip strength (31 vs. 30 kg) and walked faster (1.22 vs. 1.17 m/s). Higher eGFRdiff was significantly associated with larger thigh muscle area. In cross-sectional analyses, each 1 SD increment in eGFRdiff was associated with 30% lower odds of frailty.

Conclusions: Preliminary work has shown that the difference in estimated glomerular filtration rate by cystatin C vs by creatinine (eGFRdiff) is associated with frailty and mortality. As creatinine is influenced by muscle mass, more so than creatinine, we aim to determine whether muscle mass explains the relationship between eGFRdiff and frailty.

The Difference in eGFR by Cystatin C vs. Creatinine Is Strongly Associated with Mortality Independent of Measured GFR
O. Alison Potok, Dena E. Ritkin, Joachim H. Is, Michael Shlipak, Alice Schneider, Nina Mielke, Elke Schaeffner, 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 Francisco, San Francisco, CA.

Background: In preliminary work, we have shown that the difference in glomerular filtration rate (eGFR) estimated by cystatin C [eGFR Cys] and creatinine [eGFR 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 ioehoxel clearance (mGFR), as well as serum creatinine and cystatin C levels. eGFR Cys and eGFR Cr were calculated using CKD-EPI equations, and eGFRdiff was defined as eGFR Cys - eGFR Cr. Mortality was recorded during up to 8 years follow-up. The association between eGFRdiff and mortality was assessed using Cox regression.

Results: Average (SD) age was 79 (± 6) years, eGFR Cys 63 (± 21), and eGFR Cr 69 (± 17) for an eGFRdiff of -6 (± 12) mL/min/1.73m². Compared to participants with minimal differences in eGFR, those with a substantially positive difference eGFRdiff (a10 mL/min/1.73 m²) were younger (76 vs. 78 years), less diabetic (17% vs. 24%) and fewer took antihypertensives (59% vs. 76%). Those with a substantially negative eGFRdiff (< -10 mL/min/1.73 m²) 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).

Conclusions: In BIS, an eGFR Cys estimate that was substantially less than an eGFR 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 eGFRdiff.

Funding: Private Foundation Support

Table. Association of eGFRdiff with Mortality in Older Adults in the Berlin Initiative Study

Outcomes of Haemodialysis in Incident Elderly Haemodialysis Patients: Single-Centre Experience
Rouskas Gama, Jocelyn Heins, David Makanjuola, Subash Somalanga. St Helier 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 were 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 80-90 years (group B). Mean age was 78.1 ± 5.3 years and 74% were of white ethnicity. Baseline characteristics are 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 35% (35% in group A and 44% in group B); 1-year mortality was 35% 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.
Baseline characteristics and mortality in elderly incident haemodialysis patients.

POI1684
Cost Effectiveness Study of Hyperkalemia Management
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**Background:** Patiromer (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 Clinformatics® 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 and censored exact matching with baseline variables were used to identify the complete set of matching unexposed and exposed HK episodes. Follow-up began on index date and ended at the first censoring event (insurance disenrollment, death, 12/31/18, sodium polystyrene sulfonate or sodium zirconium cyclosilicate initiation, PAT discontinuation [exposed only], PAT initiation [unexposed only]). Cost outcomes were measured over 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 60% were male. Patients had a mean of 5 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, $9584) was observed at 6 months post-index (P<0.01). This cost difference included a pharmacy increase of $3904 ($964, $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.

POI1685
Effects of Veverimer on Serum Bicarbonate and Physical Function in Elderly Patients with Metabolic Acidosis in CKD
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**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 patient-reported objective measures of physical function in pts 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-PF which quantitates 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%), diabetes (67%), and CHF (40%). At Baseline, the mean eGFR 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-PF scores and RCS time (Table 1) compared with placebo. These effects of veverimer exceeded the minimal clinically important difference for both the KDQOL-PF (+3 to +5 points) and RCS (-1.7 seconds). Safety was similar in both treatment groups.

**Conclusions:** 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.

POI1686
Design of a Consensus-Based Geriatric Assessment Tailored for Older Patients Approaching ESKD
Carlin G. Voorhees,1 Noeleen C. Berkhout-Byrne,1 Adry Dienenbroek,2 Casper F. VanJessen,3 Wilma A.W. Jager,1 Simon Mooijart,1 Marjolijn Van Buren,1 on behalf of principal investigators of the POLDER study 1Leids Universitair Medisch Centrum, Leiden, Netherlands; 2Universitair Medisch Centrum Groningen, Groningen, Netherlands; 3Sint Antoniesziekenhuis, Nieuwegem, 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 year) 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, caregivers and health professionals. Older patients (aged ≥65 years) approaching end-stage kidney disease (eGFR < 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, psychologic, 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 practice 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 of implementation, patient satisfaction and the value for treatment decision making and outcome improvement.

**Funding:** Private Foundation Support

POI1687
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
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**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-PF, 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. The Lancet, 2019). These measures showed an ability to detect change - pts in the veverimer group improved significantly on both.

**Results:** There was a significant, direct correlation between improvement (i.e., higher score) over 1 yr on the KDQOL-PF total score and improvement on the RCS (i.e., faster time), (Pearson’s product-moment correlation, 0.33, P < 0.001). Additionally, 5 of the 10 individual KDQOL-PF activity limitations correlated significantly with RCS time: “lifting or carrying groceries”; “bending, kneeling, or stooping”; “walking one block”; “walking several blocks”, and “bathing or dressing yourself” (P-value < 0.05 for

**Key:** TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
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 survivor interview 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 an 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 4.4±3.2 points; mean scores for balance, walking and lower leg strength were 2.3±1.1, 1.8±1, and 1.3±0.7 points, respectively. Mean gait speed was 0.46±0.22 meters/second. Coding 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). Based on the literature. Interview transcripts were descriptive coded and major themes were extracted using both deductive and inductive approaches.

Funding: Other NIH Support - K23AG057813, Government Support - Non-U.S.

Key themes regarding mobility in older hemodialysis patients

<table>
<thead>
<tr>
<th>Theme</th>
<th>Quote</th>
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<tbody>
<tr>
<td>Symptomatology mobility (i.e. forearm balance and walking)</td>
<td>&quot;Oh, give me more balance or my book will fall every time I take a walk.&quot; (female, age 70)</td>
</tr>
<tr>
<td>Frequent changes in mobility</td>
<td>&quot;I get off the machine, cross the room to the car. ‘Cause I have my good legs and my bad legs they both do it...&quot; (male, age 65)</td>
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</tbody>
</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.

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 renal insufficiency (HP) by rehabilitative measures both in acute geriatrics units (AG) and in inpatient rehabilitation facilities (RG). So far it is largely unknown whether RP benefit from this type of rehabilitation to the same extent as HP. We have now examined this question by evaluating a large geriatric database.

Methods: The Geriatrics in Bavaria-Database (GiB-DAT) was established with the support of the Ministry of Health as a quality assurance project. It comprises the vast majority of anonymized records of cases treated in Bavarian AG and RG. In this study all data records for the years 2012-2019 from AG and RG were evaluated. The following parameters were examined: At admission: age, gender, cognition (Minimal Status Examination: MMSE), emotion (Geriatric Depression Scale: GDS), degree of care (DC); at discharge: number of diagnoses and medication; at admission and discharge: self-help ability (Barthel Score: BS), mobility (Timed Up and Go Test: TUG) and place of residence.

Results: Both in AG and RG, HP (AG/ RG n=11653/248831) and RP (AG/ RG n=27294/8984) did not relevantly differ in age, gender, MMSE, GDS and DC. The number of diagnoses (AG: 10.7 vs. 9.3; RG 10.3 vs. 8.3) and drugs (AG 10.1 vs. 9.3; RG 9.9 vs. 9.0) was slightly higher in RP compared to HP. No major differences between RP and HP were observed at the beginning of the rehabilitation in BS, TUG and place of residence. In RP/HP, BS improved during rehabilitation by 11.4/14.4 (AG) and +21.1/21.9 (RG) points and the number of patients "able to walk" in the TUG by +22.1/20.6% (AG) and +14.3/14.5% (RG) respectively. Living could be maintained in 66.0/68.9% (AG) and 81.6/81.5% (RG). Subgroup analysis of CKD-severity showed no relevant difference for any of the examined parameters both in AG and RG.

Conclusions: RP benefit to a similar extent as HP from rehabilitative measures both in AG and RG with respect to improvement of self-help ability, mobility as well as the preservation of private residence. This was observed regardless of the stage of renal insufficiency.

Predictors of Functional Status Change in Patients with CKD Between Two Hip Fracture Events: A 6-Year Prospective Study

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Background: Patients with chronic kidney disease (CKD) are susceptible to recurrent hip fractures (Hip#). Functional status decline after Hip# is transient, exacerbated by frailty, sarcopenia and co-morbidities. We studied the prognostic value of clinical and laboratory parameters for functional status change in CKD after recurrent Hip#.

Methods: Patients with CKD G3b-5 admitted with 2 separate Hip# events between June 2013 and Dec 2019 in a North West UK tertiary care hospital were included. Difference in Karnovsky Performance Status (KPS) Scale between 1st and 2nd Hip# admission determined functional status change. KPS is a linear scale between 0 (dead) and 100 (normally active). Parameters assessed included Clinical Frailty Scale (CFS), Hopkins Frailty Score (HFS), CKD Fl-LAB, Smerbo Score, Charlson’s Co-morbidity Index, Nottingham Hip Fracture Score, ASA Score and Abbreviated Mental Test Score. Differences in each parameter score between 1st and 2nd Hip# admission were recorded.

ROC curve analyses was performed to assess discriminative ability among individual scoring tools.

Results: 37 patients met inclusion criteria (F:M 1.8:1; mean age 84.5±10.2 yrs). 10 were receiving 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 10.6 (p=0.028). AUC values from ROC analyses are shown in Table 1.

Conclusions: There was a significant decline in functional status between Hip#. Frailty assessment tools (CFS, HFS and CKD Fl-LAB) had the best predictive performance for functional status change. Frailty measures may be utilized as risk prediction tools of functional status change from first Hip# admission. Further Research is needed to evaluate whether Hip# interventions that aim to maintain functional status and reduce subsequent fracture risk.

Funding: Government Support - Non-U.S.

<table>
<thead>
<tr>
<th>Table 1</th>
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<tbody>
<tr>
<td>Predictors</td>
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<tr>
<td>Clinical Frailty Scale</td>
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<tr>
<td>Hopkins Frailty Score</td>
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<tr>
<td>CKD Fl-LAB</td>
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<tr>
<td>Smerbo Score</td>
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<tr>
<td>Charlson’s Co-morbidity Index</td>
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<tr>
<td>Nottingham Hip Fracture Score</td>
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<tr>
<td>ASA Score</td>
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<tr>
<td>Abbreviated Mental Test Score</td>
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Which Parameters Best Predict Mortality After Hip Fracture for Patients with CKD? Insights from a 6-Year Prospective Analysis

Henry Wu,1,2 Rene Van Mierlo,1,2 Ajay P. Dhaguyige,1,2 Sandip Mitra,1,2 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...
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], I2= 73%)

Conclusions: In older patients, intensive BP control was not associated with an increase in rate 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

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Sample size</th>
<th>Mean age (years)</th>
<th>Male (%)</th>
<th>Mean BMI</th>
<th>30-day mortality</th>
<th>1-year mortality</th>
<th>3-year mortality</th>
<th>5-year mortality</th>
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<tbody>
<tr>
<td>1st study</td>
<td>RCT</td>
<td>500</td>
<td>65</td>
<td>50%</td>
<td>25</td>
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<td>60</td>
<td>55%</td>
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Table 1: AUC values of tools used to predict mortality following hip fracture

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<th>AUC (95% CI)</th>
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<td>0.65</td>
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<td>HoF Frailty Score</td>
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<td>0.72</td>
<td>0.65</td>
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<tr>
<td>DROF Score</td>
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<td>0.58</td>
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<td>Charlson's Co-morbidity Index</td>
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<td>0.65</td>
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<td>Suicide Frailty Score</td>
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<td>0.58</td>
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<tr>
<td>Sernbo Score</td>
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<td>Nottingham Hip Fracture Score</td>
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<td>CKD FI-LAB</td>
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BP: Blood pressure; RCT: Randomized controlled trial
Tailoring the Beers Criteria for Mortality Risk Stratification Among Older Adults Initiating Hemodialysis

Rasheedah K. Hall,1 Abinereki Muzala,1 Dorry L. Segey,2 Mara McAdams-DeMarco,1 Durham VA Medical Center, Durham, NC; 2Duke University School of Medicine, Durham, NC; 3Johns 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 adult aged ≥65 initiating hemodialysis (2013-2014) and enrolled in Medicare Part D by 90 days post-initiation. We used Part D claims to quantitatively assess prescription drug use (Beers Criteria). In a training cohort (60% sample), we identified which of 38 PIM classes was 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. PIM 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

Sarah Ramer, Martin Viola, Holly G. Prigerson. Weill Cornell Medicine, New York, NY.

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/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 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; 52% 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 ± 3.5 vs. 10, P=0.045) but significantly less suffering from hunger (mean 2.4 ± 3.6 of 10, P=0.012) or thirst (mean 3.2 ± 4.8 of 10, P=0.005). There was a trend towards more suffering from swelling in the dialysis patients (mean 6.2 ± 5.3 of 10, P=0.083). No 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=0.04) and swelling (β=0.20, P=0.007) in the model, the relationship between dialysis and overall suffering was attenuated (β=0.84, 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

Fahad Saeed, Basil S. Kazi, Nicole L. Mayo, Spencer Dahl. University of Rochester Medical Center, Rochester, NY.

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 (C1: -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 improve SDM in clinical settings are a top research priority.

Funding: Private Foundation Support

PO1698

Attitudes Towards Physician-Assisted Death in Patients Receiving Maintenance Dialysis

Fahad Saeed, Basil S. Kazi, Nicole L. Mayo. University of Rochester Medical Center, Rochester, NY; University of Rochester, Rochester, NY.

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 was 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, 22% expressed uncertainty, and 22% available: 37% said yes, 44% no, and 17% chose the unsure option. In the bivariate analyses, those who supported PAD had lower mean 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 or opposition/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
Underline represents presenting author.

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PO1699 Perspectives on Conservative Management of Advanced Kidney Disease: A Qualitative Study of US Patients and Family Members

Susan P. Wong,1,2 Taryn Oestreicher,1,3 George G. Gaye,1,3 Ann M. O’Hare,1,2 J. Randall Curtis,1,4 1University of Washington, Seattle, WA; 2VA Puget Sound Health Care System, Seattle, WA; 3Cambia Palliative Care Center of Excellence, Seattle, WA.

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 when 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

Katharine L. Cheung,1 Manjula Kurella Tamura,2 Michael A. Lamantia,1 Terry Rabionowiz,2 Renee Stapleton,1 Bob Gramling.1 1University of Vermont College of Medicine, Burlington, VT; 2Stanford University School of Medicine, Stanford, CA.

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 a large wall mounted screen with centrally positioned camera was used to view an iPad attached to a 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 the televisit was better. Patients felt the appointment was relevant to them, but they were less certain that they learned new things about their condition, and they were mixed about whether 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

PO1701 Abstract Withdrawn

PO1702 Modestly Low eGFR Is Not Associated with Cognitive Decline in the Elderly

Linda McEvoy Cheung,1 Taryn Oestreicher,2 Ann M. O’Hare,2 J. Randall Curtis,1,4 1University of Washington, Seattle, WA; 2VA Puget Sound Health Care System, Seattle, WA; 3Cambia Palliative Care Center of Excellence, Seattle, WA.

Background: Kidney disease is associated with cognitive impairment. Whether mild to moderate CKD is associated with cognitive decline in older adults is not clear. We evaluated changes in cognition in relation to baseline eGFR in the elderly Alzheimer’s Disease Neuroimaging Initiative (ADNI) participants.

Methods: ADNI is an NIH funded, multicenter study, which includes participants with normal and impaired cognition who were administered a comprehensive battery of neuropsychological tests every six months. We related the CKD-epi eGFR with previously validated composite scores for memory (ADNI-Mem) and executive function (ADNI-EF) in multivariable linear regression analysis.

Results: 1127 participants with a mean age of 73.8±7 years, 57% men, 97% Caucasian, and mean follow up for 6±2.6 years were included. Mean baseline eGFR was 76.4±19 ml/min/1.73 m². ADNI-Mem and ADNI-EF scores declined across all eGFR categories (figure). Older age and lower education were associated with declines in both ADNI-Mem and ADNI-EF scores. Baseline eGFR was not associated with declines in either ADNI-Mem or ADNI-EF scores (table).

Conclusions: There is no association between baseline eGFR and cognitive decline in elderly persons with mild-moderate impairment in kidney function.

Funding: Other NIH Support - K23-AI055666

Multivariable linear regression model for ADNI-Mem score and ADNI-EF score
PO1705

DNA Double-Strand Breaks of Human Glomerular Endothelial Cell-Induced Collagen Type IV Excretion and Nodular Lesions in Various Kidney Diseases

Ai Fujii,1 Yumi Sunatani,2 Kengo Furuchi,1 Keiji Fujimoto,1 Hiroki Adachi,1 Kuniyoshi Iwabuchi,1 Hitoshi Yokoyama,1 Kanazawa Medical University School of Medicine, Department of Nephrology, Kanazawa, Japan; 2Kanazawa Medical University School of Medicine, Department of Biochemistry, Kahokugan, Japan.

Background: Collagen deposition is the common histologic end-point of progressive chronic kidney diseases (CKDs). We focused on collagen type VI (COL6) which is known as components of nodular lesions. This study was performed to test the hypothesis that glomerular endothelial cells with DNA double-strand breaks (DSBs) induce the accumulation of COL6 in various kidney disease and evaluated the mechanism of COL6 accumulation after DSBs.

Methods: We examined various kidney diseases (n=180) in which DSBS and glomerular fibrosis were detected by phospho-histone H2AX (γ-H2AX) expression and COL6 accumulation. In vitro study, we investigated the relationship between DSBS and COL6 excretion and the intracellular signal pathways in human glomerular endothelial cells (HRGECs) using mitomycin C (MMC)-induced DNA damage, and other two agents; Neocarzinostatin (NCS) and camptothecin (CPT). We examined the effect of DSBS on response signal pathways, i.e. ATM, ATR and DNA-PK using their specific kinase inhibitors (KU55933, VE-821, N7441).

Results: COL6 and γ-H2AX were detected in glomeruli in which the γ-H2AX-positive area was identified as the independent factor for the % COL6-positive area (β: 0.553, t = 2.642, p = 0.009). Furthermore, COL6 was a component of the nodular lesions found in various kidney diseases. In vitro study of MMC-induced DNA damage, COL6 excretion detected 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.
PO1709
Protection of the Remnant Rat Glomeruli from Mechanical Stress Through Structural Adaptation and Pharmacological Intervention After 5/6-Nephrectomy: A Modeling Study
Owen Richfield,1 Ricardo Cortez,2 L. Gabriel Navar,3 Tulane University Biinnovation PhD Program, New Orleans, LA; Tulane University Department of Mathematics, New Orleans, LA; Tulane University Department of Physiology, New Orleans, LA.

Background: 5/6-nephrectomy leads to increased blood flow and pressure in the remaining glomeruli, ultimately resulting in scarring. 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 renalopd 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. J Am Soc Nephrol 31: 2020) 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 dynes/cm². Without structural adaptations enalapril reduced mean shear stress to 136.1 dynes/cm². The increase in glomerular capillary diameter reduced shear stress while the increased diameters combined with glomerular hypertension increased mean hoop stress from 90.9 to 104.3 kPa. The combination of enalapril and structural adaptations resulted in a mean network shear stress of 81.1 dynes/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
Cheuk Yin Wong, Susan Yung, Caleb C. Chan, Tak Mao D. Chan. The University of Hong Kong, Hong Kong, Hong Kong.

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 standard chow 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. Mice were 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, tubularatrophy, tubulo-interstitial macrophage infiltration, and increased interstitial e-smooth muscle actin, 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 TGF-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.
PO1711

Signaling at the Mesangial Cell (MC) Membrane in Light Chain Deposition Disease (LCDD) and AL-Amyloidosis (AL-Am) Involves Sorbin-Related Receptor (SORL1), Caveolins, and C-Fos

Jiunn Teng,1 Chun Zeng,1 Elba A. Turbat-Herrera,1 Takahito Moriyama,2 Luis Del Pozo-Yauney,2 Bing Liu,2 Xinggui Shen,1 Guillermo A. Herrera. Department of Pathology, 1University of South Alabama, Mobile, AL; 2Tokyo Joshi Ika Daigaku Fuzoku Kogenbyo Ryumachi Tensu Center, Shinjuku-k, Japan; 3Louisiana State University Health Sciences Center Shreveport, Shreveport, LA.

Background: AL-Am and LCDD are two diametrically opposed glomerulopathies in terms of mesangial alterations produced by glomerulopathetic 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, kapa / 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) caveoleae on the surface of MCs increased dramatically, SORL1 was activated and c-fos translocated from cytoplasm to nucleus.

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 nucleus and the downstream mesangial alterations (i.e. mesangial expansion / 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

PO1712

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, capillary transformation, 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: Proteinuria and renal COL3A1 day 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 (*, p<0.01 vs. sham) which correlated directly and significantly with renal COL3A1 mRNA expression level. Network analysis revealed a strong relative glomerular COL3A1 interactome with an average strength of 0.84±0.08 and a relatively weaker tubular COL3A1 interactome with an average strength of 0.56±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

PO1713

The Correlation Between Urinary MicroRNA-21 and Renal Parameters in Patients with IgA Nephropathy

Akira Aramai, Tsukasa Osaki, Kazunobu Ichikawa, Masafumi Watanabe, Tsuneo Konta. Yamagata University Faculty of Medicine, Yamagata, Japan.

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: Urinary microRNAs and proteins were extracted and quantified 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 eGFR change 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.

PO1714

Diagnostic Delay and the Clinical Prognosis in US Adults with Systemic Light Chain (AL) Amyloidosis with Renal Involvement

Laura Hester,1 Dina Gifkins,1 Kevin Bellew,2 Jessica Vermeulen,3 Jordan Schecter,2 Victor Dishy,1 Brendan Weiss,2 Janssen Research & Development LLC, Titusville, NJ; 3Janssen Research & Development LLC, Spring House, PA; 4Janssen Research & Development LLC, Leiden, Netherlands; 5Janssen Research & Development LLC, Rarity, NJ.

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 and associated adverse outcomes in systemic AL patients (pts) with prior signs/symptoms (S/Sx) of renal impairment.

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 inpatient or ≥2 outpatient AL codes, followed by ≥2 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 monocular 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.

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

Underline represents presenting author.

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**PO1715**

**Case of Leukocyte Cell-Derived Chemotaxin 2-Associated Renal Amyloidosis**

Anita Kamarzarian, Masoud 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. Laboratory tests showed microalbuminuria and negative ANA and dsDNA. She had been treated and is being followed for diabetics. She presented with new onset proteinuria and edema. 

**Discussion:** ALECT2 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 of chemical analysis by tandem mass spectrometry.

**PO1716**

**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 MGIgG4 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.

**PO1717**

**A Case of Secondary Focal Segmental Glomerulosclerosis and Thrombotic Microangiopathy in a Heart Transplant Patient**

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**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 Tyrosine 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.

**PO1718**

**D-Penicillamine-Induced ANA(+)ANCA(+) Crescentic Glomerulonephritis in Wilson Disease**

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**Introduction:** Wilson’s disease is an inherited autosomal recessive disorder caused by loss of function of a copper exchange adenosinetriphosphate encoded by ATP7B, which results in impaired biliary copper excretion and accumulation of copper in plasma and tissues. In the kidney, copper accumulation may affect tubular cells, but was never associated with glomerular lesions. Some patients have been reported as crescentic glomerulonephritis with Wilson’s disease treated with D-penicillamine.

**Case Description:** A 45 years old female was consulted to adult nephrology clinic on worsening chronic kidney disease. She had prescribed 800mg metalcaptase for 3 months for Wilson disease. She was consulted to our nephrology clinic with declining renal function. She initially presented with almost 50% fall in creatinine. She was started on regular dialysis and is still in remission after treatment with bortezomib, cyclophosphamide and dexamethasone.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
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, antimalperoxidase(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 fibrous or fibrocellular crescents, and 2/9 global collateral 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 glomerulonephritis, methyl-prednisolone(PSL) pulse therapy was given and preceded with 7/9 fibrous or fibrocellular crescents, and 2/9 global collateral sclerosis. Also, mild proteinase(PR3) antibody and anti-glomelular basement membrane(GBM) antibody were detected. Antimyeloperoxidase(MPO)-ANCA 350 U/ml, antinuclear factors titer 1/640. Both anti-MPO-ANCA<3.5 U/ml.Cr was improved to 1.5mg/dl in spite of presence of mild diffuse interstitial fibrosis. Hereafter 15 years, no medication except metilacaptase was given, but regrettably Cr has been deteriorated to 4.5mg/dl,MO-ANCA–15–25 U/ml. Other paraproteinemia or malignant diseases including multiple myeloma was excluded. Taken together for these 25 years, D-penicillamine-associated interstitial nephritis\cite{40} has suspected. Oral zine acetate was once truncated due to gastroenterological side effect, then planned to change to trientine.

**Discussion:** The pathogenesis of drug-induced ANCA-associated vasculitis has not been proven. There is a hypothesis that MPO binds to drug metabolites and alters the MPO antigenic property\cite{41}. Treatment of AAV is usually with mPSL pulse, cyclophosphamide, and/or rituximab. References:1)Am J Kidney Dis 2007;50:821.2) Clin Nephrol 2016;85:296.3)Kanjo Hepatology(Tokyo)1996;37:Suppl2 116.4) Japan J Nephrol 1998;40:518.

**PO1719**

**In Silico Prediction of Potential New Biomarkers of IgA Nephropathy**

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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 tissues. KEGG pathway annotation reveals that cytochrome c450 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 patients are obtained from GEO (GSE73953). Further screening of overlapping genes demonstrates that ABCD3, CLPTM1, FM04, RAR52, SFXN2 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.
upregulate signaling specifically in MD cells. MD gene profiling validated by data from Human Protein Atlas was used to confirm expression of various pathways and regulators of protein synthesis and vesicular exocytosis.

**Results:** OPP experiments in mMDβ- 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-Wntα- mice (1.36 ± 0.04) also resulted in a significant increase in MD protein synthesis as compared to control (0.67 ± 0.06). The expression of MD-specific detected proteins (Ccn1, Pappa2, Nov, Cxcl14) was enhanced in activated MD cells. Finally, results from MD gene profile analysis with HPA validation showed high and MD-specific expression of several pathways involved in mRNA translation (p=0.056, eIF3C, eEF2), chaperones (HSP70) along with markers of protein synthesis and vesicular exocytosis.

**Conclusions:** In summary, 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 Transcription-Wide Association Study Analysis Identifies Dach1 as a Kidney Disease Risk Gene**

Tomohito Doki,1 Shizheng Huang,1 Chengxiang Qiu,1 Xin Sheng,1 Hongbo Liu,1 Jianfu Zhou,2 Aili Cao,2 Jianhua Li,2 Lewis Kaufman,2 Richard G. Pestell,2 Katalin Susztak,1 University of Pennsylvania, Philadelphia, PA; 1Icahn School of Medicine at Mount Sinai, New York, NY; 2Shanghai University of Traditional Chinese Medicine, Shanghai, China; 3Pennsylvania Cancer and Regenerative Medicine Research Center, Philadelphia, PA.

**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. Transcription-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, Metaxcan. Bulk kidney epigenome mapping and single cell ATAC-seq data were used for fine-mapping. We generated tubule specific DACH1 knock-out (Kapre-Dach1i-fox) and transgenic (Pax8-TRE-Dach1) mice to define the functional role of Dach1 in kidney disease development. Murine cultured tubule cells 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 and expression 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 showed that DACH1 risk variants knock-out DACH1 regulatory region in the DCT. Mice with tubule specific Dach1 deletion developed more severe renal fibrosis when challenged with folic acid (FA) compared to controls. Mice with tubule specific Dach1 overexpression were protected from FA-induced kidney fibrosis. Single cell RNA sequencing and cultured primary tubule cell cultures showed that Dach1 plays role in controlling cell proliferation and inflammatory gene expression contributing to fibrosis development.

**Conclusions:** Integration of GWAS, TWAS, single cell, 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 cholesterol ester and triglyceride (TG) are known to cause lipotoxicity. Excessive FFA catalysis resulting from excessive lipolysis of TG is a major contributor to cell injury in obesity and diabetes. Perilipin 5 (PLIN5) is a LD-related protein that mediates FFA catabolism resulting from excessive lipolysis of TG. PLIN5 deficiency in podocytes and tubule cells may uncouple the mitochondria, leading to mitochondrial dysfunction and apoptosis. Moreover, exosomes, which in vivo improved kidney function was found in 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, Shiochi 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, a marker 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 eSMA positive myofibroblasts. Consistent with this, the analysis of single-cell transcriptomic databases showed Meflin and eSMA are expressed in distinct subsets of fibroblasts in the kidney. The expression pattern of Meflin was also confirmed by lineage tracing assay. In the UUO model, some of Meflin-lineage cells were positive for eSMA, suggesting that they give rise to myofibroblasts in the progression of fibrosis. Finally, we assessed the function of Meflin using NK49f. Meflin expression was significantly downregulated by TGF-β1 stimulation, and exogenous Meflin overexpression led to the suppression of TGF-β1 induced eSMA expression and vimentin expression.

**Conclusions:** Our present study identified a new subset of renal fibroblasts, which is positive for Meflin but negative or weakly positive for eSMA. 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**

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**Background:** CD14 is a GPl-anchored membrane protein that serves as a pattern recognition receptor in the clinical setting of sepsis. CD14 transfers lipopolysaccharide (LPS) to LPS receptors in the cell membrane 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. CD4 level is increased in SLE patients, but little is known about its clinical significance or pathogenic role in lupus nephritis (LN).

**Results:** Serum LPS and CD14 levels were determined in LN patients and healthy subjects using commercially available assays. CD4 level is increased in SLE patients, but little is known about its clinical significance or pathogenic role in lupus nephritis (LN).

**Conclusions:** Serum LPS and CD14 levels were determined in LN patients and healthy subjects using commercially available assays. CD4 level is increased in SLE patients, but little is known about its clinical significance or pathogenic role in lupus nephritis (LN).

**Funding:** Government Support - Non-U.S.
CircZNF609 Participates in the Pathogenesis of Focal Segmental Glomerulosclerosis by Sponging miR-615-5p
Junjun Luan, Hua Zhou. Department of Nephrology, Shengjing Hospital of China Medical University, Shenyang, China.

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 verify 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. Glomerulosclerosis 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 mimics 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 six weeks after FGS onset by ADR injection. Glomerulosclerosis 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.
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 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)).

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<th>Race</th>
<th>B cell return</th>
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<tr>
<td>Mac</td>
<td>1</td>
<td>1Department of Nephrology, Fujita Health University</td>
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<td></td>
<td>Graduate School of Medicine, Toyoake, Japan; 2Department of Nephrology, in Japan; 3Department of Nephrology, in other countries</td>
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Figure 1. Kaplan-Meier for B cell depletion.

POI1731
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 measured 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 undisrupted area than in glomerular crescent as contrasted with global distribution of CD163+ cells in diseased glomerulus. 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.

POI1732
Urinary Biomarkers as a Tool for Monitoring Remissions and Predicting Relapses in Autoimmune Glomerulonephritis
Suzanne Dominique Genevet,1,2 Myriam Khalili,2,1 Jean-Philippe Rioux,2,1 Jérémy Quadry,1,2 Arnaud Bonnefoy,1,2 Stephan Troyanov,1,3 Université de Montréal, Montreal, QC, Canada; 2Hôpital du Sacré-Coeur de Montreal, Montreal, QC, Canada; 3Centre Hospitalier Universitaire Sainte-Justine, Montreal, QC, Canada.

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-β (TGF-β), 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-β (all p < 0.05). Twenty percent (n=16) of inactive periods reflected relapses with subsequent relapses. Biomarker levels during the inactive period preceding relapses did not significantly change for proteinuria (+9%), urinary sC5b-9 (+15%) and MCP-1 (+21%) while they decreased for TGF-β (-30%, p<0.02). During relapses, we observed a 3.2-fold (1.98-8.3) 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-β decreased 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

POI1733
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 proteinase 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 homzygous (“GG”) were compared to heterozygotes (“CG”) and homzygous (“CC”). PRTN3 expression was measured by quantitative polymerase
chain reaction amplification of cDNA from patient peripheral blood polymorphonuclear leukocytes 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 PRTN3 expression may explain earlier disease onset.

Funding: NIDDK Support

POI1134

The Compositional and Functional Changes of Gut Microbiota in Crescentic Glomerulonephritis

Huanhuang Yin, Xiaoxiao Shi, Peng Xia, Limeng Chen. Department of Nephrology, Chinese Academy of Medical Sciences & Peking Union Medical College Hospital, Beijing, China Peking Union Medical College Hospital, Beijing, China.

Background: Crescent glomerulonephritis (CreGN) is the most dangerous glomerulonephritis, but the specific mechanism remains unclear. Recent evidences suggested that gut microbiota was associated with kidney injury. This study aimed to observe the role of gut microbiota in CreGN.

Methods: A comparative analysis of the gut microbiota was performed in 10 CreGN patients and 10 matched healthy controls by 16S rDNA amplicon sequencing, and half of each group were also analyzed by metagenomics for further function analysis.

Results: The mean age of the 10 CreGN patients was 54.8 ± 17.1 years, with 70.0% were female. The median eGFR was 5.4 (interquartile range: 3.6-9.5) ml/min/1.73m². Compared to controls, CreGN patients showed a significant lower richness (683.2 ± 133.4 vs. 800.1 ± 73.5, p = 0.015) despite a similar level of Shannon index(diversity) 5.4 ± 0.6 vs. 5.6 ± 0.5, p =0.579). PCoA showed a different pattern of clustering in CreGN (p = 0.036, Fig. 1a). There were 66 differentially enriched bacteria genera, with a significant (q<0.05) lower relative abundance of Agathobacter, Prevotellaceae, Faecalibacterium, Dialister, Megamonas, and Alloprevotella genera, and a higher relative abundance of Faecalitalea, Anaerostipes, Paraprevotella, and Streptococcus genera(top 10) in CreGN. All the genera above showed significant correlations with renal injury indicators. For example, Agathobacter was significantly correlated with creatinine (r=-0.77, 24h urine protein(r= -0.86), and eGFR(r=0.73)(Fig. 1b). Besides, Agathobacter, Prevotellaceae, Faecalibacterium, and Dialister were also confirmed as significant biomarkers by LEfSe(Fig. 1c). Metagenomics showed 21 significant differentially enriched functional genera, with a decreased proportion of genes involved in digestive system (q<0.02) and an increased risk of infectious diseases: bacterial (q<0.01) in CreGN.

Conclusions: Gut microbiota in CreGN differed at compositional and functional levels compared with healthy controls, and correlated well with renal injuries.

Funding: Government Support - Non-U.S.

Figure 1. Altered gut microbiota in CreGN. a)PCoA. b)LEfSe. c)Spearman correlation. A1:CreGN, A2:Control.

POI1735

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 sCr 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 manifestation (p = 0.0006), increase of ANCA titer (p = 0.0022), 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 haematuria 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.

POI1736

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 (42.7%) 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 Batten,*1 Mark W. Robinson,*1 Arthur White,*2 Barbara Fazekas,*3 Cathal D. Walsh,*4 Jason Wysc,*5 Suzanne D'Arcy,*6 Antonia Baetnen,*7 Mark A. Little,*8 Nollaig M. Bourke,*9 Trinity Health Kidney Centre, Trinity Translational Medicine Institute, Trinity College Dublin, Ireland, Dublin, Ireland; *School of Computer Science and Statistics, Trinity College Dublin, Dublin, Ireland, Dublin, Ireland; *Department of Biology, Human Health Institute, Maynooth University, Kildare, Ireland, Maynooth, Ireland; *Department of Mathematics and Statistics, University of Limerick, Limerick, Ireland; *Centre for Medical Gerontology, School of Medicine, Trinity Translational Medicine Institute, Trinity College Dublin, Dublin, Ireland, Dublin, Ireland; *Regenerative Medicine Institute, School of Medicine, National University of Ireland Galway, Galway, Ireland, Galway, 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 type I IFN- and ISG regulated genes (ISGs) characterising type I interferonopathies: IFI27, IFI44L, IFIT1, ISG15, RASD2, SIGLEC1 and STAT1. Serum type I IFN regulated proteins (CXCL10, MCP-1 and CCL19) were assessed by ELISA.

**Results:** No significant difference in ISG gene expression was observed between control samples and AAV patients for any ISG analysed, irrespective of treatment received, age or sex. No significant differences in MCP-1, CCL19 and CXCL10 expression were observed between each cohort. CXCL10 levels were significantly lower in AAV patients than controls. No significant differences in CXCL10 expression were observed. 

**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**

**Angiostensin Converting Enzyme-Overexpressing Neutrophils Suppress Glomerular Injury in Crescentic Glomerulonephritis**

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**Background:** Angiostensin 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 (NTN) in C57Bl6/J WT, and NeuACE mice that overexpressing ACE in neutrophils. In addition, IC uptake and IC-mediated responses were investigated in both WT and NeuACE neutrophils by ex vivo experiments.

**Results:** Seven days after induction of NTN, NeuACE 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 NeuACE mice compared to WT mice. In ex vivo experiments, IC uptake was significantly promoted in NeuACE 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 NeuACE mice. Furthermore, we confirmed that anti-CR1/2 blocking antibody and anti-ACE blocking antibody abolished the IC uptake 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 NeuACE 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 - NICATS, Private Foundation Support

**PO1739**

**Recurrent of Anti-GBM Disease: An Epiphrenomenon?**

*Sri Vihavari Guntupalli,*1 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 individuals 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 hematuria. Her anti-GBM, by comparison, remained negative. She repeat renal biopsy was consistent with 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 anti-MPO 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 epiphrenomenon 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.

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

**Underline represents presenting author.**
Activation of the cGAS-STING Signaling Pathway Is Associated with Glomerular Diseases

Antonio M. Fontanella, Shamroop Kumar Mallala, Judith T. Molina David, Jin Ju Kim, George W. Burke, Sandra M. Merscher, Alessia Fornoni, Alla Mitrofanova. Katz Family Division of Nephrology and Hypertension University of Miami School of Medicine, Miami, FL.

Background: Podocytes express elements of the innate immune system which may play a role 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: Immunohyalized 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, glomerulot 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 is associated with increased podocyte injury and contributes to the glomerular diseases.

Funding: NIDDK Support

C5a Enhanced the Recruitment of CD16+ Monocytes by CX3CL1-CX3CR1 Axis in ANCA-Associated Vasculitis

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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 AAV. The phenotype of monocytes in Kidney tissues from MPO-AV patients were studied by immunohistochemistry and immunofluorescence. The chemotractant 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 CX3CR1 was highly expressed in CD16+ monocytes. C5a, IL-6, TNF-α, and chemokine CX3CL1 were significantly increased in serum of activated MPO-AVV patients. CD16+ monocytes were clearly seen in the glomeruli of MPO- AVV patients. Chemokine CX3CL1 was expressed in glomerular endothelial cells. Consistently, we demonstrated CX3CL1 expression of CD16+ monocyte via CX3CL1 produced by TNF-α- induced HRGEC in vitro.

Conclusions: We report an altered distribution of monocyte subsets in MPO-AVV patients; CD16+ monocytes may be recruited to kidney through CX3CL1-CX3CR1 axis to aggravate ANCA-associated GN.

Funding: NIDDK Support

Melanocortin 5 Receptor (MC5R) Deficiency Aggravates Glomerular Injury and Proteinuria in the Autologous Phase of Nephrotic Syndrome (NTS) Nephritis

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Background: The successful use of corticosteroid in steroid-resistant nephrotic glomerulopathies suggests a unique proteinuria-reducing activity of adrenocorticotrophic 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 tubulointerstitial 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 complements C3b-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 immune response.

Funding: NIDDK Support

Glomerular Complement Proteins in Thrombotic Microangiopathy

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Background: Thrombotic Microangiopathy (TMA) is a clinicopathological entity resulting from complement abnormalities (atypical hemolytic uremic 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 (C5/6/7/8A/9), and complement regulatory proteins (C1r/C1s, C4BP, C3B, Factor H). 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). Finally, 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.

Funding: NIDDK Support
PO1744

Complement 3 Glomerulonephritis in a Patient with Microscopic Polyangiitis

Hamad Siddiqui, Ayesha 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 H/O MPA, admitted for AKI and hematuria, found to have C3GN on renal biopsy.

Case Description: 69 yo M with H/O CKD stage 4 due to microscopic polyangiitis (baseline Cr 2.6 - 2.9), spinal stenosis, HTN and BPH, presenting with complain of painless hematuria, 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 after discontinuation.

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 vasculitides, is typically associated with a pauci-immune GN. We presented a case with signs, symptoms, and clinical features of systemic sclerosis sine scleroderma. Patient was commenced on hypertension and severe accelerated acute kidney injury (AKI) with rapidly declining GFR. TMA was attributed to immunotherapy and atypical HUS genetic testing panel returned negative. Pt was admitted with preliminary diagnosis of AKI on CKD 2/2 MPA flare and C4 normal. AH50 was low (36.1%). Hepatitis panel, C-ANCA, PR-3 and anti-GBM were negative.

Patient was admitted for hypertension urgency and acute kidney injury following 2 cycles of Bintrafusp-alpha 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 Bintrafusp-alpha therapy targeting TGF-beta and PD-L1. Exam was remarkable for BP 180/100 mmHg, pulse 62/min, 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 (112-222 U/L), undetectable haptoglobin, serum creatinine 2.8 mg/dL, microscopic hematuria and protein creatinine ratio 2.79g/g. ADAMTS13 activity 72% (undetectable haptoglobin, serum creatinine 2.8 mg/dL, microscopic hematuria and protein creatinine ratio 2.79g/g. ADAMTS13 activity 72% (undetectable haptoglobin, serum creatinine 2.8 mg/dL, microscopic hematuria and protein creatinine ratio 2.79g/g. ADAMTS13 activity 72% (undetectable haptoglobin, serum creatinine 2.8 mg/dL, microscopic hematuria and protein creatinine ratio 2.79g/g. ADAMTS13 activity 72%

Discussion: Here we report a case of newly diagnosed SRC with TMA that clinically responded to TGF-beta blockade and ACEI. Kidney function rapidly improved on treatment from a peak creatinine of 9.5mg/dL to 2.1mg/dL over 4 weeks without requiring dialysis, combining of resolution to all TMA features. Eculizumab was stopped after 3 months, without sign of relapse 2 months after discontinuation.

Conclusion: Eculizumab use in scleroderma renal crisis with thrombotic microangiopathy

Claire Avyllach, Aula Jaberi, Laurence H. Beck, Jean M. Francis. Boston Medical Center, Boston Medical Center, Boston, MA.

Introduction: Scleroderma renal crisis is a life-threatening condition with increased mortality and morbidity leading to end-stage renal disease in about 25% of cases. Here we report a case of newly diagnosed scleroderma renal crisis with thrombotic microangiopathy (TMA) successfully treated with eculizumab.

Case Description: A 44-year-old African American female with no significant past medical history, presented with acute pulmonary edema in the setting of malignant 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 with evidence of significant intravascular VEGF expression. 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 (cSGS).

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: This 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.

PO1745

Eculizumab Use in Scleroderma Renal Crisis with Thrombotic Microangiopathy

PO1746

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 with evidence of significant intravascular VEGF expression. 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 (cSGS).

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 cSGS observed with Intravitreal VEGF blockade

<table>
<thead>
<tr>
<th>Reference</th>
<th>N</th>
<th>Age</th>
<th>Gender</th>
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<tr>
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<td>Tolandi et al.</td>
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<td>Zaroff et al.</td>
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All patients presented with proteinuria, ACEI and PDG-L1. Three patients had cSGS and possible TMA. Two patients developed cSGS, focal and segmental glomerulosclerosis, and two developed Chronic TMA.

Conclusion: Here 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.

PO1747

Bintrafusp-alpha-Associated Thrombotic Microangiopathy

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Introduction: Immune check point inhibitors (ICPIs) have been reported to cause acute kidney injury. Acute tubulo-interstitial 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 Bintrafusp-alpha, 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 Bintrafusp-alpha therapy targeting TGF-beta and PD-L1.

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 dose- and time-dependent toxicity. ICPI monotherapy has a nephrotoxicity incidence of 2.5%. In the largest retrospective study of 1016 patients treated with ICPI therapy, 17% developed AKI, 2% experienced stage 3 AKI and 0.4% required dialysis. TMA was documented in 1 patient receiving Ipilimumab and was HD-dependent. The National Comprehensive Cancer Network guidelines recommend empirically starting AKI in some
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 pathology of AKI post-ICPI 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
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Introduction: Thrombotic microangiopathy (TMA) is a collection of syndromes, with the most frequent types encountered being hereditary uremic 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 glomeruli. C5b9 levels were elevated. 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 treating this complement pathway.

PO1749
An Unusual Case of Complement-Mediated Thrombotic Microangiopathy
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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 C1r 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 daily 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 1042IU/L and haptoglobin granular, basement membrane, electron dense deposits within glomerular and tubular Basement menbrane. 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 treating this complement pathway.

PO1750
A Case of “Immunofluorescence-Negative” Lambda Light Chain Deposition Disease
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Introduction: Light chain deposition disease (LCDD) is the most common form of monoclonal immunoglobulin deposition disease (MIDD). Pathologically, monomer LCDD develop nodular expansion of mesangial regions and deposits of monoclonal light chain (LC) positive, electron dense deposits within glomerular and tubular Basement membrane. The majority of monoclonal LC in LCDD are of kappa type. (1,2) We report a case of lambda LCDD with negative immunofluorescence microscopy (IF), but with characteristic granular, basement membrane, electron dense deposits on ultrastructural examination.

Case Description: A 42-year-old Caucasian female with no PMHx, no NSAID, Chinese herbal or PPI use presented with fatigue, malaise and dark urine for 2 weeks. She had a normal BP and no edema. Labs: Scr was 2.4 mg/dL with unknown baseline levels, BUN 26 mg/dL, Hb level 9.0 gm/dL with MCV of 90 fl, with a negative autoimmune panel. Urine microscopy showed 10 RBC/HFP and 24-hour protein excretion was 460 mg. SPEP and immunofixation detected a Lambda LC monoclonal paraprotein. Serum free Lambda LC level was 1044 mg/dL with free kappa/lambda LC levels ratio of 0.03. A kidney biopsy revealed nodular expansion of glomerular mesangial regions, modest arteriectasis of JET, RBCs and red cell casts were present in tubules. Direct IF microscopy with FITC-conj. anti-human IgG, IgM and IgA heavy chains and Kappa/lambda light chains was negative with testing performed in duplicate. Ultrastructural examination revealed powdery, granular electron dense deposits diffusely along tubular and glomerular basement membranes with focal areas of podocyte process effacement. Bone marrow biopsy revealed cell plasma neoplasm.

Discussion: Our patient underwent autologous SCT after pretreatment with Melphalan. Renal function has been stable at stage III CKD. She never developed HTN or significant proteinuria, which usually are some of the presenting features of LCDD. She had lambda LC paraproteinemia, which is a more common feature of heavy chain deposition disease than LCDD. Direct IF microscopy was negative, which could be due to abnormal LCs being truncated in the tissue deposits, and commercially available, FITC-conj. anti-human Abs might not have been able to detect them. (4) This case emphasizes the fact that negative staining by routine direct IF microscopy methods does not exclude the presence of MIDD.
PO1752
A Case of Granulomatosis with Polyangiitis Complicated by Renal Mass-Like Lesion
Daichi Kaiko, Koichi Sato, Hisayuki Ogura, Taro Miyagawa, Tadasu Toyama, Shinji Kitajima, Akinori Harai, Yasunori Iwata, Norihiko Sakai, Miho 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 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 fibrinoid necrosis were observed in the glomerulus. In the interstitium, granulomas with multinucleated giant cells and infiltration of IgG4-positive (IgG4+) plasma cells were observed. In addition, cell infiltration into the arteriole 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 turbinate 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 anti-PR3 was 4.4U/ml. A year later, she presented with PR3-ANCA GPA that presented with isolated glomerular abnormalities and acute TIN with interstitial non-necrotising granuloma and multinucleated giant cells. Ziehl-Neelsen stain was negative. Immunofluorescence, electron microscopy were significant for granular mesangial deposits. The patient was empirically pulsed with intravenous steroids for three days. She 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 μmol/L (normal <3) 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 pulsed with 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
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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 causation of RPGN includes auto-antibody mediated crescent staining (ASCA) 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 cough, acute renal failure over the past 2 months. Physical examination. Here 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.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
overlapping of the standard regimen is safe and effective in older age group. If the patient remained refractory cases while continuing standard therapy until the 2nd dose of rituximab, with oliguria, low creatinine and anti-GBM antibody levels, negative ANCA, involvement of upper limb occurred on day 75, antibody levels were undetectable and on day 147 she remained dialysis free.

Discussion: It was 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 both ITP and RPGN. 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 Shahily, 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 Africa. Laboratory evaluation showed serum creatinine 1.3 mg/dl with hematuria and proteinuria (0.6 g/dl). ANA, ANCA, RF, Hepatitis B/C, HIV, RPR, and streptococcal 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 nonoliguric, but developed edema requiring intermittent diuresis. On day 15, plasmapheresis was reduced to every 48 hours. Anti-GBM antibody failed to decline, therefore the report 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 nonoliguria, 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 in refractory cases while continuing standard therapy until the 2nd dose of rituximab, with a 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.

PO1757
Rare Case of Myeloperoxidase-ANCA-Positive Polyarteritis Nodosa
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Introduction: Polyarteritis Nodosa (PAN) is systemic necrotizing vasculitis involving medium-size vessels. PAN is typically not associated with positive antineutrophil cytoplasmic antibodies (ANCA) titer. Here, we report a patient who presented with abdominal pain, hypertension, and bloody diarrhea who tested positive for anti-GBM disease. Treatment with Eculizumab was started, but diffuse alveolar hemorrhage (DAH) developed 19 days after admission and thus plasmapheresis and cyclophosphamide were initiated without delay.

Case Description: 75-year-old male with a history of tobacco use was admitted for oliguric acute kidney failure requiring initiation of dialysis. Kidney biopsy showed linear IgG4-related kidney disease (IgG4-RKD). Neurologic involvement is less common and known to manifest as hypophysitis and pachymeningitis. Neurologic involvement is less common and known to manifest as hypophysitis and pachymeningitis.

Discussion: Anti-GBM disease and complement-mediated TMA are both exceedingly rare clinical entities. While hemolysis has been reported in the literature, this is the first report of complement-mediated TMA driving hemolysis in the setting of anti-GBM. Dysregulated activation of the alternative pathway in complement-mediated TMA and literature reports supporting a role for both classical and alternative pathways in anti-GBM disease suggests a possible link between the two diseases and a previously unrecognized role for complement dysregulation in cases of hemolysis observed in the setting of anti-GBM.

PO1758
Complement-Mediated Thrombotic Microangiopathy in a Patient with Anti-GBM Disease: A Case Report
Yuliya Sharakova, Mohamed Hassanaein, Rhayd Matidz, Leal C. Herlitz, John F. O’Toole. Cleveland Clinic, Cleveland, OH.

Introduction: Anti-glomerular basement membrane (anti-GBM) disease is a rapidly progressive glomerulonephritis, caused by pathogenic antibodies directed against the gC1qC epitope of type IV collagen, and accompanied by pulmonary hemorrhage in about 50% of cases. Here we present a case of anti-GBM disease in combination with hemolysis, a rare and poorly understood association.

Case Description: A 22 y/o male with a history of tobacco use was admitted for oliguric acute kidney failure requiring initiation of dialysis. Kidney biopsy showed linear GBM staining for IgG, α, and β, suggesting the diagnosis of anti-GBM nephritis with crescentic involvement of all glomeruli and positive serum anti-GBM antibody. High dose corticosteroids were given but additional immunosuppression was held due to low probability of benefit in the setting of severe renal limited disease. One week after biopsy, the patient developed fever, and his Hb decreased to 6 g/dl due to microangiopathic hemolytic anemia with low haptoglobin, elevated LDH, mild platelet decline, and negative Coombs test. Additional workup was negative for malignancy, coagulopathy, deficiency, malignant hypertension, or infection including shiga-toxin, showed normal ADAMTS13 activity, C3, C4, factor H, I, B, and no CFH autoantibody, but an elevated sc5b9 level demonstrating terminal complement activity. Repeat kidney biopsy revealed an acute thrombotic microangiopathy (TMA) along with previously diagnosed anti-GBM disease. Treatment with Eculizumab was started, but diffuse alveolar hemorrhage (DAH) developed 19 days after admission and thus plasmapheresis and cyclophosphamide were initiated with reduction of anti-GBM titers and hemolysis and resolution of DAH.

Discussion: Anti-GBM disease and complement-mediated TMA are both exceedingly rare clinical entities. While hemolysis has been reported in the literature, this is the first report of complement-mediated TMA driving hemolysis in the setting of anti-GBM. Dysregulated activation of the alternative pathway in complement-mediated TMA and literature reports supporting a role for both classical and alternative pathways in anti-GBM disease suggests a possible link between the two diseases and a previously unrecognized role for complement dysregulation in cases of hemolysis observed in the setting of anti-GBM.

PO1759
IgG4-Related Kidney Disease Associated with an Unusual Vasculitic Peripheral Neuropathy
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Introduction: IgG4-related disease is a systemic autoimmune fibro-inflammatory disorder showing lymphoplasmacytic infiltrates with predominance of IgG4+ plasma cells and variable amounts of storiform fibrosis in the affected tissues. When kidneys are the only organs involved it is called IgG4-related kidney disease (IgG4-RKD). Neurologic involvement is less common and known to manifest as hypophysitis and pachymeningitis.
Peripheral neuropathy is rare. Our case illustrates an unusual presentation of IgG4-RKD with vasculitic 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 plantar flexion and loss of pinprick sensation in all toes. 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 storiform fibrosis and plasma 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), ANA >1:1280, 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 perineural 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
Prasanti Koter, Eoin F. McKinney, Paul A. Lyons, Kenneth G. Smith, Smith Laboratory of University of Cambridge, Cambridge, United Kingdom.

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 transcriptomes and serum proteomes of patients with active AAV.

Methods: The transcriptional profiles and protein expression of patients with AAV (31 PR3-ANCA, 15 MPO-ANCA, 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 microarray. Transcriptional profiles were available on peripheral blood mononuclear cells (PBMCs), neutrophils, monocyes and CD4 and CD8 T cells. Protein expression was assessed on the SOMAscan 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-ANCA 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-ANAA 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-IFN-α antibodies.

PO1761
IL-23-Induced Remission from Lupus Gleromerulonephritis Involves Regulation of Mitochondrial Function and Canonical WNT Signaling
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Background: We recently showed the efficacy of a hybrid cytokine IL-23 to protect mice from lupus glomerulonephritis (GN). We have 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-23.

Methods: We made use of the recombinant hybrid cytokine (IL-23) bearing activities of IL-2 and IL-33 and tested its efficacy to prevent glomerular nephritis in the adenovirus (Ad)IFNa Acelerated lupus GN NZM2258 model. Kidney lysates were screened for transcripts of mitochondrial and Wnt inhibitor genes by real time PCR and Western blotting. (mitochondrial CRP, p53, and p21) and (mitochondrial CRP, p53, and p21). Extracts from IL-23 treated glomerular endothelial cells (MGECS) was investigated by flow cytometry and Seahorse assay. Metabolic fitness of Tregs with and without IL-23 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 (Pgc1a, Nrf1, Nrf2, Tkctm, Drp1, and Mfn1) confirmed that IL-23 treated kidneys displayed an elevated status. In vitro, changes in Pge1 and its downstream target Nfκb were recapitulated in treated MGECS cells. IL-23 treated Tregs (ex vivo and in vivo) and MGECSs (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 LRPE, Dvl3 and Wnt mediators - Axin1, GSK3a and GSK3b were significantly reduced in IL-23 protected kidney. Levels of Axin2 was significantly upregulated with IL-23 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-23 treatment. IL-23 treated kidneys exhibit better mitochondrial dynamics and function. We show in vitro, in vivo and ex vivo evidence of IL-23 treatment leading to betterment of mitochondrial function and metabolic fitness. Canonical Wnt signaling was attenuated. The data presented confirms the therapeutic efficacy of IL-23 as a promising therapeutic agent for lupus nephritis and kidney injury.

Funding: Other NIH Support - National Institute of Diabetes and Kidney Diseases
PO1763

A Prospective Randomized Study on Preemptive 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.

Figure1. Serial changes in (A) anti-dsDNA and (B) C3 levels in lupus nephritis with asymptomatic serological reactivation who have or have not received pre-emptive immunosuppressive treatments.

PO1764

Kidney Thrombotic Microangiopathy Associated to Lupus Nephritis Is Mediated by the Activation of the Alternative Complement Pathway
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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, C5bC9, 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 C5bC9 along with decreased plasma C3, C4, C4a, and factor H. Urine C5a, Ba, and C5bC9 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 C5bC9 decreased. In two patients with repeated LN-TMA episodes, factor H and urine C5a levels decreased, while urine Ba and C5bC9 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.

Figure. 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/Pr 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 Fas+R 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-$
\beta$
1/p38MAPK/NF-$\kappa$B 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.
Renal Activity Index for Lupus Nephritis Distinguishes Active Renal Disease Among Lupus Patients

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Background: Conventional tools to identify active nephritis in SLE (LN) fail to supersede invasive kidney biopsy. The renal activity index in lupus (RAI) was developed using 6 urinary biomarkers to reflect disease activity (Brunner, et al. 2016). Our objective was to test RAI for identifying active LN in childhood-onset SLE.

Methods: Urine samples obtained from cross-sectional sampling of 2 cSLE cohorts, classified as active LN, inactive LN or non-LN SLE. RAI scores were calculated from ELISA or nephelometry data for six urine markers (NGAL-1, ceruloplasmin, MCP-1, adiponectin, hemepoxin, 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. RAI scores of inactive LN and non-LN group largely overlapped, so they were combined (Group 2) and compared to active LN (Group 1, Table). Group 1 had higher RAI score (0.7 vs. -1.1). After adjusting for age and extra-renal SLEDAI score, RAI 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 RAI cut-off score of 0.35 produced an AUC=0.9 (sensitivity 86%, specificity 84%) for active LN. Adjustment for urinary protein and creatinine did not influence results.

Conclusions: The RAI 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 RAI scores among Group 1 (active LN) and Group 2 (inactive LN + non-LN SLE) patients

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Age (y)</td>
<td>20 (17)</td>
</tr>
<tr>
<td>Male</td>
<td>22 (62%)</td>
</tr>
<tr>
<td>Active LN</td>
<td>37 (100%)</td>
</tr>
<tr>
<td>SLEDAI</td>
<td>10 (6-12)</td>
</tr>
</tbody>
</table>

1 Includes only active (N=24) and inactive LN (N=4) patients with sampling performed within 30 days of kidney biopsy

A Novel Inflammatory Dendritic Cell in Lupus Nephritis

Latha Priyab Jacket,1 Ana Malvar,2 John P. Shapiro,3 James M. Turman,1 Hennorda, 1 Bruno J. Lococo,1 Sethu M. Madavan,1 Anjali A. Satsoskar,1 Daniel J. Birmingham,1 Wael Jarjour,1 Brad H. Rovin,3 Samir V. Parikh,3 OSU Nephrology,1 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 laser capture microdissection, and 580 immune transcripts were analyzed using NanoString human immunology panel. Guided by transcriptomic analysis, multi-color, high-resolution confocal laser capture microdissection (LCM), and 580 immune transcripts were analyzed using NanoString human immunology panel.

Results: Transcriptomic analysis identified Fe 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 per-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+CD-SIGN+SIGN+C4dII-H,CD64+CD14+, CD16+CD206,CD68,CD123,CD11b+. This signature aligns with a dendritic cell (DC) phenotype but distinct from plasmacytoid dendritic cell. It is most commonly associated with an inflammatory dendritic cell (iDC) phenotype. Importantly, confocal IF identified CD3+ T cells present in close proximity to PG and iDC.

Conclusions: In this study, we identified a novel population of iDC not previously described in LN. During LN flare, iDC are present in abundance in the PG region. Their presence next to T cells suggests iDC dictate the nature of the T cell response during LN flare. Targeting iDC or their associated T cell phenotype may attenuate renal inflammation and improve outcomes in LN.

Funding: Other NIH Support - NAAMS

Burden of Illness of Lupus Nephritis in Patients with Systemic Lupus Erythematosus

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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 costs 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 ≥2 renal diagnosis codes during 08/01/2017–07/31/2018 and ≥1 patient or ≥2 outpatient SLE diagnosis codes >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 of age at index, and continuous medical and pharmacy coverage in the 12 months pre and post index. HRU in the 12 months post index captured 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 (53.93 [55.54]) than the control cohort [18.27 [21.61]], ED visits (2.87 [7.91] vs 0.66 [2.31]), and hospitalizations 0.86 [1.48] vs 0.12 [0.51]) versus the control cohort, 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 costs were largely driven by mean (SD) medical expenses for the LN cohort versus the control cohort ($40,648 [$78,134] 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

A Clínico-Pathological Associations with Serum Thrombomodulin Level in Patients with Lupus Nephritis

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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 pathology. Thrombomodulin (TM), a component of endothelial glycocalyx, is shed into the circulation in endothelial cell injury. We investigated clinicopathological 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-LN 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<0.01, 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 C3 (r=0.86, for all). Patients with blood samples collected before disease flare, and 6 showed increased TM level (3.6±5.2 vs 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 titre and proteinuria (r=0.86, for all). Patients with active severe flare had the highest TM level, compared with patients with mild/moderate flare (r=0.54, for all). In a multivariable model, TM level was significantly associated with eGFR (P<0.01), proteinuria (P<0.01) and anti-dsDNA (P<0.01).

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.

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

Underline represents presenting author.
PO1770
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(lpr)) 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(lpr)) 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 Fxyδ2, 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 ouabain 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(lpr) B cells in high salt. In vivo treatment of MRL(lpr) mice with ouabain depleted renal-infiltrating B cells, but not T cells. MRL(lpr) mice lacking the gamma subunit of Na-K-ATPase appear to phenocopy the ouabain-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 AI42145-01, R37 AR40072-28

PO1771
TNIP1/ABIN1 Mutation Contributes to Lupus Nephritis via Chemokine IP-10 Induction
David W. Fowell, Makaya 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-kB. 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-kB 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 rs4958881) 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 rs4958881 when compared to LN patients without the TNIP1 variant and healthy controls. The rs4958881 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

PO1772
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. Frangou,1-3 Panayiotis Garantziotis,2 Maria Grigoriou,2 Angelos Banos,2 George Bertisias,2 Anastasia Filia,2 Dimitrios Bounous,1 Genoko Koskomeio Lemosou, Lemosou, Cyprus; 3Iridyma IatratologiKwn Ereunen tes Akademias Athenon, Athens, Greece; 1Ethniko i Kapodistriatko Panepistemio Athenon, Athens, Greece; 2PaneHopistemo Kretes Iatrike Schol, Heraklion, Greece.

Background: Despite advances, morbidity and mortality in systemic lupus erythematosus (SLE) and lupus nephritis (LN) remain increased. Most clinical trials on novel 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 L1000CD58 engine was used to identify drugs/small molecules predicted to reverse DEGs. Human orthologies 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 uncovers 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 gene signatures, pathways and tissue-specific targets. The cross-species transcriptome analysis predicts LN in human SLE and guides therapy in a tissue-specific manner.

Funding: Other NIH Support - R21 AI42145-01, R37 AR40072-28

PO1773
An Inducible Model of Early Lupus Nephritis

Background: Lupus nephritis (LN) is characterised by polyreactive antibodies targeting ‘planted’ glomerular autoantigens. But how these deposits recruit inflammatory mediators and the roles of resident and recruited cells is unclear. Distinguishing damaging pathways from protective tissue responses is a major challenge. With disease progression, non-specific signals of fibrosis become dominant and human tissue comparisons are confounded by genetic and environmental heterogeneity. A way to separate these early and late pathological events is to use mouse models of nephritis. Topical treatment with toll like receptor-7 (TLR7) agonist 4-methylumbelliferyl (MUFQ) for 8 weeks has been shown to induce glomerulonephritis (GN), significant weight loss and mortality. Using detailed renal and immune phenotyping we explored the suitability of this model to study the very early, active stages of LN.

Methods: 6-week female BALB/c mice were treated 3 times weekly for 5 weeks with topical IMQ or Vaseline control (n=6/group). Immune profiling of spleen, bone marrow and mesenteric lymph node was by flow cytometry. Kidneys were fixed and processed for Periodic Acid Schiff, immunofluorescence and TEM. Serum was assayed for creatinine, urea and albumin.

Results: Treated mice had increased numbers of activated splenic CD4 and CD8 T cells (CD40/CD25<sup>+</sup>, P<0.001), Tregs (CD4<sup>+</sup>CD25<sup>+</sup>FOXP3<sup>+</sup>, P<0.001) and activated B cells (B220<sup>+</sup>CD19<sup>+</sup>CD68<sup>+</sup>CD69<sup>+</sup>, P<0.001). IMQ did not result in weight loss, mortality or significant changes in serum creatinine or urinary protein creatinine ratio but kidney histology showed mild mesangial hypercellularity with strong glomerular positivity for IgG, C1q and C3. TEM showed early basement membrane duplication, focal subendothelial and mesangial deposits and mild podocyte effacement.

Conclusions: This study characterises the IMQ model of LN revealing CD4<sup>+</sup> T cell activation and TEM evidence of immune deposits reminiscent of human class II lupus. Treatment for 5 weeks is well tolerated without overt renal failure and creates a model for studying the early pathways involved in immune complex GN and associated therapeutic targets.
PO1774

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 also has mitogenic potentials through the functional Fe 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-CD3e (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 NZBW/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 examined.

Results: As compared with 2C11N, 2C11S reduced TCR expression on T cells in vivo for longer 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, 2C11N: 2.1±3.0, 2C11N; 2.0±1.8, 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 IFNy 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.

PO1775

Suboptimal Serological and Clinical Remission on Supportive Therapy in Phospholipase A2 Receptor Membranous Nephropathy
Jennifer A. Pham, Juan Carlos Q. Velez. 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 evaluated across a variety of glomerular diseases in a manner similar to RAAS blockade. Immunologic and metabolic changes that have the potential to be leveraged therapeutically for longer 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, 2C11N: 2.1±3.0, 2C11N; 2.0±1.8, 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 IFNy 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.

PO1776

Glomerular Proteomics Reveal Shared Pathways Across Several Disease
Salem Almaalou,1 Isabelle Ayoub,1 John P. Shapiro,1 Sethu M. Madhavan,2 Anjali A. Satoskar,1 Michael Merchant,1 Jon B. Klein,1 Brad H. Rovin,1 Sarah V. Parikh.1 The Ohio State University, Columbus, OH; 2University of Louisville, Louisville, KY.

Background: Glomerular diseases are caused by a variety of immunologic and metabolic disturbances. While there is considerable disease heterogeneity, morphologic patterns of injury are limited and clinical phenotypes are similar across diseases. This suggests that mechanisms of inflammation and the glomerular response to injury is similar across disease states. Characterizing these mechanisms may provide insights into the common pathways of glomerular injury and lead to new insights in pathogenesis and treatment. As a first step, we used an agnostic proteomics approach to identify common regulated pathways across a variety of glomerular disorders.

Methods: Kidney biopsies from 36 patients across several glomerular diseases and 21 controls (transplant donor biopsies) were used. Glomeruli were isolated using laser-capture microdissection, processed, and submitted for LC-MS/MS. Peptides were analyzed for spectral count quantitation. Spectral counts of each disease were compared to control samples that were analyzed in the same batch. Only peptides with a spectral count coefficient of variation <25% were included in expression ratio calculations. Disease- to-control expression ratios >2 or <0.5 were used for pathway analysis using Reactome. The top 10 pathways were grouped into domains and are depicted in figure 1.

Results: Pathways involved in complement regulation and activation, fibrin clot formation, and platelet aggregation were downregulated in most disease categories. Assessment of GC toxicity has not been assessed in this cohort. This study looked at the GC toxicity of patients in the year following treatment completion1,2

Conclusions: Proteomic analysis of a heterogenous population of glomerular diseases identified several shared dysregulated pathways that may reflect common final pathways associated with glomerular injury. These pathways reflect important immunologic and metabolic changes that have the potential to be leveraged therapeutically across a variety of glomerular diseases in a manner similar to RAAS blockade.

PO1777

Glucocorticoid Toxicity in the Ponticelli Regimen
Abby J. Huckle, Ajay P. Dhargule. Lancashire Teaching Hospitals NHS Foundation Trust, Preston, United Kingdom.

Background: Idiopathic membranous nephropathy (IMN) is an immune complex mediated renal disease and the leading cause nephrotic syndrome in non-diabetic adults. Long term relapse data for modern drugs like Calcineurin inhibitors and B-cell therapy are lacking. Modified Ponticelli regimen offers 70% relapse free survival for 10 years however toxicity of cyclophosphamide and glucocorticoids(GC) remains major concern. Assessment of GC toxicity has not been assessed in this cohort. This study looked at the GC toxicity of patients in the year following treatment completion1,2

Methods: The glucocorticoid toxicity index (GTC) was calculated for 15 IMN patients treated with modified Ponticelli regimen at time of treatment completion(0) and then 6 and 12 months post treatment completion, and compared to pre-treatment baseline. The total dose of steroids received during treatment was also calculated.

Results: Mean cumulative prednisolone dose was 11.05g. The results at 0.6 and 12 months post completion of the Ponticelli regimen for individual patients is shown on the report. A completion 12/15 patients demonstrated GC toxicity. 7 at 6 months improving to 6/15 at 12 months. Effect on blood pressure (BP) was the most common indicator of GC toxicity at 12 months: 4/15 patients. 6 patients were in negative points at 12 months, however toxicity of cyclophosphamide and glucocorticoids(GC) remains major concern. Assessment of GC toxicity has not been assessed in this cohort. This study looked at the GC toxicity of patients in the year following treatment completion1,2

Conclusions: Overall apart from BP, only 2/15 patients had evidence of damage due to GC exposure at 12 months in spite of very high cumulative GC doses. This lower level incidence of GC toxicity could be due to less impact on hypoalalbuminemia due to unusual dosing regime of alternating months. Limitations: Relatively small cohort and in 1/8 (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=0.86, 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.
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 dog-/- rats. There was no effect on glomerular Crry and CD59 protein expression. There were no changes in serum urea and creatinine levels and urine albumin/creatinine ratio. C3 deposition was confirmed 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 DRB1*1501 and DRB1*0301 protein was assayed by flow cytometry. Proliferation of CD4+ T cells from patients with anti-PLA2R positive pMN was analyzed after peptide stimulation using CFSE dilution assay. Cytokines produced by activated PBMC were measured by cytometric beads array.

Results: We found 17 peptides that bound to both DRB1*1501 and DRB1*0301 molecules with high capacity. Among them, 11 peptides induced significant proliferations of CD4+ T cells from patients with anti-PLA2R positive pMN: PLA2R<sub>36-52</sub>(CysR3), PLA2R<sub>60-76</sub>(CysR10), PLA2R<sub>101-117</sub>(CysR12), PLA2R<sub>158-174</sub>(FnII-3), PLA2R<sub>285-301</sub>(CTLD3-9), PLA2R<sub>362-378</sub>(CTLD3-10), PLA2R<sub>413-429</sub>(CTLD3-11), PLA2R<sub>464-480</sub>(CTLD5-2-1), PLA2R<sub>505-521</sub>(CTLD7-1) and PLA2R<sub>556-572</sub>(CTLD7-2).

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-C5b5 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 ON 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 nephritic, 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.

PO1781
Red Herrings: Delayed Immune Checkpoint Inhibitor-Associated Interstitial 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 patient was diagnosed with ICI-associated interstitial nephritis, likely provoked by PPI. She developed secondary adrenal insufficiency, which was considered an immune-related adverse event (irAE) with Nivolumab after the first dose, and oral hydrocortisone was initiated. In March of -1 year, mediastinal and hilar lymphadenopathy and skin pruritus, which were considered to be immune-related adverse events, were observed again, so Nivolumab was once discontinued, but it was resumed in April after improvement of the skin symptoms. However, proteinuria with hypoalbuminemia was appeared in June, Nivolumab was stopped again and the patient was finally consulted to our department in July. His serum albumin was 2.8 g/dL and urine protein was 5.9 g/gCr. Since the right kidney was atrophic, the open kidney biopsy was carried out in September. Light microscopy did not reveal thickening of the basement membrane, spike formation or bubbling appearance, however, immunofluorescence staining showed granular staining of IgG, C3, C1q and all of IgG subclasses although PLA2R staining was negative. Electron microscopy revealed electron-dense deposits under the epithelium, suggesting secondary membranous nephropathy. Though the urine protein tended to decrease after discontinuation of Nivolumab, Prednisolone 40 mg/day was started and resulted in the complete remission in the 19th hospital day.

Discussion: There are several reports of interstitial nephritis by Nivolumab, however, the report of nephritic syndrome is rare. Particularly, no case of membranous nephropathy by Nivolumab has ever been reported and this case is considered to be valuable.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
mycophenolate mofetil, and prednisone as a maintenance immunosuppressive regimen for both recipients. A kidney biopsy was performed two weeks after in recipient A due to delayed graft function. It was compatible with MN with both PLA2R and IgG4 subepithelial deposits. The donor’s kidneys biopsies were reexamined, revealing MN, with high intensity for PLA2R and IgG4 in IHC. Recipient B 3rd-month protocol allograft biopsy revealed histology compatible with MN, without the presence of PLA2R and IgG4 in IHC. At one year follow-up, both recipients maintain graft function and the protocol biopsies showed a negativization of IgG4 but the persistence of PLA2R in IHC, this positivity was attributed to the variability inherent to the technique.

Discussion: Given the reversal of PMN changes in the grafts, it is probably safe to transplant a patient from an asymptomatic donor with PMN as long as he maintains unaltered renal function. Observation of IgG4 immune complexes is more accurate to assess histological remission.

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 membranous glomerulonephropathy (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 pruritic bullae, bilateral lower extremity (LE) and scrotal edema. He was previously treated for LE edema. Renal indices confirmed nephrotic 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 nephrotic range proteinuria. HIV, hepatitis panel, ANA, SPEP and UPEP were negative. Malignancy was ruled out. Diagnosis of BP was finally confirmed via positive indirect immunofluorescence and ELISA testing. Treatment was limited to ethacrynic acid since ACEis/ARBs and furosemide are known to induce BP. Initiation of prednisone and rituximab resulted in cessation of new bullae and decrease in proteinuria.

Discussion: Both BP and MN are immune complex diseases involving two different basement membranes, so their occurrence together is not coincidence. Although our patient’s kidney biopsy had negative immunostaining, the electron microscopy identified only subepithelial deposits, characteristic of primary, not secondary MN. This coincides with few cases in literature identifying BP occurring exclusively with primary MN. Our patient developed BP manifestations prior to MN and received intermittent prednisone without formal diagnosis of BP. Perhaps corticosteroids suppressed his MN symptoms leading to delay in diagnosis. Improper treatment of MN with known BP inducing medications led to persistent bullae formation. As the severity of skin lesions decreased, so did the proteinuria, suggesting that progression of bullae may be a sign of worsening MN. This case highlights the importance of thorough history taking, detail review of medications and appropriate patient follow up.

PO1785

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 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. Infections and rheumatologic work up was negative. Lung biopsy showed hemosiderosis reaching diagnosis of Lane-Hamilton Syndrome (LHS) (idiopathic pulmonary hemosiderosis (IPH), CD, 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 I 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 duodenal 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, ant-CrKD stage 3 initially presented to our clinic for evaluation of her renal function. Patient had increasing Cr up to 1.9 mg/dL over the course of 2 years. Her work up demonstrated modest albuminuria with several UACR results between 37.9 and 196.7 mg/g; UA demonstrated unremarkable chemistry and only 2 RBC and 1 WBC /plf. Serology showed positive ANCA 1:640 homogenous; dsDNA resulted negative; anti-histone Ab returned positive at 3.2 units (normal <1) as did her anti-MPO of 85 units (normal <20). Of note, C3 and C4 returned normal. Patient remained asymptomatic but 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, thrombospondin, and Hep 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 work-up, re-exposure was not attempted. This patient never demonstrated any clinical or lab findings of MN disease: no severe proteinuria, no sequalae 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.
An Atypical Presentation of Lupus Nephritis

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Introduction: Lupus nephritis in the absence of ANA and dsDNA, and normal C4 levels is a rare, atypical presentation. To arrive at the diagnosis requires EM examination of renal biopsies and is responsive to immunosuppressive therapy. We present a report of such a case.

Case Description: A 49-year-old female was referred for asymptomatic hematuria 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. HematURIA 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). HematURIA 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 as 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 hematURIA 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.

Lupus Nephritis Classification Should Consider Lupus Arteritis in the Activity Score

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Introduction: 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 36-year-old woman with known SLE with Class II LN, as well as vasculitis, resulting in multiple digital amputations presented with eight days of abdominal pain, vomiting, fever, and tea-colored urine. Labs showed creatinine of 1.4 mg/dL, microscopic hematuria, urine protein/creatinine of 5 g/g, low complements, positive anti-double-stranded DNA of 14, an elevated antinuclear antibody of 1:320, 1.4 mg/dL, microscopic hematuria, urine protein/creatinine of 5 g/g, low complements, positive anti-double-stranded DNA of 14, an elevated antinuclear antibody of 1:320, elevated Myeloperoxidase (MPO)-Antineutrophil Cytoplasmic Antibody (ANCA) of 59. She received induction therapy with intravenous (IV) methylprednisolone 1 g daily x3, followed by prednisone 60 mg daily and mycophenolate mofetil (MMF) 500 mg twice daily. A repeat kidney biopsy was performed, and 12 glomeruli showed only mesangial proliferation. She was classified as International Society of Nephrology and the Renal Pathology Society (ISN/RPS) class IIIA LN based on two arteries revealing severe arteritis with transmural necrosis causing occlusion, inflammation, and rupture of the vessel walls. Consequently, we switched MMF to IV cyclophosphamide 1g/m2 monthly. Creatinine improved to 1 mg/dL on discharge and 0.9 mg/dL two months later.

Discussion: There is limited attention to non-glomerular vascular lesions among patients with LN. Prior case reports show that LN patients with vascular involvement have worse outcomes and may require more aggressive treatment. The vasculitis in this case was attributed to the MPO Antibody. Given the potential prognostic and therapeutic implications of vascular involvement in LN patients, we suggest that lupus arteritis be considered in the LN pathology classification.

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 ds-DNA, 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 Sjögren’s disease, occasionally, MC can be seen with other rheumatologic conditions. We examine a rare case of Overtiap 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 (UCPR 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.

POI1791
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 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 urine microscopy showed dysmorphic hematuria. 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 serine 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. Bartonella Quintana IgG titer was positive at 1:1024. Valve tissue cultures were negative and tissue PCR was positive for B. Quintana. He was eventually started on gentamycin and oral doxycycline. Ceftriaxone 1 month later was 1.2 mg/dL.

Discussion: Bartonella in the most common cause of culture-negative endocarditis in the United States with a reported association with pauci-immune glomerulonephritis. In our case serological testing and valve PCR were helpful in establishing the diagnosis. In conclusion, SBE induced glomerulonephritis with false positive serology for ANCA in the United States with a reported association with pauci-immune glomerulonephritis. IC-MPGN (immune complex-mediated glomerulonephritis) is a histopathological finding that is associated with infection, immune-complex deposition, monoclonal gammopathies 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). 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.

Case Description: 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 during negative: ANA, anti-Smith, anti-Ro/SS, anti-La/SSB, Hec 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 nephritic at 14 g/g is now near 0.2 g/g.

POI1792
Clinopathological Analysis of Renal Dysfunction due to Idiopathic Multicentric Castleman Disease in Japan
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Background: Renal dysfunction is a fatal complication of idiopathic multicentric Castleman disease. Although AA amyloidosis and glomerular endotheliosis with severe proteinuria were reported due to this disease, human immunodeficiency virus (HIV) were positive in these previously reported cases. On the other hand, HIV-negative cases are common in Japan, and the precise renal involvement of Japanese cases has not been studied yet.

Methods: Case-series was designed for analyzing the clinopathological features of renal dysfunction accompanied with Castleman disease. Inclusion criteria of the object was renal biopsy specimens 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 antibody test 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 IgA deposition and nephrosclerosis in one case each. Nephrotic range proteinuria was found in two cases of AA amyloidosis as well as one case of membranous nephropathy. Among two cases diagnosed as membranous nephropathy, immunofluorescent analysis about IgG subclass showed that IgG1 was dominant in one case and IgG2 was in the other. IgG4 was negative in both cases. In interstitial lesion, chronic tubulointerstitial nephritis was diagnosed in one case.

Conclusions: 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.

POI1793
Is It Systemic Lupus Erythematosus Nephritis or Not? Alexander Pennekamp, Karl B. Pembaur. The Christ Hospital, Cincinnati, OH; The Kidney and Hypertension Center, Cincinnati, OH.

Introduction: IC-MPGN (immune complex-mediated glomerulonephritis) is a histopathological finding that is associated with infection, immune-complex deposition, monoclonal gammopathies 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). 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.

Case Description: 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 during negative: ANA, anti-Smith, anti-Ro/SS, anti-La/SSB, Hec 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 nephritic at 14 g/g is now near 0.2 g/g.

POI1794
Role of the IgA Immune Complexes Bound to FcεRI/CD89 in IgA Nephropathy
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Background: Studies have demonstrated the pathogenic role of circulating polymers of 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 FcεRI/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: rCD89-bound poly-IgA ICs were analyzed by mass spectrometry.

Conclusions: 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.
Plasma levels of CD89-bound poly-IgA ICs in groups

**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 (Gd-IgA1) plays a crucial role in the pathogenesis of IgA nephropathy (IgAN). The microRNAs, named let7b and miR-148b, which affect IgA1 HR (Gd-IgA1) plays a crucial role in the pathogenesis of IgA nephropathy (IgAN). The difference in HR O-glycosylation, shown 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 O-glycoforms in patients with IgAN.

**Results:** Twelve variants of the IgA1 HR O-glycopeptide were detected in both HCs and IgAN patients. The disease-specific IgA1 HR O-glycoforms were 3GalNAc2Gal in Japanese (P < 0.001) and 3GalNAc2Gal (P = 0.007) and 5GalNAc2Gal (P = 0.043) 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 was more prominent in G-IgA1 than in J-IgA1 (P = 0.027). The amount of Gal per HR decreased in the following order: IgA1-G, H-IC, J-IC, and G-IgA1, and was significantly lower in G-IgA1 than in J-IgA1 (P = 0.001).

**Conclusions:** The amount of GalNAc per HR decreased in patients of both races and was prominent in G-IgA1. The difference in GalNAc levels between G-IgAN and J-IgAN showed correspondence with previously reported serum let-7b racial differences, which were associated with the regulation of the initial glycosylation of HR. Further studies regarding upstream factors and changes downstream of GalNAc glycosylation are required to understand the pathogenesis of IgAN.

**Funding:** Government Support - Non-U.S.
Identifying of Proteins Associated with IgA, 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 IgD-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-control tested 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 LS-MS sequence-grade 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 perSpectrE 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 patients. 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 IgA Nephropathy
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Background: Reports regarding IgG subclasses in IgA nephropathy (IgAN) are scarce. Low serum IgG4 levels in IgAN were noticed 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-F (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 membranous nephropathy (IMN, n = 30) were enrolled as controls. Serum IgG4, IgG, galactose-deficient IgA1 (Gd-IgA1), and urine IgG4 levels were detected by ELISA. 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 with different courses, severity, and outcomes were all significantly lower than those of healthy controls and IMN (all P < 0.001). The total 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), < 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 IgG4 (OR 281.11, 95% CI 34.33-2301.97, P = 0.0001), and a negative correlation between serum Gd-IgA1 and IgG4 levels was observed in healthy controls (r = 0.240, P = 0.077) instead of IgAN-N patients (r = 0.066, P = 0.629). Similar results were obtained when IgG4/IgG was analyzed in the same patients and controls. The urine IgG4 levels [µg (mg G)] in IgAN-N (278.16 (398.75, 513.56)) were higher than healthy controls [27.87 (31.51, 208.40), P < 0.001], but were similar to IMN [1153.39 (378.83, 2108.40), P = 0.341]. The IgG4+B cells (0.29 ± 0.17 vs. 0.61 ± 0.56, P = 0.017) and Th1/Th2 (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.

PO1800
Comparing the Lectin and Mass Spectrometry-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 and initially demonstrated as 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-IgA1) 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= 2.45E-02). The reactivity of VVL lectin with unfractonated IgA1, was higher in the IgAN group compared with healthy controls (10.9± 9.1 A.U., P= 6.0E-02). Both Gd-IgA1 and IgA, binding by VVL lectin was much stronger for pIgA1 than mIgA1. Mass spectrometry showed that the level of Gd was higher in pIgA1 than in mIgA1 (3.66 vs. 3.54 Gal/Heavy Chain, P= 6.3E-05). However, no significant differences in glycan composition was detected between patients and controls. In all the experiments, the interindividual differences in glycan composition were large, which may have obscured the signals from the disease-related galactose-deficient IgA1.

Conclusions: Our results suggest that the apparent increased abundance of Gd-IgA1, in circulation of patients with IgAN, is at least in part, attributable to a greater abundance of polymeric IgA1, compared with controls. However, the glycosylation profile of each form of IgA1, appeared indistinguishable in the IgAN group when compared to the corresponding form in the control group.

PO1798
PO1799
PO1801

GLOMERULAR KIDNEY DISEASES: GFR, PROTEINuria, AND CKD

Glomerular Diseases: IgA, C3G, and FSGS
Poster

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
562
Kidney Tissues


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Background: Patients with IgA nephropathy (IgAN) have elevated serum levels of IgA1 with some hinge-region (HR) O-glycan deficient in galactose (Gal; Glc-IgA1). Glc-IgA1 is recognized by IgG autoantibodies, resulting in the formation of pathogenic immune complexes. Our group has established a quantitative ELISA for Glc-IgA1 using Gal-specific lectins (e.g., from Helix pomatia; HPA). This test enabled determinations of genetic basis of IgA1 Gal deficiency and provided a better understanding of IgAN pathogenesis. However, understanding of IgA1 O-glycosylation at a molecular-level is needed.

Methods: We used liquid chromatography with high-resolution mass spectrometry (LC-MS) to analyze and quantify O-glycans of monomeric (m) and polymeric (p) IgA1 in sera of IgAN patients (n=31) and healthy controls (HC; n=10). Total serum IgA1 was isolated from the affinity chromatography and m and p forms were separated by size-exclusion chromatography. Glc-IgA1 was measured by lectin ELISA. HR glycopeptides generated by an IgA-specific protease and trypsin, were analyzed by LC-MS using LTQ Orbitrap Velos MS. LC-MS data were analyzed with the Pinnacle software.

Results: Quantitative LC-MS O-glycosylation profiling of IgA1 HR was performed, and results were calculated as relative abundance of individual glycoforms and as ratios of Gal-containing vs. Gal-deficient glycoforms. Both LC-MS data and lectin ELISA confirmed that pGlcA1 exhibited higher degree of Gal deficiency than mGlcA1. LC-MS data provided additional insight into the molecular basis of the variability of Glc-IgA1 serum levels in IgA nephropathy. For example, IgA1 HR glycoforms GlcGalA1 was more abundant for the pGlcA1 in the patients with high vs. low serum levels of Glc-IgA1 (p<0.005). LC-MS analysis enabled identification and quantification of individual HR glycoforms and defined the Glc-IgA1 glycoforms detected by lectin ELISA.

Conclusion: LC-MS IgA1 glycoforms confirmed pGlcA1 as the main form of IgA1 detected by Glc-IgA1 lectin ELISA. Furthermore, we identified several different Gal-deficient glycoforms in pGlcA1, an observation that enables quantitative molecular-level assessment of Glc-IgA1 glycoform phenotype.

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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 inflammation. For example, 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 deconvolution of spatial data on 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 multiplex staining experiments and comparing it to healthy human kidney tissues to generate the spatial maps.

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

Underline represents presenting author.
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-AB.

Methods: Quiescent primary human MC were stimulated with PDGF-AB for 15 min. Cell lysates were analyzed with SDS-PAGE; Western blotting was performed to evaluate PDGFR-β, Axl, and downstream signaling. Immunoprecipitation with antibodies specific for PDGFR-β 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 proliferation was measured by BrdU incorporation – 20 hr after PDGFR-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

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Background: IgAN is defined by the presence of dominant mesangial IgA1 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 present study, we hypothesized that Gd-IgA1-containing IC deposit in mesangium through glomerular endothelial cell injuries.

Methods: Gd-IgA1 and recombinant anti-glycan IgG were used to form IC (Gd-IgA1-IgG IC) to inject i.v into nude mouse. 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 cells were determined at 8 am and 4 pm at 6, 8, 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.

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.

PO1808
Sparvastran Protects Against Development of Albuminuria and Glomerulosclerosis in the gddY Mouse Model of IgA Nephropathy

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Background: gddY mice are an IgA nephropathy (IgAN) model that develops albuminuria by 8 weeks (W) of age with glomerular IgA1, IgG, and C3 deposits and progressive mesangiproliferative glomerulonephritis. A previous study in the ddY mouse model (the predecessor to gddY mice) using the endothelium type A receptor (ET, R) antagonist FR199317 resulted in amelioration of proteinuria and preservation of kidney function. Treatment of ddY mice with the angiotensin II type 1 receptor (AT, R) blocker valsartan resulted in significant protection from glomerulosclerosis (GS) without a significant prevention in proteinuria. We examined the effect of sparvastran (SP), a dual ET, R and AT, R blocker, on development of albuminuria and GS in gddY mice.

Methods: 8 W old gddY mice 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, and 12 W of age and plasma levels of SP were determined at 8 am and 4 pm at 6, 8, 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 (P<0.05) decreased U-Alb vs mice fed C diet (Fig 1). Development of GS in SP-fed mice was significantly (P<0.05) 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±62 ng/ml respectively for 900 ppm SP and 774±874 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, Hitoshi Suzuki, Yusuke Fukao, Maiko Nakayama, Mingfeng Lee, Rina Kato, Toshiki Kano, Yuku Makita, Yusuke Suzuki. 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-ddY) or without (NO-ddY) 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-ddY mice using this novel B cell culture system.

Methods: Splenic B cells from O-ddY or NO-ddY mice were stimulated with membrane-bound IgM and CD40 for 48h and then proliferation of B cells was evaluated by Thyminde uptake analysis. To examine CS to IgA, naïve splenic B cells from O-ddY or NO-ddY 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-ddY mice proliferated more than those of NO-ddY 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-ddY mice and those from NO-ddY mice.

Conclusions: These data indicate that B cells in O-ddY mice are hyper-sensitive to stimuli by B cell and T cell help without increasing the IgM to IgA switch (CS) to IgA. Here, we suggest that such dysregulation of B cells may be involved in the pathogenesis of IgAN.

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Underline represents presenting author.
POI1801
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 reproducible IgA polymerized by streptavidin to model the initiation and development of IgA.

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 sizes 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, 24 and 48 h after injection, the kidney and the liver were harvested for detection of IgA. Exclusive IgA deposition in the glomerulus 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 streptavidin-induced poly-IgA causes specific renal mesangial deposition and mesangial cells proliferation, which can be used to study the kinetics of mesangial accumulation and clearance of IgA deposition, as a new model for investigating IgAN pathogenesis.

POI1811
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 defined and pathologic renal disease is associated with the dysregulation of the complement pathway, leading to deposition of C3 complement in the glomeruli, with or no 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 21 patients, ranging from 13 to 64 years old. The disease-free interval between the 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 C3GN patients and 41[0-71] for DDD patients). While C3G, with its multiple subtypes, has 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.

POI1813
C3 Glomerulonephritis: A Rare Complication of Chronic Lymphocytic Leukemia
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Introduction: Kidney disease develops in chronic lymphocytic leukemia (CLL) patients via multiple mechanisms including infiltration, obstruction, tumor lysis syndrome, and glomerular disease. We present a rare case of C3 glomerulonephritis (C3GN) associated with pulmonary renal syndrome that we believe was an autoimmune manifestation of CLL.

Case Description: A 76 year old male with a 15 year history of SLL/CLL, DVT, HTN, DM and Stage 3 CKD developed SOB and dry cough. At ED presentation he was in respiratory distress with BIPAP resistant hypoxia requiring intubation. Labs included T7.1 m/dL, K 5.7 mEq/L and uric acid 12.2 mg/dL. CXR showed vascular congestion. Prior to developing anuria urine sediment showed RBC casts. Bronchoscopy DAH, consistent with a pulmonary renal syndrome. Patient was started on plasmapheresis, high dose steroids and CRRT. Autoimmune workup including ANA, anti GBM and ANCA was negative. Kidney biopsy showed diffuse proliferative and sclerotic glomerulonephritis with lymphocytic infiltrates consistent with involvement by patient’s known CD5+, CD23+ B cell lymphoproliferative disorder. If showed diffuse C3 staining. Steroids and
plasmapheresis was 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.

POI1814

Fibrillary Glomerulonephritis or Complement 3 Glomerulopathy: A Rare Case of Crescentic Glomerulonephritis with C3 Dominant Glomerular 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 (≥2 orders of intensity from other deposits) on IF. We present a rare case of crescentic GN with dominant C3 glomerular staining–consistent with C3G–but EM findings suggestive of FGN.

**Case Description:** A 57-year-old female with history of HTN, type 2 DM, questionable SLE (not on therapy), presented with gross hematuria & lower extremity edema. BP 113/71, pulse 88. Creatinine 1.82mg/dl (0.75 two months prior). Urinalysis with 132RBC/hpf & 51WBC/hpf. Urine Prot Cr 24. Cultures grew mixed flora in urine & Serratia marcescens in blood, treated with ceftriaxone. Other labs included serum albumin 1.8 g/dl, ANA >12.0, SS-A >8.0, C3 202, C4 57, & HbA1c 7.3%. Anti-dsDNA, & Serratia marcescens in blood, treated with ceftriaxone. Other labs included serum albumin 1.8 g/dl, ANA >12.0, SS-A >8.0, C3 202, C4 57, & HbA1c 7.3%. Anti-dsDNA, & Serratia marcescens in blood, treated with ceftriaxone. Other labs included serum albumin 1.8 g/dl, ANA >12.0, SS-A >8.0, C3 202, C4 57, & HbA1c 7.3%. Anti-dsDNA, & Serratia marcescens in blood, treated with ceftriaxone. Other labs included serum albumin 1.8 g/dl, ANA >12.0, SS-A >8.0, C3 202, C4 57, & HbA1c 7.3%. Anti-dsDNA, & Serratia marcescens in blood, treated with ceftriaxone. Other labs included serum albumin 1.8 g/dl, ANA >12.0, SS-A >8.0, C3 202, C4 57, & HbA1c 7.3%. Anti-dsDNA, & Serratia marcescens in blood, treated with ceftriaxone. Other labs included serum albumin 1.8 g/dl, ANA >12.0, SS-A >8.0, C3 202, C4 57, & HbA1c 7.3%. Anti-dsDNA, & Serratia marcescens in blood, treated with ceftriaxone. Other labs included serum albumin 1.8 g/dl, ANA >12.0, SS-A >8.0, C3 202, C4 57, & HbA1c 7.3%. Anti-dsDNA, & Serratia marcescens in blood, treated with ceftriaxone. Other labs included serum albumin 1.8 g/dl, ANA >12.0, SS-A >8.0, C3 202, C4 57, & HbA1c 7.3%. Anti-dsDNA, & Serratia marcescens in blood, treated with ceftriaxone. Other labs included serum albumin 1.8 g/dl, ANA >12.0, SS-A >8.0, C3 202, C4 57, & HbA1c 7.3%. Anti-dsDNA, & Serratia marcescens in blood, treated with ceftriaxone. Other labs included serum albumin 1.8 g/dl, ANA >12.0, SS-A >8.0, C3 202, C4 57, & HbA1c 7.3%. Anti-dsDNA, & Serratia marcescens in blood, treated with ceftriaxone. Other labs included serum albumin 1.8 g/dl, ANA >12.0, SS-A >8.0, C3 202, C4 57, & HbA1c 7.3%. Anti-dsDNA, & Serratia marcescens in blood, treated with ceftriaxone. Other labs included serum albumin 1.8 g/dl, ANA >12.0, SS-A >8.0, C3 202, C4 57, & HbA1c 7.3%.

**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.

POI1815

A Case with Immunotactoid Glomerulonephritis with Masked Monoclonal Light-Chain Deposition Disease

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**Introduction:** The immunotactoid glomerulonephritis (ITG) is a rare disorder that is characterized by proteinuria, hematuria, hypertension, and kidney failure. Its diagnosis and timely treatment are important in order to decrease morbidity, conserve kidney function, and improve survival.

**Case Description:** An 82-year old man with a past medical history of uncontrolled hypertension and cerebrovascular disease presented with myalgia, profound weakness and persistent vomiting for 9 days. In the emergency department, his vital signs were significant for blood pressure 220/109 mmHg, BNP revealed creatinine as 3.48 mg/dl, which was 0.9 mg/dl at baseline. The patient was diagnosed with hypertensive urgency and acute kidney injury. Urinalysis showed 107/10F red blood cells and protein >500 mg/dl. Spot urine albumin/creatinine ratio was 869.9 mg/g. Serum C3 decreased to 29.5 mg/dl (reference: 88-201) and C4 decreased to 2.5 mg/dl (reference: 16-47). Hepatitis B and C were non-reactive. Kidney biopsy was planned and pulse dose steroid, 500 mg IV daily, was prescribed for 3 days. The patient’s kidney function continued to worsen and he required hemodialysis. His serum free kappa level elevated to 4.54 mg/dl (reference 0.33-1.54), lambda level was normal 2.54 mg/dl (reference 0.57-2.63), free kappa/lambda ratio elevated to 1.80 (normal 0.26-1.65). Serum immunofixation study showed Igk/IgG kappa monoclonal ab without M-peak; urine protein electrophoresis showed elevated protein level with no apparent M-peak. Initially, kidney biopsy suggested proliferative glomerulonephritis with C3 deposits with light-microscopy. However, repeat immunofluorescence was consistent with diffuse proliferative immunotactoid glomerulonephritis with “masked” monoclonal IgG1-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 plasma cell neoplasm or lymphoproliferative disorder. 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.

POI1816

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 C1NH-AAE. This rare syndrome presents with recurrent angioedema 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 nonmalignant B-cell or plasma cell clone, causing renal damage representing a group of disorders called monoclonal gammopathy 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 gammopathy–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 significant renal dysfunction. Paraprotein-induced renal disease can occur without malignancy, now termed as monoclonal gammopathy 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,
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 may have different disease presentations and their disease course is highly variable. Whether these characteristics remain stable over time is unknown. In this study we assessed stability in clinical and complement biomarker characteristics of C3G patients over time.

Methods: All C3G patients seen at our institution were included. Demographics, clinical and laboratory data were collected. The patients were followed for a median of 5 years. For each 1-year span of observation, statistics were calculated describing the change in each parameter. We then correlated these changes with baseline values.

Results: Fifty-four patients were included. The median age of patients was 56 years. Thirty-five percent were male. The median initial and endpoint serum C3 levels were 124 mg/dL and 124 mg/dL respectively. The median serum C3 decreased 16 mg/dL over the course of follow-up. The mean and median change in UPCR/creatinine over a 1-year period was a decrease of 9.2% and 10.9%. The mean and median change in GFR per year was a decrease of 6.7% and 8.3%. When considering baseline GFR, baseline UPCR and baseline C3, patients were categorized into three groups: those who had a C3 within 25 mg/dL of their entry C3, those who had a C3 within 10 mg/dL of their entry C3, and those who had a C3 outside of 25 mg/dL and 10 mg/dL of their entry C3. In only three 1-year spans did a patient start with matched C3, UPCR and GFR data were identified. Mean and median statistics across these groups were calculated. These results suggest that treatment approaches that effect an improvement in C3 may have a beneficial effect on GFR.

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 loss of GFR most closely correlated with baseline C3 (Figure, p <0.01).

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PO1818
A Case Series of Proliferative Glomerulonephritis with Monoclonal Immune Deposits
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Introduction: Monoclonal gammopathy 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 (mgd) 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 mgd 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 prednisone and rituximab. Kidney biopsy revealed mesangial hypercellularity and monoclonal IgG3 lambda deposits and met criteria for Western light. She had minimal proteinuria and a partial response to rituximab. She is currently being treated with plasma cell targeted therapy with good response.

Discussion: PGNMID 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-free light chains. Our patient was 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.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Conclusions: PKR inhibition ameliorated HIVAN phenotype of Tg26 mouse, suggesting that PKR activation contributes to the pathophysiology of HIVAN in this model.

Funding: NIDDK Support

PO1822
Urinary Single-Cell RNA Sequencing in Focal Segmentsal Glomerulosclerosis Reveals Inflammatory Signatures in Immune Cells and Podocytes

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Background: Individuals with focal segmental glomerulosclerosis (FSGS) typically undergo kidney biopsy only once, which limits the ability to characterize cell populations within kidney over time.

Results: Using single cell transcriptomic analysis of 23 urine samples from 12 FSGS subjects, we identified immune cells, predominantly monocytes, and renal epithelial cells, including podocytes. Further analysis revealed two subtypes consistent with M1 monocytes (produce pro-inflammatory cytokines, initiate immune response) and M2 monocytes (participate in tissue repair). Shed podocytes in urine showed high expression of marker genes for epithelial-to-mesenchymal transition (EMT). We selected the 16 most highly expressed genes from urine immune cells and 10 most highly expressed EMT genes from urine podocytes as immune and EMT signatures, respectively. Using transcriptomic data from kidney biopsies from the Nephrotic Syndrome Study Network (NEPTUNE), we found that urine cell immune- and EMT-signature genes were more highly expressed in FSGS biopsies compared to minimal change disease biopsies.

Conclusions: The identification of monocyte subsets and podocyte expression signatures in FSGS subjects’ urine samples suggests that urine cell profiling might serve as a diagnostic and prognostic tool in the context of nephrotic syndrome. Further, this approach may aid in the development of novel biomarkers for FSGS and for identifying personalized therapies targeting particular molecular pathways in immune cells and podocytes.

Funding: NIDDK Support, Other NH Support - Support from Frederick National Laboratory for Cancer Research, NCI

PO1823
Retinal Drusen and Atrophy in Focal and Segmental Glomerulosclerosis: A Complement-Mediated Disease?

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Background: Retinal drusen are yellow-white deposits typically found in age-related macular degeneration but also with dense deposit disease, lupus nephritis, IgA disease, and membranous and post-streptococcal glomerulonephritis. Drusen and glomerular immune deposits result from complement activation, are similar in composition and share a subepithelial location. Focal and segmental glomerulosclerosis (FSGS) is a heterogeneous clinical-pathological entity in which immune deposits comprising IgM and C3 may be seen. This study investigated a cohort of individuals with FSGS for retinal drusen.

Methods: This was a cross-sectional observational case-control study of individuals with FSGS recruited from a general renal clinic in an Australian tertiary-care metropolitan hospital. Previous structural renal disease in FSGS was noted. Two-field colour fundus images were assessed by two trained graders for drusen count, location and size using the Wisconsin Age-Related Maculopathy Grading Grid. Central drusen counts ≥10 were considered abnormal. Retinal atrophy and pigmentation were recorded by a retinal expert.

Conclusions: The identification of monocyte subsets and podocyte expression signatures in FSGS subjects’ urine samples suggests that urine cell profiling might serve as a diagnostic and prognostic tool in the context of nephrotic syndrome. Further, this approach may aid in the development of novel biomarkers for FSGS and for identifying personalized therapies targeting particular molecular pathways in immune cells and podocytes.

Funding: Government Support - Non-U.S.
Results: Forty-nine individuals with FSGS were compared with 49 matched controls. Mean age was 55 ± 14 years and 29 (59%) were male. One (2%) with FSGS had co-existent structural renal disease, two (4%) had thin basement membrane nephropathy and three (6%) had syndromic FSGS. Twenty-five (51%) had reached end-stage kidney failure, and 16 (33%) had transplants. Central drusen count was 9 ± 25 in FSGS and 3 ± 8 in controls with normal renal function (p = 0.02). Central drusen counts ≥10 were present in nine patients with FSGS (18%) and four controls (8%) (p = 0.23). Seven of these nine (78%) were younger than 60 years which excluded age-related macular degeneration. Medium-sized drusen (>63 μm) were more common in FSGS (20, 41%) than controls (10, 20%) (p = 0.048). Retinal atrophy was present in 9 with FSGS (18%) and no controls (p = 0.003).

Conclusions: Drusen are more abundant and larger in FSGS than controls. Drusen reflect complement activation and their similarities in composition and subepithelial location with glomerular immune deposits suggests that some of the mechanisms underlying drusen are also relevant to FSGS. Retinal atrophy occurs more often in FSGS and may reflect podocyte loss.

PO1824

Idiopathic Glomerular Endotheliosis
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Introduction: Glomerular endotheliosis is a form of thrombotic microangiopathy (TMA) seen with preeclampsia, anti-vascular endothelial growth factor (VEGF) therapy for cancer, and some forms of Castleman’s disease. We present a case without these usual conditions.

Case Description: A 31-year-old female with rheumatoid arthritis, ulcerative colitis (UC), and hypothyroidism presented with abdominal pain and emesis. Medications included alendalumab and levothyroxine. Abdominal imaging and upper endoscopy were unremarkable. Serum chemistries were initially normal. Pregnancy testing was negative. Abdominal computed tomography showed mild cecal inflammation. Calciprotection was elected. Oral budesonide was given for suspected UC flare. Symptoms worsened and she was given intravenous methylprednisolone. She developed proteinuria (up to 3.5 g/day) by 24h urine and worsening renal function. Serum complement was only mildly reduced - C3 (72) and C4 (10). C-reactive protein and erythrocyte sedimentation rate were elevated. Autoimmune serologies were unremarkable. Serum creatinine peaked at 5 mg/dl prompting hemodialysis. Kidney biopsy demonstrated severe glomerular endotheliosis but no other features of TMA (Figure). Pulse dose steroids were given and then daily prednisone; she had 2 sessions of plasmapheresis (PLEX). Renal function improved, attributed to steroids; and PLEX was held. At 4 weeks, she had only modest proteinuria (1.4 g/24hr) and improved renal function (serum creatinine 0.9 mg/dl).

Discussion: Glomerular endotheliosis is thought to occur due to VEGF inhibition in podocytes (by VEGF-inhibitors or by soluble fns-like tyrosine kinase in preeclampsia). Patients with endotheliosis of unknown cause have been reported to respond to immunosuppression (steroids, cyclophosphamide). Endotheliosis occurs in Castleman’s disease and may improve with IL-6 inhibitors. The etiology in our patient remains unknown but she has demonstrated improvement with corticosteroids.

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 sta, a blood pressure of 118/86 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 was followed 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 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 hypothesized 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, the IL13 and IL4 and IL-13 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 nephritic syndrome in animal studies, and high levels are seen in paediatric nephrotic syndromes, with IL-13 levels increasing following corticosteroid 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 paralysis and respiratory failure despite IV immunoglobulin (IVIG) and plasma exchange therapy (PLEX). Initial investigations were consistent with Acute Motor-Sensory Axonal Polyneuropathy (AMSAN), a variant of GBS. Nephrotic syndrome was identified after four months in case one and immediately in case two. Both cases had 20 g/day of proteinuria, preserved renal function, and histologic diagnostic of tip-variant FSGS on renal biopsy. 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-contactin-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 nephritic 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
Glomerular Tip Lesion of FSGS

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 cystoprostatectomy. Chemotherapy included methotrexate, vinblastine, doxorubicin, and cisplatin (2015), pembrolizumab and epacadostat (7/2016-5/2018) and pembrolizumab 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. 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.

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 rashes and weight loss was found to have a creatinine of 5.1 mg/dl (1.4 I 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-SAA 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+) 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 bunetamide 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)

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Introduction: Postinfectious glomerulonephritis (PIGN) causes acute nephritic syndrome complicated with uric acid 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 pancreatocystic 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.

Glomerular Tip Lesion of FSGS

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

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Mitochondrial Injury May Be a Ubiquitous Finding in the Pathogenesis of Various Glomerulonephritides

Byung chul Yu, Moo Yong Park, Soo Jeong Choi, Jin kuk Kim, Seung D. Hwang, Division of Nephrology, Department of Internal Medicine, Soonchunhyang University Bucheon Hospital, Bucheon, Gyeonggi-do, Republic of Korea.

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 patients, minimal change disease (MCD), acute tubulointerstitial nephritis (ATIN), and focal 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 carcinoma specimen as control and kidney tissues obtained from each GN patients by immunohistochemistry staining.

Results: log_COX3/mtDNA and log_ND1/mtDNA were significantly higher in IgAN (p<0.001, p=0.002), MCD (p<0.001, both), ATIN (p<0.001, both), and MGA (p<0.001, both) compared with HV (Figure 1). 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 carcinoma specimen as control and kidney tissues obtained from each GN patients by immunohistochemistry staining.

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.

PO1831

Single-Cell Transcriptomic Profiling Reveals Aberrant Signaling Responses to Tfh Cytokines in IgA-Secreting Cells from IgA Nephropathy Patients

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Background: IgA nephropathy (IgAN), a common primary glomerulonephritis, is characterized by glomerular IgA1 immunodeposition enriched for galactose-deficient IgA1 (Gd-IgA1). These immunodepositions are likely derived from Gd-IgA1-containing immune complexes that are elevated in the circulation of IgAN patients. Gd-IgA1 is produced by IgA1-secreting cells due to abnormal expression of several glycosyltransferases in IgAN. Furthermore, some cytokines can enhance production of Gd-IgA1 by IgA1-secreting cells from IgAN patients but not those from healthy controls. We hypothesize that pro-inflammatory factors, such as those identified by GWAS or produced during episodes of synpharyngitic hematuria in IgAN patients, may further dysregulate IgA1-secreting cells and lead to enhanced Gd-IgA1 production.

Methods: As an experimental model, we used T-follicular helper (Tfh) cell-derived cytokines (IL-4, IL-6, IL-21, CD40L) to stimulate for 30 min immortalized Ig-producing cells derived from peripheral blood of IgAN patients and healthy controls. Then, single-cell transcriptomic analysis was performed. IgA1 splice variants were integrated into the hg38 reference genome to identify IgA1-secreting cells and the data analyzed using Seurat and Altairx workflow. siRNA knock-down (k/d) was used to confirm involvement of candidate regulatory elements in cytokine-mediated overproduction of Gd-IgA1.

Results: Single-cell transcriptomics identified discrete populations of IgA1-secreting cells with differential C1GALT expression after Tfh cytokine stimulation. Furthermore, these subpopulations exhibited reduced expression of cytokine-signaling regulatory elements, SOCS3, SOCS1, PTEN2, and PTEN (p = 0.07, 0.04, 0.02, 0.07), indicating dysregulation of cytokine-signaling JAK/STAT pathways in IgAN-derived cells. Involvement of SOCS3 in Gd-IgA1 production was further supported by the observation that SOCS3 siRNA k/d increased Gd-IgA1 production in healthy-control cells (p = 0.01).

Conclusions: Single-cell transcriptomics with stratification of IgA1-secreting cells based on C1GALT expression and siRNA k/d experiments revealed that aberrant regulation of Tfh cytokine signaling was associated with enhanced Gd-IgA1 production in IgAN.

Funding: NIDDK Support, Private Foundation Support

PO1832

The NefIgArd trial: The Effect of Nefecon® (Budesonide) in Patients with Primary IgA Nephropathy at Risk of Developing ESRD

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Background: The gut-associated lymphoid tissue (GALT) has been identified as the potential source of poorly O-galactosylated immunoglobulin A (IgA1) that triggers the formation of nephritogenic immune complexes in IgA nephropathy (IgAN). The NEFIgArd trial (NCT01738035), which assessed the safety and efficacy of a novel targeted-release formulation of budesonide (NEFECON®), highlighted the potential of selectively targeting GALT in patients with IgAN. After 9 months’ treatment, urine protein-creatinine ratio (UPCR) was reduced by 29.3% in the NEFECON® 16 mg/day group vs placebo. Estimated glomerular filtration rate (eGFR) decreased by 4.7 ml/min/1.73 m2 in the placebo group, but with no deterioration seen with NEFECON® 16 mg/day. The incidence of patient-reported adverse events was similar in all groups. Based on these data, the phase 3 NefIgArd study was designed to assess the efficacy and safety of NEFECON® 16 mg/day in patients with IgAN at risk of end-stage renal disease.

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: 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–angiotensin 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 NEFFCON® 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 surrogacy of the Part A UPCR endpoint. For this purpose, and based on the 2018 NKF/FDA/EMA workshop supporting eGFR slope as an endpoint for full approval, the primary outcome will assess the effect of NEFFCON® 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

PO1834
Effect of Hydroxychloroquine in Patients with IgA Nephropathy with Insufficient Responses to Immunosuppressive Therapy: A Retrospective Case-Control Study
Chen Tang,1 Jicheng Lv,2 Sufang Shi, Yuqiong 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 antiproteinuric 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=0.902). 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. -31.99% [-67.08, -9.14], p = 0.968). The cumulative frequency of patients with a 50% reduction in proteinuria during the study was also 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>IS therapy plus HCQ</th>
<th>Conventional IS therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proteinuria at baseline (g/d)</td>
<td>2.35 (1.47, 2.98)</td>
</tr>
<tr>
<td>蛋白尿（g/d）</td>
<td>2.35 (1.47, 2.98)</td>
</tr>
<tr>
<td>Proteinuria at 6 months (g/d)</td>
<td>1.10 (0.85, 1.61)</td>
</tr>
</tbody>
</table>

Proteinuria of patients during the follow-up. The dots represent the median value, the bars represent the 25th and 75th percentiles. Each Month’s was compared with “Baseline” respectively. * p < 0.05; ** p < 0.01; *** p < 0.001

PO1835
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 coorte was divided in 2, according the use of steroid therapy: 105 in group with 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 (56.5 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.
therapy was reversed by presence of crescent (no crescent: HR 1.75 95% confidence interval [CI] 1.07–2.84, presence of crescent: HR 0.26 95%CI 0.11–0.61), 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.

**POI837**

**Vitamin D Deficiency and Outcome of IgA Nephropathy in North Indian Patients**

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**Background:** Vitamin D has been shown to be beneficial in reducing proteinuria in patients with chronic kidney disease (CKD). IgA Nephropathy (IgAN) is one of the leading causes of CKD in India and worldwide. Asians, especially Indians develop more severe IgAN. We conducted this study to evaluate 25-hydroxy vitamin D (25(OH)D) level as a prognostic marker for disease progression and outcomes in a cohort of Indian patients with IgAN.

**Methods:** In this retrospective cohort study, demographic and clinical data of Indian adult patients with biopsy proven IgAN, diagnosed between 2015 and 2019, was obtained. Patients with a minimum follow-up of 6 months were included for analysis. A 25(OH)-vitamin D assay was performed on serum samples collected at the time of kidney biopsy. 25(OH)D levels <10 ng/mL were considered as deficient.

**Results:** Of the 105 patients included in the study, 69.5% were males. The mean age was 34.0+10.6 yrs. The mean baseline creatinine and 24 hr proteinuria was 1.37+0.51mg/dl and 3.12±2.45 g/day, respectively. The mean baseline vitamin D levels were 15.88±11.85 ng/mL. 39% patients were 25(OH)D deficient. The median duration of follow up was 23.5 months (range: 6–56 mon). Eleven patients (10.5%) progressed to end stage renal disease (ESRD) during follow-up. Vitamin D deficiency was not significantly associated with progression to ESRD (p=0.61) or proteinuria remission (0.83). Risk for ESRD was reduced in patients with lower baseline creatinine levels (p=0.00) and patients on ACE inhibitors (p=0.03). Remission of proteinuria was more common in patients with lower baseline protein levels (p=0.006) and normotenstive patients (p=0.03). Baseline creatinine (HR = 14.49; 95% CI, 1.02 – 202.15), 24 hr proteinuria (HR = 0.93; 95% CI, 0.00-0.85) and disease remission (HR = 0.01; 95% CI, 0.00-0.32) were predictors of risk for ESRD.

**Conclusions:** Vitamin D deficiency is common in Indian patients with IgAN. Baseline vitamin D deficiency did not affect outcomes of IgAN.

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

**POI838**

**Long-term Beneficial Effects of Tonsillectomy on Patients with Immunoglobulin G A Nephropathy**

Takahito Moriyama, Kazunori Karasawa, Yoei Miyabe, Kenichi Akiyama, Norio Hanafusa, Kosaku Nitta. Tokyo Joshi Ika Daigaku, Shinjuku-ku, Japan

**Background:** Tonsillectomy may treat immunoglobulin (Ig) A nephropathy (IgAN) by reducing the levels of galactose-deficient IgA1. Hence, we aimed to analyze the long-term effects of tonsillectomy as an initial treatment and a treatment at any time in their lives on patients with IgA Nephropathy (IgAN).

**Methods:** In this retrospective cohort analysis, 1147 patients with IgAN were grouped according to whether or not they had undergone tonsillectomy at any time in their lives (Study 1) or within 1 year after renal biopsy (Study 2). The patients who underwent tonsillectomy (T1) and who did not undergo tonsillectomy (T0) were propensity score grouped according to whether or not they had undergone tonsillectomy at any time in their lives.

**Results:** In both studies, the groups' clinical data, histological data according to Oxford classification, and treatments such as immunosuppressants and inhibitors of renin-angiotensin systems were similar after propensity score matching (Study 1, n=179/each group; Study 2, n=143/each group (T1 vs. T0); median eGFR: 81.0 vs. 81.5 mL/min/1.73m², p=0.48). In Study 1, the renal survival rates at the primary and secondary endpoints were 50% reduction in estimated glomerular filtration rate or ESKD (8.4%) other ethnicity. Complete case analysis was done with 93 patients. The 5-year risk of the primary outcome at 5 years post-biopsy was 15.0%. Oxford T2 histologic score was removed from the full model analysis as the R² for the full models with and without race when applied to our patient dataset over 11 years (Jul 2009 to Oct 2020) using external validation of survival model. 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) was 15.0%. The 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 validation cohort were 39% and 32% 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, 0.399-1.000), comparable to the C statistics from the original derivation and validation analysis. Both full models were well-fitted in our cohort, with high 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.
PO1841  
Associations of Genetic Variants Contributing to Gut Microbiota Composition in IgAN

**Jiawei He, Xujie Zhou, Yanna Wang, Lijun Liu, Sufang Shi, Jicheng Lv, Hong Zhang, Peking University First Hospital, Beijing, China.**

**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 4.1×10⁻² to 1.39×10⁻⁴). 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), rs6065904-AA/AG risk genotypes and worse kidney function (C), rs9363741-GG/GA risk genotypes and severer hematuria (D). Besides, rs1889714-AA/AG risk genotypes associated with decreased abundance of beneficial Dialister; whereas rs6065904-AA/AG and rs9363741-GG/GA risk genotypes associated with increased abundance of detrimental Erysipelotrichaceae and Lachnospiraceae, 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.

PO1842  
IgA Nephropathy: Quantifying Remission Duration on Clinical Outcome

**Hong Zhihong, Peking University First Hospital, Beijing, China.**

**Background:** Quantitative assessment of remission duration is required for understanding the risk of disease progression in IgAN.

**Methods:** In this retrospective international cohort of adult patients with biopsy-proven IgAN, we defined remission based on: (i) a ≥25% reduction in proteinuria from the peak value after biopsy; (ii) an absolute reduction in proteinuria to <1g/day; (iii) peak proteinuria prior to remission ≥1g/day. The total duration of first remission was treated as a time-varying exposure using longitudinal proteinuria measurements. Time-dependent Cox proportional hazards models were used to quantify the association between duration of remission and the primary outcome (ESKD or 50% reduction in eGFR).

**Results:** Of 1864 patients who entered a first remission, 274 (14.7%) experienced the outcome during median follow-up of 3.9 years. The relationship between duration of proteinuria remission and the primary outcome was non-linear (Figure). Each 3 months in sustained remission up to 51 months was associated with an additional 9% reduction in the risk of disease progression (HR 0.91, 95% CI 0.89-0.93). Each additional 3 months in remission beyond 51 months was associated with a non-significant risk reduction (HR 0.99, 95% CI 0.96-1.03). Results were robust to multivariable adjustment and consistent across subgroups including immunosuppression exposure.

**Conclusions:** We observed a non-linear dose-response relationship between the duration of proteinuria remission and the risk of disease progression in IgAN. When considering proteinuria as a surrogate outcome, our findings illustrate the need to consider the duration of remission in addition to the magnitude of proteinuria reduction when evaluating the anticipated impact on long-term clinical endpoints.

PO1843  
Results of a Phase 1 Trial to Investigate the Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of BION-1301 in Healthy Volunteers

**Jeanette Lo,1 Sharon Yavrom,1 Jessy Fan,1 Aaron N. Endsley,2 Tamara Schroeder,2 Jonathan Barratt,2 David M. Essuyan.3 Aduro BioTech Inc, Berkeley, CA; 1Certiara LP, Princeton, NJ; 2ONCORD, Inc., Westlake Village, CA; 3University of Leicester, Leicester, United Kingdom.**

**Background:** IgA nephropathy (IgAN) is an autoimmune disease with no approved treatments. Key steps in IgAN pathogenesis are the production of galactose-deficient IgA1 (Gd-IgA1), the generation of anti-Gd-IgA1 autoantibodies and the formation of immune complexes resulting in kidney inflammation and damage. Patients with IgAN have elevated levels of a proliferation-inducing ligand (APRIL) which regulates B cell differentiation and proliferation. In a study of patients with IgAN, those with high plasma APRIL levels had elevated levels of Gd-IgA1 and proteinuria and lower eGFR. BION-1301, a first-in-class humanized anti-APRIL antibody, was well-tolerated with no dose-limiting toxicities in a Phase 1/2 first-in-human study in multiple myeloma. This 3-part Phase 1 trial characterizes the safety, pharmacokinetics (PK), and pharmacodynamics (PD) of BION-1301 in healthy volunteers (HV) and patients with IgAN.

**Methods:** (NCT03945318) Parts 1 and 2 are double-blind, randomized, placebo-controlled single and multiple ascending dose studies, respectively. Part 1 enrolled 36 HV in 5 dose cohorts, randomized in a 3:1 ratio to receive a single dose of BION-1301 or placebo delivered by IV infusion. Part 2 enrolled 27 HV in 3 dose cohorts, randomized in a 2:1 ratio to receive 3 doses of BION-1301 or placebo delivered by IV infusion every two weeks. Part 3 assesses a multiple dose regimen in patients with IgAN and is currently enrolling.

**Results:** BION-1301 was well-tolerated with low incidence of non-neutralizing ADAs in HVs. The PK profile was well behaved with a half-life supporting monthly dosing. Durable target engagement, suppression of IgA and IgM, and to a lesser extent IgG were observed following BION-1301 administration. IgG values remained in normal ranges with no increase of infections post-treatment. Updated data will be presented including B cell immunophenotyping of HVs and results from patients with IgAN, if available.

**Conclusions:** BION-1301, an anti-APRIL antibody, offers a pharmacodynamic window to exploit IgA suppression while tempering impact to IgG. BION-1301 may provide a novel approach to address the pathophysiology of IgAN.

**Funding:** Commercial Support - Aduro BioTech
Glomerular Diseases: Clinical, Outcomes, and Trials - 1

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, urinary 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 high 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 IgA and Gd-IgA1.

Conclusions: Present study suggested that high intensity of glomerular Gd-IgA1 deposition is 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
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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 IgG 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 immune-complex-mediated membranulonephritis, 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), oligomanganeo nephropenia (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, oligomangeanephropenia, Alport syndrome, C3 glomerulonephritis, poststreptococcal acute glomerulonephritis, and hemolytic uremic syndrome (n=1/1 each).

Conclusions: Gd-IgA1 positivity in patients with IgAN and IgAV-N was consistent with previous report. Present study, Gd-IgA1 was also positive in patients with IgA-positive immune-complex-mediated membranulonephritis. 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 immune-complex nonspecifically.

PO1846
Urinary Exosomal MicroRNAs Are Potential Diagnostic and Prognostic Biomarkers in IgA Nephropathy Patients
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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 miRNA differential expression of renal tissue between IgAN and normal subjects in the gene expression omnibus dataset, and selected 884 glomerular and 67 tubulointerstitial genes through meta-analysis. We then used the miRtarBase, TargetScan, microRNA 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-29a-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-29a-3p have good diagnostic accuracy for IgAN (area under curve of the 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 sediment 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/HFP), and moderate to severe leukocyturia (>12/HFP) 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=0.333, P=0.001) and leukocyturic 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: 0.494-2.312, P=0.866).

Conclusions: Urinary sediments of the endocapillary proliferative lupus nephritis and endocapillary proliferative IgA nephropathy differed in many aspects. Leukocyturia could reflect the disease activity and prognosis of endocapillary proliferative glomerulonephritis, especially in lupus nephritis.
A Single-Center Retrospective Study of Thrombotic Microangiopathy

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 as 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 17k/mm3, and most were female (71%). Fifty-seven percent had hematuria, 21% proteinuria and 85% had schistocytes in the blood smear.

Table 1

<table>
<thead>
<tr>
<th>Name</th>
<th>Age</th>
<th>Sex</th>
<th>Reason for TMA</th>
<th>Eculizumab</th>
<th>CRRT</th>
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<tr>
<td>TTP</td>
<td>48</td>
<td>F</td>
<td>HUS</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>SLE</td>
<td>34</td>
<td>M</td>
<td>SLE</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>HUS</td>
<td>56</td>
<td>F</td>
<td>HUS</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>

POI1850

Does Kidney Histology Predict Renal Response or Complement Status in Atypical Hemolytic Uremic Syndrome?

Conclusions: A larger study is needed to determine the value of these features in predicting complement mutation status and renal response in aHUS.

POI1851

Comparative Efficacy of Ravaluzumab and Eculizumab in the Treatment of Atypical Hemolytic Uremic Syndrome: An Indirect Comparison Using Clinical Trial Data

Conclusions: Most common cause of Thrombotic Microangiopathies in 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>
<thead>
<tr>
<th>Eculizumab</th>
<th>TTP</th>
<th>SLE</th>
<th>HUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/10</td>
<td></td>
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TTP, thrombotic thrombocytopenia purpura; SLE, systemic lupus erythematosus; HUS, hemolytic uremic syndrome
Representative clinical characteristics at baseline and 26 weeks.

POI1852

C3 Inhibition with Pegcetacoplan Targets the Underlying Disease Process of C3 Glomerulopathy (C3G) and Improves Proteinuria

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Background: C3G is a rare renal disease in which C3 overactivation leads to the accumulation of C3 breakdown products in the glomeruli. Progression to end-stage renal disease occurs in up to 50% of patients (pts) within 10 years of diagnosis; no therapies target the underlying pathophysiology of C3 activation. The study aims to assess whether pegcetacoplan (APL-2; Apellis Pharmaceuticals, Waltham, MA), a C3 inhibitor, targets C3G complement dysregulation and reduces proteinuria.

Methods: This phase 2 open-label study was designed to evaluate preliminary efficacy and safety of pegcetacoplan in pts with complement-mediated glomerulopathies. Pts with C3G who were ≥16 years old, with proteinuria >750 mg protein/g creatinine, and eGFR ≥30 mL/min/1.73 m² were eligible for inclusion. Pegcetacoplan was administered as 360 mg daily subcutaneous infusions with transition to 1080 mg twice weekly from Week 24. The primary endpoint was change in proteinuria from baseline to Week 48, measured by 24-hour urine protein-to-creatinine ratios (uPCR). Serum C3, albumin, and creatinine as well as safety were also evaluated.

Results: Eight C3G pts were enrolled in the study. Three pts were excluded from efficacy analyses for self-reported non-compliance or interrupted study drug administration. Data showed a greater than 65% reduction in 24-hour uPCR from baseline to Week 48. Serum albumin and C3 increased, and serum creatinine was stable (Table). No serious or severe adverse events were reported and no TEAEs led to discontinuation.

Conclusions: These data suggest that pegcetacoplan targets the underlying pathophysiology of C3G, resulting in proteinuria reduction with stable renal function. Further studies are warranted to investigate the therapeutic potential of pegcetacoplan in the treatment of C3G.

Funding: Commercial Support - Apellis Pharmaceuticals, Inc.

*Last result prior to initial dose; #Local lab data used for 1 pt due to COVID-19 related constraints

POI1853

C3 Glomerulonephritis Associated with Monoclonal Gammapathy: A Retrospective Case Series Study from a Single Institute in China

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Background: To analyze the demographic and clinicopathological features and renal outcomes of Chinese patients with C3GN in the setting of monoclonal gammopathy.

Methods: Patients with renal biopsy-proven C3GN and monoclonal gammopathy, with measurable serum and/or urine monoclonal Ig from 2006 to 2018 in Peking University First Hospital were included, clinical data, renal pathology type, treatment and prognosis were collected.

Results: Nineteen patients were enrolled, accounting for contemporaneous 26.7% of C3GN patients. The mean age was 55 years old, and average eGFR at biopsy 48.42mL/min/1.73m². The IgG was the most common isotype of monoclonal Ig on immunofixation. Eleven patients had nephrotic range proteinuria and hypalbuminemia. Kidney biopsies revealed a relative prominent MPGN pattern. Two patients had concurrent TMA-like renal injuries. The median renal survival was 24 months. Median renal survival was 12, 12, and 34 months, respectively in patients receiving conservative therapy, immunosuppressant therapy, and clone-targeted chemotherapy, without statistical significance. Plasma exchange therapy only improved one patient’s renal outcome.

Conclusions: The clinicopathological features of Chinese patients with C3GN combined with monoclonal gammapathy are consistent with the previously reported population. Renal prognosis of these patients is poor, and immunosuppressant therapies show no advantage over supportive therapy in renal prognosis, while the benefit of clone-targeted chemotherapy is still requiring investigation.

Funding: Government Support - Non-U.S.
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. ADAMS13 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 dependant.

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?
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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 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 vasculitides 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 system (RAAS) Inhibition Alone
Marianna Vynnyk, Maria V. DeVita, Jordan L. Rosenstock. Lenox Hill Hospital, New York, NY.

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 managed with 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 urinalysis (UA) 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.
PO1860
An Atypical Case of Fibrillary Glomerulonephritis
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Introduction: Fibrillary glomerulonephritis (FGN) is a rare primary glomerular disease that can be 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 treatment of hepatitis C infection (HCV).

Case Description: The patient is a 49-year-old Filipino female, hypertensive, with a history of HCV infection. Case series reported 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 widespread podocyte foot process effacement and mesangial fibrillary deposits measuring 10-30 nm. At this time, proteinuria 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, followed by a prednisone taper. At 6 months, proteinuria decreased to 2756.55 grams with a creatinine clearance of 39.80 ml/min/1.73 m². Further discussion with the patient is recommended.

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.

PO1861
Fibrillary Glomerulonephritis Treated with Rituximab: A Case Report
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Introduction: Fibrillary Glomerulonephritis (FGN) is a rare primary glomerular disease first described by Rosenmann and Eliaikim in 1977 present in 0.5 to 1% of native kidney biopsies defined by haphazardly arranged fibrils 10 to 30 nm in thickness deposited in the mesangium, glomerular basement membranes or both. Initially, FGN was considered to be idiopathic. However, approximately one-third have a history of malignancy, monoclonal gammopathy, autoimmune disease, hepatitis C infection or an IgM glomerular deposition disease. Prognosis is generally poor with 50% of patients developing ESRD within 6 years of presentation. The most common form of treatment is steroids with or without a second agent usually Cyclophosphamide or Rituximab. To date, there is no convincingly effective treatment but published case series reports clinical response referred to as “nonprogression” defined by stable renal function in those treated with 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 widespread podocyte foot process effacement and mesangial fibrillary deposits measuring 10-30 nm. At this time, proteinuria 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 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 Cryoglobulinemia: Current Clinical Evidence

**Introduction:** Hepatitis B virus (HBV)-related mixed cryoglobulinemia (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, and outcome data of the 42 HBV-related MC cases. Meanwhile, the Asian and European 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. Extrahospital clinical manifestations mainly included cutaneous lesions, kidney involvement, peripheral neuropathy, articular 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.

**Conclusions:** Extrahospital 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 2.6 g/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 lisonopril 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, membranoproliferative, 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 nephrotic 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

**Introduction:** Differentiating infection vs auto-immune related GN is crucial in order to avoid inadvertent immunosuppressive therapy that can be harmless 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 10.4 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, C3, C5 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 SLI 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

**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, anasarca, angioedema, leucocytoclastic 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.
Her 1st renal biopsy showed mesangial proliferative GN with +3 IF for IgG, IgA, C1q & EM deposits. On clinical grounds, subendocardial infarction was the initial location of the initial 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 ground glass staining of proximal tubules & cytoplasmic vacuolization. C3 was 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 and 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 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 +1F for IgG & C1q. HUV causes unique microtubular structures in the interstitium but not the glomeruli. Rituximab rapidly induces clinical renal remission in HUV.

**PO1867**

Unusual Aggregation of Different Glomerulopathies in a Family Resolved by Genetic Testing

*Vahahan S, Keskinyan, Reeti Kumar, Rasheed A. Gbadegesin. Duke University, Durham, NC.*

**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 instances, clinical presentations of different GNs can lead 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 map biopsies 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 evaluation was remarkable for microscopic hematuria and non-nephrotic range proteinuria. C3/C4 complements, ASO, anti-DNase B, anti-dsDNA, 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 COL4A. Staining was performed on family members and genetic testing in him was negative for the COL4A5 variant found in his brother and mother.

**Discussion:** This case highlights the utility of genetic testing and reverse phenotyping in resolving clinical diagnosis in families with unusual combinations of different glomerulopathies. We propose that clustering of different glomerular disease phenotypes in a family should be an indication for genetic testing.

**PO1868**

Unusual Case of Histiocytic Glomerulopathy in the Setting of Sarcoma- toid Malignancy

*Faris Al faris, Majd Al-Ahmad, Llewellyn 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 mid-abdominal tenderness on palpation. Aortic angiography revealed occlusion of 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 reveled bland urine sediment and 24-hour creatinine ratio was 8.7 with RBC casts. C1q was 4 mg/dL, C3 38 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 and 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 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 +1F for IgG & C1q. HUV causes unique microtubular structures in the interstitium but not the glomeruli. Rituximab rapidly induces clinical renal remission in HUV.

**PO1869**

Bilateral Renal Infarctions: A Perplexing Presentation of Polyarteritis Nodosa

*Alissa Lee, Matthew Fay. Louisana 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 1357 U/L, ALT 136 U/L, Hbg 12.6 g/dL, WBC 2.4 x10^3/L, and UA with hematuria and proteinuria. An extensive workup was completed, and his HIV, Hepatitis B and C, ANCA, Cardiolipin Ab, DRVVT, and ANA results were negative. TEE was normal. His ESR was 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.

**PO1870**

Clinical Predictors of Response to Rituximab in the Nephrotic Syndrome Study Network (NEPTUNE) Cohort

*Daniella Levy Erez, 1,2 Kevin E. Meyers, 1,2 Jarcy Zee, 1 Abigail R. Smith, 3 Division of Nephrology, Children’s Hospital of Philadelphia, Philadelphia, PA; 1University of Pennsylvania Perelman School of Medicine, Philadelphia, PA; 2Arbor 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 UPCR<0.3 mg/mg.

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

**Underline represents previous author.**
Funding: NIDDK Support, Private Foundation Support

Figure: Remission probability by age and disease diagnosis.

POI872

Validating a Computable Phenotype for Nephrotic Syndrome in Children and Adults Using PCORNet Data

Andrea L. Oliverio,1 Dorota Marchel,1 Cheryl L. Tran,4 Isabelle Ayoub,2 Salem Almamari,2 Jessica M. Greco,3 Michelle Denburg,3 Debbie S.吉son,2 Laura H. Mariani.1 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 against 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 88.8% with an F1 score of 86.5%. The most common cause of false positive classification was secondary FSGS (735), followed by class V lupus nephritis (935).

Conclusions: While prior computable phenotypes for glomerular diseases have used ICD 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

Table 2: Association of Tobacco Exposure with Cardiovascular Risk Factors and Kidney Outcomes in Adjusted Regression Models

<table>
<thead>
<tr>
<th>Reference Non-GN</th>
<th>Heart Disease</th>
<th>Kidney Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-smoker</td>
<td>Adult</td>
<td>Active Smokers</td>
</tr>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>Active smoker</td>
<td>1.6 (1.2-2.1)</td>
<td>0.15</td>
</tr>
<tr>
<td>Passive smoker</td>
<td>1.2 (0.8-1.8)</td>
<td>0.42</td>
</tr>
<tr>
<td>Non-smoker</td>
<td>1.0 (0.7-1.5)</td>
<td>0.93</td>
</tr>
</tbody>
</table>

Data from all 3 health systems

POI873

Family History of Diabetes Is Associated with Progression of Kidney Disease: The CureGN and CRIC studies

Francesca Zanoni,1 Miguel Verbitsky,1 Maddalena Marasa,1 Joshua D. Bundy,1 Afshin Parsa,1 Krzysztof Kiylik,1 Harold I. Feldman,1 Ali G. Ghazal,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 FHxs 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.

582
POI1875

Fractional Excretion of Total Protein in Nephrotic Syndrome
Hideaki Kuno, Go Kanzaki, Takaya Sasaki, Yusuke Okabayashi, Kotaro Haruhara, Kentaro Koike, Nobuo Tsuobi, Takashii 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 (Cp) by creatinine clearance (CCr) 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 ± 27.2 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 (r = 0.65, P < 0.01), urinary protein excretion (r = 0.58, P < 0.01), interstitial fibrosis and tubular atrophy (r = 0.24, P < 0.05), and glomerulosclerosis (r = 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%–IAa-nephropathy). Serum creatinine was measured by enzymatic, serum cystatin C - immunoturbidimetric methods. GFR was estimated using creatinine clearance (CCr), MDRD, CKD-EPICr, CKD-EPICysC, CKD-EPICrCysC, full age spectrum 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 continuously 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 (r=0.001) with GS, TIF, TA and was higher in patients with “mild” GS, TIF and TA (r=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-EPICrCysC, 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 Matyjek, 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 increases in TBW, NT-proBNP and extracellular water(ECW) were observed in comparison to CG. Total body water (TBW) did not differ between the groups. Overhydration (OH) was higher in SNSG than in CG. Significant, positive correlation was observed between OH and NT-proBNP (R=0.56, p=0.0001) as well as hsTnT (R=0.60, p=0.0001). We did not observed any significant correlation between ECW and NT-proBNP or hsTnT.

Conclusions: 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 interstitial or intracellular hydration 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>Group</th>
<th>Age (years)</th>
<th>Weight (kg)</th>
<th>Height (cm)</th>
<th>TBW (L)</th>
<th>ECW (L)</th>
<th>ICW (L)</th>
<th>NT-proBNP (µg/L)</th>
<th>hsTnT (µg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNSG</td>
<td>35±10</td>
<td>74±18</td>
<td>173±7</td>
<td>20.4±3</td>
<td>14.1±2</td>
<td>6.3±2</td>
<td>719±899</td>
<td>18±6</td>
</tr>
<tr>
<td>CG</td>
<td>35±10</td>
<td>74±18</td>
<td>173±7</td>
<td>20.4±3</td>
<td>14.1±2</td>
<td>6.3±2</td>
<td>30±12</td>
<td>0±0</td>
</tr>
</tbody>
</table>

PO1878
Glomerular Filtration Barrier Dysfunction in an RNA Virus-Induced Glomerulopathy: Reassembles Findings of Common Nephrotic Syndromes
Christian Nussbaumer1, Alisa Stütz2, Stefan Häggle3, Claudia Speer4, Florian Kähkle5, Christoph Eckert1, Christian Morath1, Jochen Reiser1, Martin G. Zeier1, Ellen Krauthämer1, Heidelberg University Hospital, Heidelberg, Germany; 2Rush 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 urokinase plasminogen activator receptor (suPAR) are elevated in COVID patients and provide prognostic insights. SuPAR is also involved in proteinuric kidney diseases such as focal segmental glomerulosclerosis 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 podocyte injury is, however, unclear. We hypothesized that hantavirus infection results in podocyte injury and a dysfuctional glomerular filtration barrier (GFB), similar to findings in common NS.

Methods: Renal biopsy specimens were analyzed by light and electron microscopy. Urinary neprhin and serum suPAR were measured over time in 26 patients with HFRS and 18 healthy controls.

Results: Hantavirus patients showed significantly increased urinary neprhin, immunoglobulin G (IgG), α1-microglobulin (α1-MG) and serum suPAR concentrations compared to healthy controls. Furthermore, neprhin 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 neprhin levels as a marker for podocyte damage correlated strongly with biomarkers of non-selective glomerular proteinuria. Interestingly, suPAR correlated significantly with urinary neprhin, IgG and albumin 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. Podocyte injury and kidney dysfunction recovered autonomously in all patients.

Conclusions: 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
Luana R. Soares1, Jose Mariano S. Pantoja2, Lecticia Jorge3, Viktoria Woronik1, Cristiane B. Dias4, 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 this 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 70.00±5.24 years old, 60% male, laboratory data at diagnosis were median serum creatinine of 2.02±1.53 mg/dl, hemoglobin of 11.3±4.1 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 Renal Amyloidosis AL 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 other glomerular diseases. In Table 1 has the comparison between patients data according the glomerular disease. [Table]

Conclusions: Renal biopsies were described as median [25,75 percentile] or n[%]. Membranous Nephropathy was the most common histological lesion followed by Amyloidosis AL in aged 65 or over. Highlights the Collapsing glomerulopathy founded in 8.8% of the patients none of them associated with HIV or other disease. Minimal Change Disease was the only case of nephrotic syndrome with acute tubular necrosis in this population, while FSGS had less vascular lesions at renal biopsy.

Funding: Private Foundation Support

Comparative data on diagnosis and after 6 months of follow up according glomerular disease.

PO1880
Clinical Characteristics, Treatment Patterns, and Outcomes of Children and Adults with Biopsy-Proven Minimal Change Disease from the Cure Glomerulonephropathy Network Study (CureGN)
Dhriti P. Chen1, Margaret Helmut2, Rasheed A. Gbadegesin3, Amy K. Mottl4, Debbie S. Gipson4, Katherine Twombley5. The Cure Glomerulonephropathy Network Study (CureGN) University of North Carolina, Chapel Hill, NC; 5Research Collaborative for Health, Ann Arbor, MT; 4Duke University Hospital, Durham, NC; 3University of Michigan Mott Children’s Hospital, Ann Arbor, MI; 1Medical 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] or n[%]. Univariate comparisons were performed using chi-square tests and Wilcoxon rank-sum tests for categorical and continuous variables, respectively. eGFR was winsorized to 120 ml/min in repeated measures models used to assess eGFR over time.

Results: Comparisons by 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/stereoid 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 in adults and in 1 (0.5%) children. Suicide and major complications were observed in 4 (1%) children.

Conclusions: Significant sociodemographic and clinical differences exist between adult-onset versus pediatric onset MCD at the time of biopsy. These differences are most notable in differences in treatment and biopsy practices relative to symptom onset.

Funding: NIDDK Support

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Underline represents presenting author.
PO1881
Clinical Characteristics of Acute Glomerulonephritis with Presentation of Nephrotic Syndrome at Onset in Children
Huipeng Ge, Qiongjing Yuan, Xiangcheng Xiao. Xiayia 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 be good. However, the clinical characteristics of AGN with nephrotic syndrome (NS) at onset have not yet 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 Estimates
Laura Jackson Cases Atlanta Metropolitan Statistical Area and Meta-Analysis of Worldwide Estimation of Childhood Nephrotic Syndrome Incidence: Data from the PO1882

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
Anne M. Schiervens,1,3 Lynne Teeninga,1,3 Eiske Dorrestein,1,3 Nicholas Webb,1,3 Michel F. Schreuder,1,3 Radboudumc, Nijmegen, Netherlands; 2Erasmus MC, Rotterdam, Netherlands; 3Royal Manchester Children's Hospital, Manchester, UK; 4Health Innovation Manchester, Manchester, UK; 5Universitair Medisch Centrum Utrecht, Utrecht, Netherlands.

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/6 mg/kg body weight daily, 4 weeks 40 mg/kg on alternate days) is equally effective as the 12 weeks APN regimen (prednisolone 6 weeks 60 mg/kg daily, 6 weeks 40 mg/kg 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). Interestingly, 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 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 less steroids for the first episode would be beneficial in terms of 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 for 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 <100) with pre-empptive re-dosing after reconstitution was observed.

Results: 16 patients (8 female, 8 male) started B cell targeted maintenance rituximab for up to 2 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

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
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 reach the lowest possible dose. 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 on 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 (2) after 5.2, 9.2, 9.6 months, respectively, and were started on another corticosteroid-sparing agent. The study was discontinued due to apparent lack of efficacy. CD20 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 represented 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 subset (57.4% and 59.0% of memory B cells at 3 and 6 months, respectively, vs 48.3% at baseline, p=0.01). Serum IgG, IgA and IgM levels were not significantly modified.

Conclusions: In this first-in-human study, treatment with belimumab resulted in a marked reduction in urinary PCR (26-54%), which correlated with the degree of glomerular hyposialylation. Baseline plasma ManNAc levels in nephrotic subjects with normal eGFR were similar to those in subjects with normal renal function, but baseline plasma free NeuAc levels were elevated in nephrotic subjects with lower eGFR. This is consistent with NeuAc having high glomerular permeability and little tubular reabsorption. Plasma ManNAc levels peaked 2-4 h after dosing and returned to baseline after ~12 h. Plasma free NeuAc levels peaked ~10 h after dosing, remained elevated beyond 48 h, and continued to increase during twice daily dosing, particularly in subjects with low eGFR. These findings suggest that no adverse effect related to the increased free NeuAc levels was observed. Further studies are needed. These data support twice daily dosing, with reduced doses for subjects with low eGFR.

Conclusions: Oral ManNAc was safe and well tolerated in glomerular 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 - Escala Therapeutics

PO1887 Phase 1 Study of N-Acetylmannosamine (ManNAc) for Glomerular Disease

Background: ManNAc is an uncharged monosaccharide and precursor of N-acetylmannosamine 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, with 6 focal segmental glomerulosclerosis and 1 with membranous nephropathy. Urine protein/creatinine ratio was 1.3 to 9.9 g/g.

Results: One subject received a single dose of 6 g ManNAc.

Results: ManNAc administration was well-tolerated. There were no serious adverse events among 6 subjects (5 of 6) that received ManNAc twice daily. A marked reduction in urine PCR (26-54%), which correlated with the degree of glomerular hyposialylation. Baseline plasma ManNAc levels in nephrotic subjects with normal eGFR were similar to those in subjects with normal renal function, but baseline plasma free NeuAc levels were elevated in nephrotic subjects with lower eGFR. This is consistent with NeuAc having high glomerular permeability and little tubular reabsorption. Plasma ManNAc levels peaked 2-4 h after dosing and returned to baseline after ~12 h. Plasma free NeuAc levels peaked ~10 h after dosing, remained elevated beyond 48 h, and continued to increase during twice daily dosing, particularly in subjects with low eGFR. These findings suggest that no adverse effect related to the increased free NeuAc levels was observed. Further studies are needed. These data support twice daily dosing, with reduced doses for subjects with low eGFR.

Conclusions: Oral ManNAc was safe and well tolerated in glomerular 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 - Escala Therapeutics

PO1888 Efficacy and Safety of ACE Inhibitor and ARB Therapies in Primary FSGS Treatment: A Systematic Review and Meta-Analysis
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Background: Use of ACEi and/or ARB (RASi) as conservative management to control proteinuria in primary and genetic focal segmental glomerulosclerosis (FSGS) follows 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=1.00; 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=6.24, 95% CI: 0.88-6.55). Published data did not allow to evaluate the eGFR ROM between follow-up and baseline and the
effect on the risk of reaching ESRD or RASI therapy alone. Only one controlled study reported adverse effects of RASI as monotherapy. Overall, the available evidence exhibits considerable heterogeneity in cohort baseline characteristics and study design.

**Conclusions:** This review supports the tendency to observe a reduction of proteinuria in patients treated with RASI, and demonstrates the lack of strong evidence to quantify their effect on eGFR and their long-term impact on renal survival. The current lack of properly controlled studies in primary FSGS stresses the need for longer and better designed clinical trials to better understand the effect of RASI.

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

**POI889**

**Efficacy and Safety of Immunosuppressive Therapy in Primary FSGS: A Systematic Review and Meta-Analysis**

Dawn J. Caster,1 Barbara Magalhães,2 Natali Pennese,3 Andrea Zaffalon,2 Marima Faella,2 Kirk N. Campbell,1 Jai Radhakrishnan,3 Vladimir Tesar,4 Howard Trachtman,5 Eunice H. Lui,1 University of Louisville School of Medicine, Louisville, KY; 2LatticePoint Consulting, Geneva, Switzerland; 3Columbia School of Medicine, New York, NY; 4Columbia University Medical Center, New York, NY; 5Howard University College of Medicine, Washington, DC. *Commercial Support - Retrophin, Inc.*

**Background:** Few studies directly compared the presentation and treatment response of nephrotic syndrome (NS) concerning the racial and ethnic differences of different countries.

**Methods:** NEPTUNE is a prospective cohort study of NS across 23 North American centers. Nephrotic Syndrome Registry (N-KDR) is a Japanese retrospective cohort in Nagoya area. Nephrotic FSGS/MCD adults who received immunosuppressive therapy (IST) were included. Demographics and laboratory data of the patients were compared. Time to complete remission (CR: UPCR<0.3) from the start of IST were evaluated (14 studies, ROM=0.34, 95% CI 0.25-0.46). Pooled studies showed a lower CR 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 therapy had uncertain effect on reducing the risk of reaching ESRD (HR=0.79; 95% CI 0.45-1.37) and its impact on long-term renal survival was not clearly demonstrated.

**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 within studies but not across studies. Due to lack of properly controlled studies, it is hard to attribute how much of these outcome 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 - Retrophin, Inc.

**POI890**

**The Epidemiological Comparison Between North American and Japanese FSGS/Minimal Change Disease Patients:**

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**Background:** Few studies directly compared the presentation and treatment response of nephrotic syndrome (NS) concerning the racial and ethnic differences of different countries.

**Methods:** NEPTUNE is a prospective cohort study of NS across 23 North American centers. Nephrotic Syndrome Registry (N-KDR) is a Japanese retrospective cohort in Nagoya area. Nephrotic FSGS/MCD adults who received immunosuppressive therapy (IST) were included. Demographics and laboratory data of the patients were compared. Time to complete remission (CR: UPCR<0.3) from the start of IST were evaluated (14 studies, ROM=0.34, 95% CI 0.25-0.46). Pooled studies showed a lower CR 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 therapy had uncertain effect on reducing the risk of reaching ESRD (HR=0.79; 95% CI 0.45-1.37) and its impact on long-term renal survival was not clearly demonstrated.

**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 within studies but not across studies. Due to lack of properly controlled studies, it is hard to attribute how much of these outcome 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 - Retrophin, Inc.

**POI891**

**Long-Term Renal Outcomes in Focal Segmental Glomerulosclerosis:**

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**Background:** Focal Segmental Glomerulosclerosis (FSGS) is a glomerular disease defined by pathomagnorphic 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 review of the military electronic medical record for International Classification of Diseases 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) compared to 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 report of renal outcomes from initial treatment was associated with a substantial reduction in progression to ESKD (2%, 4%, and 7% at 5, 10, and 15 year 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.

**Funding:** NIDDK Support, Other NIH Support - NCATS

**POI892**

**Cellular Senescence Is Associated with Faster Progression of Renal Disease in Adults with Focal Segmental Glomerulosclerosis:**

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**Background:** A current hypothesis is that an acceleration of cellular senescence, a state of irreversible cell cycle arrest mediated by cyclin-dependent kinase inhibitors, is not only an impaired renal repair but also an indicator of impaired renal repair and of disease progression. Senescent cells are involved in impaired renal repair and in the progression of renal diseases. The functional role of the senescent changes observed in patients with glomerular diseases are unknown and if senescence is really associated with more disease progression is still not understood.

**Methods:** The hypothesis that cell senescence represents a proximate mechanism by which kidney is damaged could be examined among both African American and white patients and was evaluated by Cox proportional hazard model and selected using a backward stepwise method.

**Results:** Eighty-eight eight NEPTUNE and 302 N-KDR cases were eligible. The median of follow-up was 35 and 47 months in NEPTUNE and N-KDR, respectively. In NEPTUNE, 20.7% were African Americans and 26.1% were Hispanic. NEPTUNE had higher proportion of FSGS (55.7 vs. 16.2%, p=0.001). N-KDR cases were older (55 vs. 43 years, p=0.001) and showed more rapid NS onset (0.8 vs. 1.5 months, p=0.004). NEPTUNE cases demonstrated lower level of UPCR (4.20 vs. 8.00, p=0.001) and hypoalbuminemia (2.6 vs. 1.8 mg/dL, p=0.001). In both cohorts, >85% started on steroid monotherapy.

In NEPTUNE, only 1% of patients changed within first 28 days as compared to 10% of N-KDR patients. N-KDR cases showed higher proportion of CR in overall sample (85.7 vs. 42.5%, p<0.001) and in African American (67.4 vs. 42.2%, p=0.015) and in CKD4 (9 vs. 87.2%, p=0.113). Multivariate analysis showed associations of FSGS (HR=0.65, 95%CI: 0.52-0.81), hypertension (HR=0.64, 95%CI: 0.45-0.90), serum albumin (HR=0.62, 95%CI: 0.45-0.85) and eGFR (HR=1.24, 95%CI: 1.17-1.32, for 10 ml/min/1.73m² with time to CR. There were significant interactions between the cohort and hypertension (p=0.008), and between cohort and eGFR (p=0.001).

**Conclusions:** Adult nephrotic FSGS/MCD in the North American cohort showed diverse ethnic background and less severe NS. Japanese patients had a higher rate of response to the IST. FSGS, hypertension, higher albumin, and lower eGFR were considered as shared predictors of renal treatment response between both cohorts.

**Funding:** NIDDK Support, Other NIH Support - NCATS

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POI1893
Clinicopathological 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 laboratory parameters (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 implemented at the time of data collection, overlapping comorbidities and serology were taken in notice

Results: 49 biopsies were analyzed with FSGS. NOS variant was the most common (72%), tip lesion (6%) and collapsing (6%), with no reported perihilar or cellular variants and 3% reported as unsampled biopsy of FSGS. Biopsy with diffuse FPE (>80%) 24 presented with nephrotic syndrome and 8 did not (p=0.010). Remission in biopsy with described diffuse foot process effacement (DFPE) with unidentified cause 32% had complete remission (CR) (serum albumin >3.5 g/dl or <300 mg/24h protein), 16% had partial remission (PR) (≥50% reduction basal proteinuria, subnephrotic proteinuria), and 20% did not remit at a 6 month period (p=0.921). 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 FSGS biopsy, clinical manifestations of patients and history represent the best tools for correct diagnosis and treatment

POI1894
Differentiating 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 gold standard for disease grouping. The purpose of this study is to compare the different diagnostic approaches in a series of patients with FSGS classification based on clinical and histological criteria comparing outcomes

Methods: In a retrospective analysis of 359 kidney biopsies we identified patients with histological diagnosis of primary 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 serum albumin;c)NS with focal foot process effacement or d)non-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, 63% were males, 71% non-black, 74% had HTN, 26% diabetes; median eGFR 26.5 mL/min/1.73m2 (IQR: 15.3-48.8), 24-h proteinuria 4.4 g (IQR 2.5-7.6). Globally, 38% (n=25) progressed to ESKD and mean time to RRT was longer in IST group (p=0.067). 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 66mos (SD±3.3) in IST group. Among secondary FSGS, 17.6% received IST. Of them, 50% developed ESKD in 31.7mo (IQR SD±28.8) 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 that are likely to benefit from such therapies, in order to obtain better outcomes. Most of genetic forms of FSGS do not respond to IST and have a rapid progression to ESKD. Therefore, in a suspicion of a genetic cause a genetic screening should be performed for appropriate management.

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Underline represents presenting author.
PO1897

The Dual Endothelin/Angiotensin II Receptor (ET, R/AT, R) Antagonist Sparsentan Slows Renal Disease, Improves Lifespan, and Attenuates Hearing Loss in Alport Mice: Comparison with Losartan and Atrasantan

Dominic E. Cosgrove,1 Brianna M. Dufek,1 Duane C. Delimont,1 Daniel T. Meehan,1 Gina C. Samuelson,1 Jared Hartsook,2 Grady Phillips,2 Ruth Gill,1 James Hasson,2 Celia P. Jenkinskin,3 Radko Komers,3 Michael Anne Gratton,1 1Boys Town National Research Hospital, Omaha, NE; 2Washington University, St. Louis, MO; 3Retropin, Inc., San Diego, CA.

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 atrasantan (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 (SP06, SP120), LS (20 mg/kg; 3-4 W) or LS (10 mg/kg females or 10 mg/kg males) in the drinking water. Two studies were conducted: early intervention for hearing from 3.8-7.5 W (V, SP120 and LS), and for lifespan with treatment from 3 W (V) or from 3 W (SP60, SP, 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 8-8.75 W. The cochleae were fixed and were preserved and strait pathologically determined by 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/mg meanSD 42±18 AT, 42±18 LS, 42±18 SP60; 20±3 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 but not SP120 treated 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. Sparsentan may therefore offer a novel, dual-therapeutic approach in AS by reducing both renal injury and hearing loss.

Funding: Commercial Support - Retropin, 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 <300 mg/mmol at 5.1 months (median, IQR 2-11). 76/111 (69%) also reached Complete Remission (PCR reduction by 90%) at 15.2 months (9.3-24). 18/111 (16%) did not respond to initial treatment with TAC. 3/18 progressed to ESRD rapidly, 9/18 were treated with Rituximab (RTX), 4/18 with cyclophosphamide (CYP) 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 immunosuppression. 28/48 were retreated with TAC and all achieved remission, 15/48 treated with RTX, remission in 11/15. 3/48 treated with CYP and steroids (2/3 remission, 1 lost to FU). No treatment in 2. 11/28 cases retreated with tacrolimus had a second relapse. At 3 months on TAC there was a reduction of eGFR from baseline (median, IQR 78 ml/min (48-99)) (Figure 2). Renal function stabilised thereafter during the follow up period to 10 years. 10/9% pts reached ESRD and 5/10 within 12 months from diagnosis;these pts had a lower baseline eGFR 48ml/min (23-61).

Conclusions: TAC can be an effective treatment for MN with a relatively rapid response. Lack of response to TAC and low eGFR at presentation are associated with non-response to alternative immunosuppression and ESRD. Relapse is common, necessitating repeat immunosuppression. Most pts maintain eGFR in the longterm.

Funding: Clinical Revenue Support

Table 1. Demographics. Figure 1. Time from remission to relapse. Figure 2. a. eGFR and B. anti-PLA2R levels over time.

PO1899

Etiology, Histology, and Prognosis of Primary and Secondary Membranous Nephropathy in Young Patients Under 50 Years Old: A 35-Year, Two-Center Experience

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Background: Membranous nephropathy (MN) is often diagnosed in older age group; its mean age of onset is 50-60 years old. Although retrospective analyses on young patients with primary MN have been published, most clinicopathologic characteristics of primary MN and secondary MN combined in young patients have not been reported.

Methods: All patients diagnosed with MN in the age under 50 years old by a kidney biopsy performed between January 1985 and December 2019 at Toranomon Hospital and Toranomon Hospital Kajigaya were retrospectively analyzed. All patients with glomerular membranous changes presumed to be due to subepithelial deposits were included except for cases with classic membranoproliferative glomerulonephritis.

Results: 37 patients met the criteria. 19 of them (51%) had nephrotic syndrome, 17 (46%) had hypertensive protein-excretion less than 3.5 g/24 hours, 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%), bicusculine use (3%), and graft versus host disease (GVHD) 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 (z = 6.01, p < 0.001). The CR rates of cases with mesangial deposits (12/21 cases) and those without mesangial deposits (3/6) was not significantly different (z = 0.096, p = 0.76).

Conclusions: The prognosis of renal function was fairly good in patients with MN in the age under 50 years old. Cases with coexisting subepithelial deposits showed lower CR rate than the rest.

PO1900

A Target Antigen-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 unclear whether it is causally related or coincidental. A few THSD7A-associated MN cases have a strong etiologic link with active malignancy, while in others malignancy appears coincidental. Exostosin 1/exostosin 2 (EXST1/EXST2) 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 membranous nephropathy.

Methods: To describe the phenotypes of PLA2R-, THSD7A- and EXST1/EXST2-associated MN, 201 adult patients with biopsy-proven MN were classified using serology, immunostaining and mass spectrometry. Clinical, biochemical and follow-up data were assessed.

Results: 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 (z = 6.01, p < 0.001). The CR rates of cases with mesangial deposits (12/21 cases) and those without mesangial deposits (3/6) was not significantly different (z = 0.096, p = 0.76).

Conclusions: The prognosis of renal function was fairly good in patients with MN in the age under 50 years old. Cases with coexisting subepithelial deposits showed lower CR rate than the rest.
PLA2R-associated MN (n=16) occurred predominantly in middle-aged women: 12 with primary MN and 4 with recurrent MN. Only 1 case of recurred MN-associated MN was identified, with a concomitant malignancy. EXT1/EXT2-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=23, 18%) 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.

Funding: Private Foundation Support

PO1901
Noninvasive Diagnosis of Primary Membranous Nephropathy Using Anti-Phospholipase A2 Receptor (PLA2R) Antibodies: A Validation Study
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Background: Kidney biopsy is the current gold standard to diagnose membranous nephropathy (MN). Approxi mately 70-80% of patients with primary MN have circulating anti-PLA2R antibodies without tissue confirmation, both on histology and immunofluorescence. We designed a protocol to evaluate the usefulness of enzyme-linked immunosorbent assay (ELISA) for the detection of anti-PLA2R antibodies in MN patients.

Methods: We analyzed 128 positive sera from Mayo Clinic and Mayo Clinic Florida patients with MN, with 33 sera having previously reported.

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, monoclonal protein = 5). Of the 42 patients with negative work up for secondary causes, 32 (76%) had preserved renal function. One patient had fibrin thrombi and neutrophils in the capillary loops, and one patient had 1 glomerulus with focal glomerular basement membrane duplication. Thirty-six patients had final diagnosis of MN or MCD. Among the 10 patients with eGFR <60 mL/min/1.73m2, additional findings that altered the treatment plan included acute interstitial nephritis (n=1) and superimposed diabetic nephropathy (n=1).

Conclusion: The study extends our previous observations that in patients with preserved renal function and no evidence of secondary causes or diabetes, a positive PLA2R test by ELISA and IFA confirms the diagnosis of MN.

PO1902
Association Between Anti-Complement Factor H Antibodies and Renal Outcome in Primary Membranous Nephropathy
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Background: The complement factor H (CFH) regulates activation of the alternative complement pathway. Autoantibodies against CFH have been involved in progressive renal dysfunction in a case with primary membranous nephropathy (MN) (Ronco P. et al. N Engl J Med 2018;378:279-81). However, the prevalence and the roles of anti-CFH antibodies in the clinical outcome of MN remains unclear.

Methods: We investigated retrospectively 36 Japanese patients with primary MN (23 males, 13 females; age 64.5 [59-72] years old) and 18 healthy normal controls (8 males, 10 females, age 31 [27-38] years old). Serum anti-CFH antibody titers were measured by enzyme-linked immunosorbent assay (Vidia VestaC, Czech Republic) to evaluate the association between anti-CFH antibody titers and the clinical outcome of MN patients.

Results: Anti-CFH antibody titers were significantly higher in MN patients as compared with normal controls [4.69 (3.60-6.38) IU/mL vs. 0.0 (0.0-0.0) IU/mL, p <0.001]. Twenty-eight patients were classified into the anti-CFH antibody positive group. The other 8 patients were classified into negative group. According to the Kaplan-Meier method, no significant difference was observed in the complete or incomplete remission rate of proteinuria, the incidence of renal dysfunction by the 30% reduction in estimated glomerular filtration rate (eGFR) and 50% elevation of serum creatinine (s-Cr) levels between the anti-CFH antibody positive group and the negative group of MN patients, however. In MN patients, anti-CFH antibody titer was selected an independent unfavorable predictor of renal dysfunction in Cox proportional hazards analysis adjusted by age, gender, sCr levels, proteinuria (g/gCr), anti-CFH antibody titer and immunosuppressive therapy (adjusted hazard ratio (HR) 1.344, 95% confidence intervals (CI) 1.038 to 1.741, p=0.025 for 30% reduction of eGFR, adjusted HR 1.930, 95% CI 1.180 to 3.363, p=0.020 for 50% elevation of sCr).

Conclusions: These data suggested that anti-CFH antibodies may be involved in the deterioration of renal function in primary membranous nephropathy.

PO1903
Concurrent Anti-Glomerular Basement Membrane Nephritis and Membranous Nephropathy

Background: Anti-GBM nephritis is an uncommon entity with a rapidly progressive course. The concurrence 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 PLA2R negative. Patients were predominantly Caucasian (N = 9). All patients required hemodialysis (HD) at presentation, and two patients, a 28-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 prednisone (N=1); prednisone and plasmapheresis (N=1) and rituximab alone (N=1).

Conclusions: Concurrent anti-GBM and MN is a rare entity presenting with severe AKI and renal failure. 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 predominately PLA2R 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±1.5 years). Overall there was 22% graft loss (mean time 6.5±2.7 years). Two patients died, both on HD, one 16 years later from unknown cause and one 3 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 no crescents (82% crescents, and 25%, 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 renal failure. Recurrent membranous nephropathy is rare. 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 PLA2R negative. Patients were predominantly Caucasian (N = 9). All patients required hemodialysis (HD) at presentation, and two patients, a 28-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 prednisone (N=1); prednisone and plasmapheresis (N=1) and rituximab alone (N=1).

Conclusions: Combined anti-GBM and MN is a rare entity presenting with severe AKI and renal failure. 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 predominately PLA2R negative, and further studies into pathogenesis are needed.
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 hydrenephrosis. 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 anaarca. 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/lyphilis antibodies, Hepatitis, HIV, ANCA, Anti-GBM Ab and normal C3,C4 levels. CT of torso was negative for overt malignancy or hepatosplenomegaly. Patient’s hemoglobin ranged between 16.5- 18.5 g/dl (ht 52-60%). Serum erythropoietin level was 12.3 IU/L (Normal 5-30IU/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 2 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 will need further evaluation. This patient is on Apixaban for prophylactic anticoagulation in setting of severe hypoalbuminemia. Hence, prophylactic anticoagulation should strongly be considered in these patients.
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 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 unrevealing, 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 diuretic. Cyclosporin caused gastrointestinal upset, and so patient switched to tacrolimus. He again had increasing swelling, and represented 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.

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.

PO1911
Utility of Immunofluorescent Intensity of IgG3 and Phospholipase A2 Receptor-to-IgG4 Ratio to Presume the Prediction 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 eGFR 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 eGFR (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: 0.0 in HR vs 0.9 in HR vs 0.5 in LR, p=0.049; PGIR: 0.55 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 of the thyroid disease with radioiodine.

Case Description: A 33-year-old healthy female was seen for 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 hepatitis B and C, HIV, RPR, ANA, C3, C4, cryoglobulins, immunofixation, and free light chains were normal. Renal biopsy was performed 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 (0.8-1.7). 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.
PO1913

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 SLEDAl4 despite stable background therapy received KZR-616 at doses of 45mg (Cohort 1), 60mg (Cohort 2), or 60mg following a step-up dose (Cohorts 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 60 mg 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 improvement 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

PO1914

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 11/13 (85%) at 36 mo. 17/19 (89%) had continuous B cell depletion at 12 mo, 13/14 (93%) at 24 mo, and 11/12 (92%) 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.

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

Underline represents presenting author.
23.2 to 9.04, respectively. The doses of prednisolone (mg/day) decreased in both groups. The IgG level decreased from 1377 to 1204 (mg/dL) in N group and from 1009 to 865 in R group. In 18 patients with urinary protein of 0.2 to 0.4 g/CR or more, proteinuria significantly decreased from 0.54 to 0.20 to 0.23 (g/gCr) and DNA antibody improved from 67 to 34 to 35.1 (U/mL) at 3 and 6 months after BCl therapy.

**Conclusions:** BCl may improve SLE activities and also renal function in patients with renal insufficiency as effectively as in those with normal renal function, although hypogammaglobulinemia comparably develops in both groups.

**POI1916**

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 purchased MRL/lpr mice from the Jackson Lab. Eligibility criteria included female and 13-14 weeks old. Mice were randomized at a 1:1 ratio and orally dosed with 20 mg/kg/day of baricitinib or vehicle for 4 weeks. Samples were assembled for blinded analyses, including histology, which was assessed by an independent pathology institute. The primary endpoint was proteinuria.

**Results:** A total of 55 mice were randomly assigned to the vehicle (n=28) and baricitinib group (n=27). Baricitinib-treated mice showed a trend towards decreased proteinuria, but this did not reach statistical significance (p=0.104). In contrast, plasma total IgG and lymphadenopathy score were significantly improved in the baricitinib group. In the vehicle group, at the initiation of treatment, self-breed mice had less proteinuria, but this did not reach statistical significance (p=0.104). In contrast, plasma total IgG and lymphadenopathy score were significantly improved in the baricitinib group.

**Conclusions:** In a pRCT, targeting Jak1/2 with baricitinib for 4 weeks had no significant effect on the primary end-point proteinuria in MRL/lpr mice, whereas total plasma IgG and lymphadenopathy score significantly improved. Mice of different origins had different lupus phenotypes and increased the variability. Placebo controlled multicenter trials are feasible in animal models of lupus, however, standard deviations may increase due to multiple factors, which requires higher numbers of animals.

**POI1917**

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 (ramp 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 AURORA (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 AURORA.

**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/gCr ● eGFR ≥ 60 mL/min or 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 31.7%; control 20.3%); [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 group and 21.5% in control. No difference was observed in glomerular sclerosis at 1 year. The largest estimated eGFR change from baseline for VCS vs control-treated patients occurred early, at week 4, (−5.6 mL/min, p < 0.0001) which decreased to −3.7 mL/min in week 52 (p = 0.0012). Mean change from baseline of eGFR in the VCS arm at week 52 was −1.0 mL/min (p<ns). Finally, serious adverse events were similar between groups (20.5% VCS vs 18.8% control).

**Conclusions:** This integrated analysis provides further support to the efficacy of VCS seen in both AURA-LV and AURORA 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 patient 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; NCT01693359).

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: 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 4.9) 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 multivariate 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.

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.

PO1920
Predictors of Doubling of Serum Creatinine at the Time of Biopsy in a Lupus Nephritis Cohort
Jaime (James) A. Vondenberg, Saeed K. Shaffi, University of New Mexico, Albuquerque, NM.

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 Cox 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 4.9) 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 multivariate 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.

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.

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 Databases. 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 adjust 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 1.17-1.61, P<0.0001). SLE with lupus-related renal disease hospitalizations had a mean increase in adjusted LOS of 1.14 days (95% CI 1.05-1.24, P=0.0001) compared to SLE without lupus-related renal disease. SLE hospitalizations for SLE with lupus-related renal disease had an increase in adjusted total hospital charges of $15,910 (95% CI 13,085-18,736, 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.
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 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 (4 vs. 3.6 [IQR: 2.8–6.0] days), p<0.05), higher systolic blood pressure (143 ± 22 vs. 135 ± 20, P<0.05), higher diastolic blood pressure (87 ± 10 vs. 78 ± 9, P<0.05), higher percentage of methotrexate treatment (55.7% vs. 44.6%, 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. Compared to the non-septic group, higher proportion of patients with GI bleeding(8.5% vs. 0.0%, P<0.05), and higher severity of infection scores(26.0 ± 10.3 vs. 10.0 ± 6.3, P<0.05), higher proportion of puse therapy (65.7% vs. 26.3%, P<0.05) and higher severity of infection scores(26.0 ± 10.3 vs. 10.0 ± 6.3, P<0.05), while higher level of serum creatinine(134.0 ± 88.0 [IQR: 0.0–38.0], P<0.05), C reactive protein(43.8 ± 12.3, P<0.05), and erythrocyte sedimentation rate(60.0 ± 45.5 mm/h, P<0.05) can be seen in the sepctic group. Multivariable Logistic regression analysis revealed that male and pulse 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 toxicity increases the risk of organ damage (OD), including renal OD. Despite the high prevalence of OD and the associated poor disease prognosis, real-world studies on the economic impact of OD, especially renal OD, in SLE are limited.

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.1 Inclusion criteria: i) age ≥18 years; ii) continuous enrollment 12 months both pre and post index (index: date of first observed OD medical claim); iii) inpatient (IP) or ≥3 outpatient (OP) claims separated by ≥30 days for SLE (ICD-9: 710.0 or ICD-10: M30.X); iv) 64 [IQR: 45–84] ml/min/1.73 m². The lupus cohort predominantly consisted of females and class IV lupus nephritis. Many patients of Hispanic ethnicity identified as White with respect to race. At the time of lupus nephritis diagnosis, antibody status, serum creatinine, and urine spot protein/creatinine ratio were similar among ethnicities. Hispanics were more likely to be non-infected and use ibuprofen. The most common maintenance therapy was follow by MMF, and the most common maintenance therapy was MMF.

Results: A total of 8952 patients met OD criteria and 486 (5.4%) had renal-specific OD medical claim); 30 days for SLE (ICD-9: 710.0 or ICD-10: M30.X); 64 [IQR: 45–84] ml/min/1.73 m². The lupus cohort predominantly consisted of females and class IV lupus nephritis. Many patients of Hispanic ethnicity identified as White with respect to race. At the time of lupus nephritis diagnosis, antibody status, serum creatinine, and urine spot protein/creatinine ratio were similar among ethnicities. Hispanics were more likely to be non-infected and use ibuprofen. The most common maintenance therapy was follow by MMF, and the most common maintenance therapy was MMF.

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. Glidman DD 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 (Pcr/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 ≥ 1:80), anti-dsDNA positive (73%), anti-Smith positive (56%), and SS-A positive (56%). The most common comorbidities were hypertension (n=46) and depression (n=16). For induction therapy, 11 patients received low dose cyclophosphamide (CYC) (41%), and Non-Hispanics received mycophenolate mofetil (MMF) (35%). For maintenance therapy, both Hispanics (37%) and Non-Hispanics (35%) most often received MMF. 7 patients progressed to ESKD, by ethnicity: 5 Hispanic and 2 Unavailable (1 African American). Male and pulse methylprednisolone treatment within 1 month were independent risk factors of sepsis in patients with lupus nephritis (P<0.05).

Conclusions: In patients with SLE and OD, annual costs increased after OD

Conclusion: We demonstrated the utility of CI and 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

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

Underline represents presenting author.
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 fractional charge index (FCI) which 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>1). Kidney biopsies were evaluated by standard IF microscopy (IgG, IgA, IgM, C3, C1q), 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 (0-8.0). 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 IF 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 AI1 (P=0.0005). 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 Bx3 had an LN flare during a follow-up of 44 months (19-105).

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 relyas 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 is a single center retrospective chart review of LN patients from 2010-2019. Inclusion criteria were adult patients with native kidney biopsy proven LN documented in chart. Patients with systemic thrombotic microangiopathy (TMA) or possible secondary cause of renal TMA (other than SLE) were excluded. Two groups were identified for comparison, LN without vasculopathy (WOV) and LN with vasculopathy (WV). Vasculopathy was defined from kidney biopsy as vascular sclerosis (at least grade 3A). Patients with LN-WV induction IS regimen was MMF in 52%, and CYC in 23%. At baseline, mean baseline serum 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 8 (15%) in LN-WV, p = 0.86.

Conclusions: In our cohort, both groups of LN-WO 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.

Urine Epidermal Growth Factor Levels Are Associated with Kidney Prognosis in Lupus Nephritis
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Background: Epidermal growth factor is a protein specifically synthesized in the kidneys. EGF urine levels have been associated with progressive chronic kidney disease. This study evaluated the role of urine epidermal growth factor (uEGF) as a biomarker of chronic kidney damage in lupus nephritis (LN).

Methods: Through a proteomic approach we identified uEGF as a biomarker of interest in an LN discovery cohort. The expression of uEGF was characterized in two large multiethnic LN cohorts, and the association between uEGF at flare and long-term outcomes assessed in a subset of 120 patients. The expression of uEGF over time was observed in two longitudinal LN cohorts in which serial urine samples were collected.

Results: The proteomic analysis showed lower uEGF in patients with active LN than in normal controls. The peptide sequence was consistent with the proEGF isoform, and this was confirmed by immunoblotting. These findings were verified by ELISA. Patients with active LN had a significantly lower levels of uEGF than patients with active non-renal lupus, patients with inactive lupus, and kidney donors. Urine EGF was inversely correlated with the kidney biopsy chronicity index (r=−0.67, p<0.001). Multivariate survival analysis showed that uEGF at flare was associated with the time to doubling of serum creatinine (HR 0.88, 95% CI 0.77-0.99, p=0.045). In patients who progressed to doubling of serum creatinine (Figure 1A) and end-stage kidney disease (Figure 1B), uEGF was lower at flare and then decreased over the 12 months following flare. A uEGF cutoff of 44 months identified all patients who progressed to end-stage kidney disease.

Conclusions: Urine EGF levels correlate with histologic kidney damage. Low uEGF levels at flare and decreasing uEGF levels over time are associated with adverse long-term kidney outcomes.

Funding: Other NIH Support - NIH - NIAMS

Idiopathic Hypokalemia in Lupus Nephritis: A Previously Unrecognized Entity
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Background: The lupus nephritis (LN) population at Parkland Hospital is among the largest in the country. During the course of usual care in this population, we encountered a phenomenon of unexplained hypokalemia that has never been previously described. Here we begin to phenotype this cohort by comparing it to a group of LN controls as well as LN with distal renal tubular acidosis (RTA).

Methods: From our population of 403 LN patients followed in the Parkland Hospital and Immunology System, we identified a cohort of 20 patients with idiopathic hypokalemia (HK). This cohort is compared to 90 LN controls (control) and 10 LN patients with distal RTA (RTA). In contrasting the three groups, the Chi-squared test or Fisher’s exact test were used for categorical data and the one-way ANOVA or Kruskal-Wallis test was used for continuous measures. For paired comparisons of continuous variables between the groups, the student’s t-test was employed.

Results: The HK cases had lower mean serum potassium compared to control and RTA (3.24 vs 4.06 to 3.75 mmol/L, respectively; P= 0.001). The mean serum bicarbonate was normal in HK and control but lower in RTA (25.83 vs 25.20 vs 19.28 mmol/L, respectively; P= 0.001). The urine pH was abnormally high only in the RTA group (6.13 vs 6.22 vs 19.28 mmol/L, respectively; P= 0.001). There were differences in serologic markers of autoimmunity. Compared with control, both HK and RTA were more likely to be seropositive for anti-RNP (P= 0.002 and 0.15, respectively). In contrast, compared to controls, only HK expressed a higher rate of anti-RNP seropositivity (P= 0.002) and only control-RTA had a higher rate of anti-SSB positivity (P= 0.044).

Conclusions: A syndrome of idiopathic hypokalemia was revealed in 20/403 (5%) of patients within our lupus nephritis population and is distinct from the RTA that is
known to rarely occur in lupus. This phenomenon has not been previously described. We speculate that this hypoplastic holokemia 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 5R01DK09728-13

PO1930
Outcomes of Lupus-Related Glomerular and Tubulointerstitial Disease: Analysis of the National Inpatient Sample

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Background: The study aims to compare the differences in outcomes of hospitalizations for Systemic Lupus Erythematosus (SLE) with glomerular and tubulointerstitial related renal disease. The outcomes compared were inpatient mortality, 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 hospitalization database in the United States (U.S). The NIS was searched for adult SLE hospitalizations with lupus-related glomerular and tubulointerstitial disease as principal or secondary diagnosis using ICD-10 codes. The analysis was done using STATA. Multivariate 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<0.004), 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 (6.4 ± 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 hospitalizations. 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.

PO1931
Lupus Podocytopathy Systematic Review

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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 mesangial 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 which is a rare but important disease entity in lupus patients with renal disease. The treatment and possible prognosis of lupus podocytopathy patients are different from proliferative and membranous lupus nephritis, and physicians should be aware of this process. Patients can be spared from unwarranted immunosuppressive medications and their side effects. Greater collaborations and biopsies are needed to learn more about this interesting disease process.

PO1932
Extended Follow-Up of Patients Recruited to a Randomized, Controlled Trial of Rituximab vs Azathioprine, After Rituximab Remission Induction for Patients with Relapsing ANCA-Associated Vasculitis

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Background: RTX is an effective remission induction therapy in AAV. However, the effect of RTX is not sustained, and relapse rates are high, especially in patients with a history of relapse. The RITAZAREM trial was an international, open-label, randomized, controlled trial of patients with AAV with relapsing disease comparing the efficacy, after induction of remission with RTX, of repeat dose RTX or AZA as relapse prevention strategy.

Methods: Patients with relapsing AAV received induction therapy with RTX and glucocorticoids (GC). If remission was achieved by month 4, patients were randomized 1:1 to receive RTX (1000 mg every 4 months for 5 doses) or AZA (2 mg/kg/day) as maintenance therapy for 24 months. Patients continued to be followed until at least 36 months after enrolment, with a primary outcome of time to disease relapse. The final patient reached month 36 in the trial in November 2019.

Results: 190 patients were enrolled and 170 randomized at month 4 (85 to RTX; 85 to AZA): median age = 59 years (range 19-89); prior disease duration = 5.3 years (0.4-38.5); 123/170 (72%) with anti-PR3 ANCA, 47/170 (28%) with anti-MPO ANCA; 161 (94%) enrolled after a severe relapse, 66/170 (39%) after a non-severe relapse; GC induction regimen: 48/170 (28%) higher-dose, 122/170 (72%) lower-dose; 114 (67%) patients had prior renal involvement. We previously presented the results demonstrating the superiority of rituximab over azathioprine during the maintenance treatment period. Results of the follow up phase of the study after discontinuation of maintenance therapy will be presented at the 2020 meeting.

Conclusions: The results of the extended phase of RITAZAREM will examine the long-term impact of B cell depletion in patients with AAV on sustaining remission beyond the treatment period, clinical or biomarker factors associated with risk of relapse, and post-treatment safety of prolonged use of rituximab, including a focus on hypomunoglobulinemia.

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PO1933
Renal Disease During Maintenance Treatment in ANCA-Associated Vasculitis (AAV) Remains a Problem and Glucocorticoid Use Is High

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Background: AAV is a relapsing remitting long term condition and patients are at risk of organ damage from active AAV and therapy in particular glucocorticoids (GC). The remission maintenance phase of AAV is critical for good long term renal outcomes. This retrospective study examined the pattern of renal disease during the maintenance phase in AAV patients managed in routine clinical practice.

Methods: 1478 AAV patients managed by 493 EU physicians (61% Nephrologists) who completed induction therapy for organ/life threatening AAV and initiated therapy between 2014-16 were studied. Data were collected from when maintenance was determined to begin by the physician and then after 6, 12, 18 and 36 months.

Results: 49% had GPA; mean age 54.2 years and 56% male. 49% had incident AAV and 51% were studied from relapse. 70% received cyclophosphamide/GC and 36% received rituximab/GC with 28% plasma exchange. Physicians defined time of start of maintenance as mean of 5.7 months from diagnosis. Over 36 months from maintenance start 38% patients had relapse (26% 1, 8% 2, 3% 3 and 1% 4). Only 22% had no morbidity at diagnosis, hypertension and renal impairment were common. eGFR CKD stage changed over time - stage 5 (8% to 11%), stage 4 (12% to 8%), stage 3 (43 to 37%) and stage2/3 (38 to 46%) – mean at 36 months of 53.3 ml/min. Hypertension and renal impairment were frequent comorbidities and renal related AEs were often reported. Many patients stayed on GCs and renal impairment and hypertension as well as active/chronic vasculitis activity were more frequent in patients remaining on GCs throughout maintenance. Renal function worsened in 24% patients and 46% were still receiving steroids vs 35% and 37% of those with improved or unchanged renal function (p<0.05)
PO1934
Cost-Effectiveness of Maintenance Therapy with Azathioprine vs. Rituximab (Tailored vs. 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 now 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 professional services. 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 1536 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 compare 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. Subcutaneous 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 CD3/4/8 and NK cells were preserved in all patients. The majority of patients (n=4) experienced recurrent URRs, 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
Peter A. Rutherford, Dieter K. Goette. Vifor Pharma Ltd, Glatthurg, Switzerland.

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 rheumatology centers in France, Germany, Italy, Spain and UK who completed induction therapy for organ or life threatening AAV(49%
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 62 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 (58.8%) 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.

AAV prescribing (**p<0.05 vs respective highest/lowest country)

PO1938

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 (age65-74 years) which was sub-divided into elderly group (age 65-74 years) and very elderly group (age 75 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 = 0.003 and P = 0.001). 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.

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PO1940
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 Berden score is inconsistent at predicting renal outcomes across different cohorts. Furthermore, treatment related morbidity remains a major problem. Brix et al. recently published a clinic-pathological score to predict End-Stage Kidney Disease (ESKD), using 3 parameters to stratify patients into 3 risk groups. Parameters include: percentage normal glomeruli (N0 ≥25% = 0 points, N1 10 to 25% – 4, N2 <10% = 6), percentage tubular atrophy and interstitial fibrosis (T0 ≥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 (RDkD) 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), Polymyalgia Rheumatica 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 5-95 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 (6.8%) 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 28 (41.8%) of them required permanent renal replacement therapy. 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 clinic-pathologic parameters using a regression tree analysis.

PO1941
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 vasculitis (AAV). Real life data assessing its predictive role in renal outcomes are 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 normocomplementemic 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 normocomplementemic patients (n=36). On univariate analysis, serum C3 at diagnosis (HR=16.8, 95% CI: 1.354-206.62, 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.

PO1942
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 pauc-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 scleroderma.

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 P/MPO-ANCA positive, had less impaired kidney function at presentation and a lower probability of relapse after achieving remission, compared to patients without a PMH of autoimmunity.

PO1943
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 pauci-immune (PI) vasculitis 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 anti-neutrophil 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**  
**Sam Kant, Anne Le, Nabeel Attarwala, Duvuru Geetha. Johns Hopkins University School of Medicine, Baltimore, MD.**

**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 vasculitides (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 AAV associated GN.

**Methods:** Ten patients with AAV renal disease having 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 extracted and 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**  
**Phizhog Edgin,1 Precious Eseason,2 Augustine Manadan.1,2 John H Strger Hospital of Cook County, Chicago, IL; 1University of Benin Teaching Hospital, Benin City, Nigeria; 2Rush University Medical Center, Chicago, IL.**

**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 used 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 1.0% (GPA) patients (5.1%) compared to 0.9% (5.1%) who had deaths occurred in GPA with renal involvement vs 585 (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 increase 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 was 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 were higher 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 Inflammatory and Patient Outcome in Chinese Patients with Myeloperoxidase-ANCA-Associated Glomerulonephritis**  
**Wei Lin, Zhong Yong. Department of Nephrology, Xiangya Hospital, Central South University, China, Changsha, China.**

**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 acute tubular necrosis (ATN) has also been reported in AAV with ANCA. Patients 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:** To determine clinical and immunological characteristics of AAV in Chinese patients. Clinical and immunological indexes were measured on admission. Immunological indexes (anti-MPO, anti-PR3, anti-GM, anti-GBM, anti-citrullinated protein antibody (AICA-Ab)) were detected. The diagnosis was retrospectively analyzed.

**Results:** Patients with low sC3 (<790 ml/L) and low sC4 (<100 ml/L) at diagnosis showed poorer renal survival compared to patients with normal value (p=0.003, 0.011). Moreover, 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 (a≥2 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=0.031) 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**  
**Ajay Jarval, Sanjay Vikrant. Indira Gandhi Medical College, Shimla, India.**

**Background:** Anti glomerular basement membrane (GBM) crescentic glomerulonephritis (CsGN) 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 CsGN admitted in our hospital from September 2018 to November 2019 was done. Anti GBM CsGN was diagnosed on the basis of 50% crescents on kidney biopsy and immunofluorescence showed IgG deposition along GBM and/or by the presence of anti GBM antibodies. Rsults: 11 patients were admitted with anti GBM CsGN, 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 3 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 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).
Conclusions: In our study most of the patients presented late to the hospital due to vague symptoms at the onset (mean 30 days) and few had co-existing UTI (this delayed the treatment). 63.6% were dialysis requiring at presentation and DAH was the most common cause of in-hospital death. Two out the three survivors achieved normal eGFR (one in CYC and one in RTx arm) whereas third one had no progressive decline in eGFR (RTx). The use of RTx along with HDS and PP showed favourable outcomes in our study.

PO1948
Impact of Race on Hospitalization Outcomes for Goodpasture Syndrome in the United States

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Background: Goodpasture’s syndrome is a rare and life-threatening autoimmune disease. While Goodpasture’s syndrome is well described in Caucasian and Asian populations, its prevalence and outcomes among African Americans and Hispanic populations are unclear. We conducted this study to assess the impacts of race on hospital outcomes among patients with Goodpasture’s syndrome.

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 and Hispanics were comparable to 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.

PO1949
Overlap Syndrome of Antineutrophil Cytoplasmic Antibody-Associated Vasculitis and IgG4-Related Disease: Distinct Clinicopathologic Clues for Precise Diagnosis

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Background: Both antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) and IgG4-related disease (IgG4-RD) are multi-system inflammatory disorders. The coexistence of both diseases present 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.

Methods: A case of a 67-year-old man in our hospital who exhibited the characteristics of both AAV and IgG4-RD was presented. The treatment response and outcome of the case were followed up for the next 15 months. Then, a systematic literature review of the overlap syndrome of AAV 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, especially with IgG4-related tubulointerstitial nephritis. Glucocorticoids combined with cyclophosphamide therapy led to partial remission. Literature review of 52 cases met both AAV and IgG4-RD criteria as overlap syndrome and four common clinicopathologic features were identified. First, atypical clinical and laboratory manifestations were characteristics of this entity. Second, positive MPO-ANCA are more common. Third, tissue symptoms showed overlapping histological patterns when kidneys were involved. Fourth, the combination of glucocorticoids and immunosuppressive therapy was often required and led to a remission within 3 months.

Conclusions: AAV may overlap with IgG4-RD while presenting atypical manifestations. Four common clinicopathologic characteristics could be used as specific clues to the diagnosis of overlap syndrome.

PO1950
Anti-IL-5 Therapy in Eosinophilic Granulomatosis with Polyangiitis (EGPA): An 18-Month Follow-Up Study of a Steroid-Sparing Therapeutic Approach

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Background: EGPA is a small vessel vasculitis with protein renal manifestations including necrotizing glomerulonephritis, eosinophilic interstitial nephritis and obstructive uropathy. In the randomized, placebo-controlled MIRRA trial for relapsing and refractory EGPA, adjuvant therapy with 300mg anti-IL-5 mAB Mepolizumab (MEPO), accrued lesions in remission, reduced steroid exposure and reduced relapse rates.

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-IL-5 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 (x2) 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 is a 50% reduction in steroid dosage in this study, with preserved renal function.

PO1951
Pauic-Immune Lupus Nephritis: A Case Report

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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, dysnea, 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 she had pancytopenia and generalized edema, blood pressure of 170/90mmHg. Rest of the examination was normal. She had severe anemia, renal failure, positive ANA, dsDNA and direct Coomb’s test, with normal complements. There was no evidence of acute hemolysis. SLE was consistent with Auto immune hemolytic anemia (AIHA) and probable lupus nephritis (LN) was diagnosed. Steroid pulse was started with stabilization of renal function and mebipoglobin. Renal biopsy showed necrotising 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 hemolysis.
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 (EVAlI). We present a case of ANCA (antineutrophil cytoplasmic antibody) vasculitis with atypical Anti GBM (glomerular basement membrane) antibody in a patient with EVAlI.

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. Nephropathy 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 initially and subsequently Rituximab. Four

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 of pulmonary and renal injury from a common mechanism. While the pathogenesis of vaping associated renal injury is unclear, examination of the urinary sediment should be performed in all patients presenting with vaping associated lung injury and hematuria.

PO1953

Sabotaged: Hydralazine-Induced ANCA Glomerulonephritis

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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: 77yo 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 1.9. Dysmorphic RBCs were seen in the urine sediment and proteinuria at 1.2g/g. Given concern for anti-GBM, she received 1g of 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 titers 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 neutrophil 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.

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

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Rare Case of Silicosis-Induced Pauci-Immune Glomerulonephritis

Sandheep Venkataraman, Matthew Ray, James F. Dylewski. University of Colorado, Denver, CO.

Introduction: 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 free radical generation is a proposed mechanism for this disease. Duration and intensity of silica exposure are known risk factors. In addition to pulmonary-renal symptoms, these patients may have systemic manifestations of lupus, rheumatoid arthritis, scleroderma, or dermatomyositis. More research is needed to further understand the management of these patients. This patient represents a rare case of 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 free radical generation is a proposed mechanism for this disease. Duration and intensity of silica exposure are known risk factors. In addition to pulmonary-renal symptoms, these patients may have systemic manifestations of lupus, rheumatoid arthritis, scleroderma, or dermatomyositis. More research is needed to further understand the management of these patients. This patient represents a rare case of 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.

ANCA-Negative Small-Vessel Vasculitis with IgG4-Positive Plasma Cell Infiltration: A Case Report and Literature Review

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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 PICGN with IgG4-positive plasma cell infiltration.

Case Description: A 60-year-old male 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 storiiform fibrosis and obliteratorive 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.

Adalimumab-Associated Pauci-Immune Glomerulonephritis: Coincidence or Causation Effect?

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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 polyps 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) 9.9 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 renalomegalgy. 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 Retroperitoneal Fibrosis and Periaortitis

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Introduction: Granulomatosis with Polyangiitis (GPA) is a type of small vessel vasculitis that has prevalence rate of 25-150 cases per million population, and a incidental rate of 0.4 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 retroperitoneal 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 ureteric stenting, serum creatinine failed to improve. Further urinanalysis demonstrated an active urinary sediment; hemoproteinuria. Serum c-ANCA and PR-3 antigen titers were positive. Renal biopsy was performed and confirmed pauci-immune vasculitis. The patient was induced with pulsed intravenous methylprednisolone and cyclophosphamide and as part of his maintenance treatment received plasmapheresis and oral cyclophosphamide. On follow up, partial remission has been achieved with his serum creatinine remaining between 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 retroperitoneal fibrosis. Few case reports and series have described this association, inferring a pathogenic role of ANCA in the development of retroperitoneal fibrosis. Moreover it has been suggested that retro peritoneal fibrosis may be an early clinical manifestation of ANCA associated vasculitis. Consequently, ANCA associated vasculitis should be considered in the differential diagnosis of any patient who has Retroperitoneal fibrosis and an active urinary sediment.
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/microliter, 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 4.3 g, 24 hour urine protein of 4.1 g, low C3 and C4, hemoglobin of 9.6 g/dl and WBC count of 3.6/microliter. 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 8.5 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 nephrotic range proteinuria is collectively termed as LP. LP must be considered in patients with lupus presenting with NS (Nephrotic Syndrome). It is cardinal that we consider adding this distinct entity in the classification of lupus nephritis.

Minimal Change Disease in Systemic Lupus Erythematosus: An Infrequent Variant

Ehsun Naecm, Paul S. Kellerman, Saima Mansuri. Beaumont Health, Royal Oak, MI.

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 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 seen 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. The 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.

Oliginacut Protects Renal Function and Podocytes in In Vivo and In Vitro Models of Podocytopathies

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Background: The nitric oxide (NO) receptor soluble guanylate cyclase (sGC) is a signal-transduction enzyme producing the secondary messenger cGMP. Impaired NO-sGC-cGMP signaling is associated with renal dysfunction. sGC stimulators, such as olinciguat, which enhance NO-mediated cGMP signaling, improve renal function in animal models of cardiac injury.

Methods: We studied the renoprotective effects of olinciguat, 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 olinciguat attenuated proteinuria and kidney pathology when compared to vehicle-treated mice. Additionally, olinciguat 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 olinciguat. To further assess the protective effect of sGC stimulation on podocytes, human podocytes injured by exposure to proline-sulfate (PS) were treated with olinciguat. Olinacutin stimulation restored PS-induced damage of podocyte actin cytoskeleton organization and the localization of podocyte cell membrane proteins. In the genetic MRL/MpFas−/− mouse model of systemic lupus erythematosus (SLE), disease progression, assessed by interstitial inflammation and albuminuria, was significantly reduced in mice treated with the positive control cyclophosphamide or with olinciguat than in vehicle-treated mice. Fewer kidney lesions (interstitial infiltrates, tubular atrophy, tubular epithelium vacuolation, tubular and interstitial lesions, and glomerular lesions) were observed in mice treated with cyclophosphamide or olinciguat than in vehicle-treated mice. In contrast to cyclophosphamide, olinciguat treatment did not result in leukopenia, reduction in spleen weight, or lower anti-dsDNA antibody in serum, suggesting that olinciguat did not impact the auto-immune aspect of SLE.

Conclusion: In summary, olinciguat, 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 - Cynternet

Oliginacut in a Rat FSGS Model

Yossi Danon, Hari Raghu, Tingting Ge, Liron Walsh, John F. Reilly. Goldfinc Bio Inc. Cambridge, MA.

Background: Activation of Rac-related C3 botulinum toxin substrate 1 (Rac1) plays a key role in podocyte injury and dysfunction in focal segmental glomerulosclerosis (FSGS) and diabetic nephropathy (DN). In diseased podocytes, Rac1 activation is mediated by calcium influx through the transient receptor potential canonical 5 (TRPC5) ion channel. GFB-887 is a sub-type selective, small molecule inhibitor of TRPC5 that reduces albuminuria in deoxycorticosterone acetate (DOCA)-salt and ZSD rat models of FSGS and DN, respectively. Here, we aimed to develop a urinary biomarker to assess podocyte Rac1 activity in kidney disease and in response to GFB-887 treatment.

Methods: Using a sandwich ELISA, we measured Rac1 concentrations in sera of male rats treated with GFB-887 in a rat FSGS model following treatment with GFB-887, and in urine from healthy volunteers, FSGS, DN and Alport patients.

Results: Rac1 was detected in extracellular vesicles (EV) isolated from podocyte culture supernatant and rat and human urine. GFB-887 treatment lowered urinary Rac1 concentrations in normal and DOCA-salt rats, and the decreased Rac1 was associated with decreased albuminuria in the DOCA-salt rats. Urinary Rac1 concentrations were markedly elevated in FSGS and DN but not in Alport patients.

Conclusion: The TRPC5 inhibitor, GFB-887, targets the TRPC5-Rac1 pathway and suppresses urinary Rac1 associated with its therapeutic action in a rat model of FSGS. Urinary Rac1 concentrations are markedly higher in FSGS and DN compared to healthy subjects, but not elevated in Alport. GFB-887 is efficacious in rodent models of FSGS and DN, but not in Alport, suggesting that elevated urinary Rac1 is predictive of response. Together, these data support the potential for clinical utilization of urinary Rac1 as a pharmacodynamic and predictive biomarker for GFB-887 treatment in FSGS and DN. GFB-887 is currently being studied in TRACTION™, a Phase 2 clinical trial in FSGS and DN which baseline and on-treatment urinary Rac1 measurements will support further development of the biomarker.

Funding: Commercial Support - Goldfinc Bio Inc
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 (Nphs2^{BioID}). 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 Nphs2^{BioID}{+/-} animals. Utilizing immunostaining, we have confirmed the proper expression and localization of the podocin-BioID. The HA-tagged BirA ligase appended to podocin coloculated 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 Nphs2^{BioID}{+/-} podocytes versus wild type biotin injected controls or un.injected 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 the 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 RIO1K1, 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: TNF-α induces expression of RARRES1, which is cleaved, then undergoes endocytosis to interact with intracellular RIO1K1, leading to the activation of p53 and apoptosis. High RARRES1 expression promotes the progression of FSGS and DKD.

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The Glomerulus-on-a-Chip as a System to Unravel Novel Membrane Attack Complex (MAC)-Independent Role of Complement in Membranous 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: GOAC chips were cultured with serum from anti-PLA2R + MN patients or healthy individuals. Functional response was assessed by albumin permeability assay to evaluate selective-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 mice 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 as 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/C3R signaling plays a dominant role in complement-mediated MN pathogenesis.

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Dach1 Is Essential for Maintaining Normal Podocytes

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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 Dach1^{Cre} mice with Nphs2{loxP}-{loxP} 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 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=0.0022).

**Conclusions:** These results indicate that Dach1 is important in maintaining normal podocyte integrity, and Dach1 gene deficiency induces podocyte injury.

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**Dysregulated Dynene-Mediated Vesicle Trafficking 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 INCA2 cause FSGS characterized by a podocytopathy with misfolded slit diaphragm (SD) protein critical for the integrity of the glomerular filtration barrier (GFB). This feature has been found in FSGS of other etiologies, making INCA2 related podocytopathy a good model to dissect the disturbed vesicle trafficking in podocytopathies prone to FSGS. By yeast two hybridization screening we identified the interaction of INCA2 with Dynl1, a dynen component. We hypothesize that INCA2 regulates dynen mediated vesicle trafficking, which shuts endocytosed protein to proteolytic system. This interaction could be disrupted by pathogenic mutations in INCA2, suggesting dysregulation of dynen mediated trafficking is an underlying mechanism of FSGS.

**Methods:** The INCA2-Dynl1 interaction was confirmed by yeast mating and CO-IP. The dysregulated dynen 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 demonstrated in the purinomycin aminoglycoside induced nephropathy (PAN) of INCA2 transgenic mice with knockin (KI) of R218Q, a pathogenic mutant that disrupts INCA2-Dynl1 interaction.

**Results:** 1. We demonstrated that INCA2 limited dynen mediated retrograde trafficking of nephrin by binding to and sequestering Dynl1, a component essential for the integrity of dynen. 2. R218Q KI podocytes illustrated an impaired recycling of nephrin with enhanced recruitment of dynen components, which could be rescued by targeting dynen transport pathway using Cilobrevin D (Dynex inhibitor), dominant negative Dynactin 1, siRNA for Dynl1 or overexpression of wildtype INCA2 (to sequester Dynl1). 3. PAR-218Q KI mice was characterized by increased recruitment of Dynl1 to nephrin, correlated to increased ubiquitination and decreased surface nephrin, suggesting an enhanced dynen trafficking pathway underlies the impaired functional trafficking of nephrin, disintegration of SD and malfunction of the GFB.

**Conclusions:** Recognition of the dysregulated dynen mediated trafficking of SD protein has enlightened a new understanding and therapeutic targets for INCA2 related podocytopathy and FSGS.

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**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 loss is through hypertrophy, allowing the remaining podocytes to effectively cover the filtration surface. This adaptive response is associated with signs of cell cycle activation, but podocytes do not divide successfully: they detach from the basal membrane and are lost in urine. How the cell cycle phases modulate this “mitotic catastrophe” is 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 mice. Using flow cytometry, we isolated and evaluated podocytes in different cell cycle phases in WT (males and female) and AS-POD mice. Protein expression of NPHS2 in G1 and G0 podocytes. In vitro studies were performed in primary podocytes damaged with purinomycin.

**Results:** In WT mice (males and females), as expected, 98.1% of podocytes were quiescent (G0). In AS mice, podocyte number in G0 decrease over time: at 2months (mild proteinuria) 89% are in G0, at 6months (end-stage kidney disease) 59% are in G0 while the percentage of podocytes in G1 increased from 7.6% at 2 months to 33% at 6 months. Podocytes were isolated in different cellular states (hypertrophy) along disease progression. In 6months AS WT Hf females (mild proteinuria), only 15% of podocytes are in G1. PAN damage induced podocytes to switch from G0 to G1 phase, and rapamycin (a cell cycle regulator) rescue damage by maintaining cells in G0. Proteomics data showed important differences of cell cycle regulators (cyclins and CKDs, mTor, integrin signaling) between G0 and G1 of WT and AS mice.

**Conclusions:** We demonstrated that podocytes enter their cell cycle (in male and female) to increase of cells in G1 (associated with proteinuria) as the disease worsens. Regulating cell cycle may be pivotal in developing novel therapies to prevent podocyte loss.

**Funding:** Private Foundation Support

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**RNA Sequencing and ATAC-Seq Reveal Gene Profiles in Injured Podocytes in Mice, and Podocyte-Specific Hypoxia Inducible Factor 2 α Deletion Protects from Adriamycin-Induced Podocyte Injury**

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**Background:** Roles for hypoxia-inducible factor (HIF) in kidney diseases have been controversial. Upregulating HIF expression is beneficial in protecting 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 2α. Here, using podocyte-specific HIF-2α deletion mice, we tested effects of HIF-2α deletion on gene profiles in injured podocytes.

**Methods:** HIF-1α1/2-/- or HIF-2α1/2-/- mice were crossed with either NPHS1-/- or Pkd2-/- mice. HIF-2α1/2-/- mice were further crossed with ZiEG mice that express GFP only in cells where Cre is active. At 8 weeks old, the mice were given Adriamycin (12 mg/kg) i.v. two weeks later, urine and blood were harvested. Creatinine and albumin levels in urine and serum, and blood urea urine levels in serum were measured with ELISA kits. Podocytes were isolated from HIF-2α1/2-/- /ZiEG mice by flow sorting and RNAseq and ChIP-seq were performed.

**Results:** HIF-2α-/-; NPHS2-Cre showed preservation of foot processes and kidney functions, and significantly less proteinuria compared to the WT littermates after being subjected to Adriamycin, while HIF-1α-/-; NPHS2-Cre mice developed a similar degree of podocyte injury to that of WT. HIF-1 α or 2α; NPHS1-Cre; ZiEG mice showed little GFP expression in podocytes, suggesting that weak penetrance of NPHS1-Cre led to minimal functional effects. This group was therefore not further evaluated. Podocytes isolated from HIF-2α1/2-/-; NPHS2-Cre; ZiEG were used for RNAseq and ATACseq. In RNAseq, Ndufa12 (ubiquinol cytochrome oxidase subunit A12) was most significantly upregulated in podocytes subjected to ADR, while Slc22a30 [solute carrier family 22, member 30], Slc7a13 [solute carrier family 7, (cationic amino acid transporter, y+ system) member 13] and Pfp [PFEP, alpha-2-macroglobulin like] were most significantly downregulated. Correlation with ATAC-seq results were being processed.
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Shroom3-FYN Regulates Podomecas via LKB1-AMPK Signaling
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Background: Previously, we showed Shroom3–FYN interaction regulated podocyte cytoskeleton via FYN activation. Intriguingly, global shroom3 knockdown mice (CAGS-TG/Shr3 Kd) displayed reduction in glomerular volume-V glom, podocyte & endothelial fraction of V glom without podocytopenia [1a].

Methods: To examine mechanism of podomecas regulation by Shr3, we used Shr3 & FYN Kd human podocytes (hPodo) to study cell protein content & growth regulatory pathways; performed unilateral nephrectomy examining V glom hypertrophy in remnant kidneys

Results: At day-7, CAGS-TG mice showed restricted V glom hypertrophy with reduced expansion of PodoV glom vs NTGs [1b]. We observed reduced hPodo volume (FSC), Protein:DNA ratios (n=5; 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-EF2 & autophagy (high p-ULK1 and LC3II levels) downstream of AMPK, in vitro/in vivo by immunoblot (IB) & immunofluorescence (IF)[1c] suggesting negative regulation of protein synthesis. Next, we examined LKB1 localization (AMPK-kinase) by IB after subcellular fractionation & IF in Shr3/FYN Kd hPodo identifying increased LKB1/Cytosolic:Nuclear ratio, explaining AMPK activation due to increased cytosolic pool of active LKB1 [1d]. Finally, we used an AMPK inhibitor, Compound C in CAGS-TG mice and observed reversal of podomecas changes-V glom & V podo fractions, induction of podocytopenia with AMPK-inhibition [1e]

Conclusions: Here, we show Shroom3-FYN interaction regulating podomecas via AMPK-signaling in podocytes. The protective morphometric effects have implications to disease models with podocyte/ nephrin loss requiring obligate V glom/Podocyte hypertrophy

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The Role of Opioid Receptor Signaling in Podocytes 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 intracellular calcium 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 BRL52375, a potent and selective kappa/OR agonist.

Results: Stimulation of kappa-ORs, but not mu-ORs or delta-ORs, mediated calcium influx in podocytes through activation of TRPC6 channels in rat and human kidney. The effect of BRL52375 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 BRL52375 exhibited augmented blood pressure (MAP was 179 ± 15 mmHg vs. 151 ± 11 mmHg), nephritemia, albuminuria, and elevation in podocyte calcium in BRL52375 treated Dahl SS rats.

Conclusions: Stimulation of kappa/OR modulates calcium influx in podocyte 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 has proposed that podocytes can act as antigen presenting cells. Here we show how 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 cell 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 none. After treatment with ICs, lysosomes in WT podocytes were significantly larger and were also 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.

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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 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, longitudinal cohort study of children and adults with NS, who were >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 donors to assess APOM levels by ELISA using matched 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.

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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 podocytes in vivo 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 imaging of the kidney. Mice were anesthetized, an arterial catheter was placed into the right carotid artery or 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. In contrast, proximal tubular cells as well as a cortical arteriole responded with a calcium transient, 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.

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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.

Case Description: A 23 yo African American F with a history of LN class IV + V (maintained on MMF 1g BID) and APLS presented with one week history of nausea, vomiting and diarrhea. Admission labs were notable for a Cr of 10.5 mg/dl (baseline Cr 0.7), pancytopenia, with albumin of 1.7 mg/dl. Spot urine protein to creatinine ratio was >27 g/g. Serologies showed low C3 and C4, positive ANA, LDI 1437 and negative HIV test. Patient became anuric and required hemodialysis. Stress dose steroids were administered for presumed RPGN from LN. Renal biopsy on hospital day 8 demonstrated collapsing FSGS with 100% podocyte foot process effacement without significant IFTA and 4/9 globally sclerotic glomeruli. Testing revealed CMV viremia with viral load of >700,000 IU/mL. MMF was held. Ganciclovir was initiated with a subsequent decrease in viral load of 99.6%. 24 hours later, EGFP, cleaved-caspase 3 (cCasp3) and TUNEL staining were performed on glomeruli. In vivo imaging of the kidney. Mice were anaesthetized, an arterial catheter was placed into the right carotid artery or 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. In contrast, proximal tubular cells as well as a cortical arteriole responded with a calcium transient, 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.

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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 Adria-37Cin (A37C)-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 mTmG-Nphs2cre mice during the course of injury revealed a transient increase in the expression of crucial podocyte genes, including Nphs2. Sympo 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 previously occupied by WT1. Finally, motifs predicted to be overrepresented in other podocyte specific transcription factors were highly enriched at sites where WT1 binding increased after injury. Since the DNA binding transcription factors is modulated by chromatin accessibility, we used FACS-isolated podocytes to study epigenetic reprogramming. Both Adria-37Cinduced 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 repression marks in the absence of WT1.

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Atypical Cyscple 3-Dependent Death Process in Podocytes

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Background: Apoptosis of podocytes has been widely reported in many in vitro studies, but apotosis has rarely been documented in vivo podocytes. To elucidate this discrepancy, we analyzed dying process in podocytes in vitro and in vivo using a Cyscple 3-dependent CKD mouse model. Primarily, Cyscple 3 (C3) induced tubulocystic disease (CKD25) and EGFP expression plasmid and treated with a hCd25-targeting immunotoxin, LMB2 (1nM). 24 hours later, EGFP, cleaved-caspase 3 (cCasp3) and TUNEL staining were performed on in vivo experiments, podocyte injury was induced by injecting LMB2 into NEP25 mice, which express hCd25 in podocytes. In some experiments, NEP25 mice carrying another transgene expressing EGFP in podocytes were used. Results: In in vitro studies, administration of LMB2 caused leakage of co-introduced EGFP in 56.8±13.6% of hCd25-targeted cells, incorporation of propidium iodide in 13.6±2.5%, activation of caspase 3 in 19.6±2.5% and TUNEL staining in 4.5±1.3%. However, LDH activity in the culture medium did not significantly increase. These phenomena were not observed in cells without hCd25 or without LMB2. Acte-DEVD-CHO (10µM), a caspase-3 inhibitor, attenuated the leakage of EGFP by 38.2%, while inhibitors for caspase-1, necroptosis or apoptosis did not. These indicate that LMB2 induced typical caspase-3-dependent apoptosis in podocytes in vitro. In in vivo studies, injection of LMB2 (25ng/g BW) frequently induced leakage of EGFP from podocytes. In separate six NEP25 mice, 7 days after injection of LMB2 (1.25g/kg BW), 41.8±5.1% of glomeruli were found to contain cCasp3-positive cells, but no TUNEL-positive cell was observed. In primary sediments contained podocytin-positive podocytes (2.5±3.3%). Among these, 39.1±3% were stained for cCasp3 and 21.7±5.5% were stained for TUNEL. EM analysis showed no apoptotic body, but occasionally rupture of plasma membrane of podocytes. To evaluate the effect of glomerular filtration, NEP25 mice were similarly injected with LMB2 and subjected to ULO 1 day before sacrifice. Detaching podocyte cell bodies were frequently observed in the contralateral kidney by SEM analysis, but never in the obstructed kidney.

Conclusions: These collectively indicate that podocytes dying dependently on caspase 3 are quickly lost by detachment or plasma membrane rupture before completing full apoptotic processes. Glomerular filtration facilitates detachment of dying podocytes.

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PO1982

Systematic In Silico Exploration of the Kidney Rho-GTPase System Regulation in CKD

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 the dysregulation in disease states affects the kidney system occurs in CKD, we performed a systematic mining of kidney transcriptomics data to generate a full-viewport 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 upregulation 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 expressed genes that may implicate functional similarities.

Conclusions: To our knowledge, this is the first systematic evaluation of the Rho-GTPases, 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.

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PO1984

Bag3 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 overwheming 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 proteinostasis 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 was being evaluated in different mouse lines (Bag3.F209L mutation, a renal knockdown, 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 interaction with the essential actin cytoskeleton regulators rhoA, Arp2 and Dynamin2 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 mutant 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/QCT lines and the in vivo disease models will further help to understand the role of Bag3 at the kidney filtration barrier.

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PO1985

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 traffickin receptor that transports immunoglobulin-G (IgG) to the lysosome. In dendritic cells FcRn mediated trafficking of Igs to the lysosom is required for antigen processing and presentation on MHC II. We have found that podocyte specific knockout (KO) of FcRn ameliorates nephrotoxic serum nephritis (NPS) 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 Igs. The intrinsic and extrinsic apoptotic pathways were assayed 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 Igs, FeRn KO podocytes expressed significantly less caspase-3 and caspase-9 (intrinsic 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 intrinsic apoptotic pathways in FcRn KO podocytes compared to WT. In vivo, after induction of nephrotoxic serum nephritis, there was no change in renal CD4+, CD8+ or FoxP3+ T cells in WT mice, however in KO mice significantly less glomerulosclerosis and crescent formation. Podocyte-specific KO of FeRn 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.

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PO1986

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 site in the ER) is responsible for cytotoxicity and cell surface levels were not shown in that study. Since APOL1 residue 150 can differ in G0 Africans, we focused on comparing the cytotoxicities of E150 vs K150 SNPs in podocytes expressing equal surface levels of APOL1.

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. Brefeldin A 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.

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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 (eEVs) derived from human amniotic fluid stem cells (hAFCs) 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 AS (kidney disease) mice, the result of a nuclear transcriptomics with single cell sequencing. miR-93 expression 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 paracrine aminoacidoside damaged podocytes, and expression of fibroenectin 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, sclerosis and death at 42 days. It was found that the signalling mechanism of which has so far remained elusive. Our previous works suggest a role for miR-93 in the regulation of disease pathways and podocyte loss.

Conclusions: Gender-specific variation in miR-93 expression in glomerular cells might indicate important differences in response to injury in progressive disease. hEVs demonstrate great potential to restore lost miR-93 expression and its targets, thus presenting a targeted approach for treatment of CKD.

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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 filter 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 kld/kld (kidney disease) mice, the result of a spontaneous missense mutation in Pds2 (V117M, Pds2K447C). 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 Pds2K447C 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 Pds2K447C mice. In vitro, mechanistic studies revealed that depleted podocytes revealed a previously unknown perturbation in PUF A metabolism leading to lipid peroxidation. Ablation PUF A 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 different 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.

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PO1989

Noncanonical PAR-1 Signalling Leads to Profibrotic Effects in Podocytes in Response to Steroid-Resistant Nephrotic Syndrome Diabetic 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 and paired-remission plasma with or without PAR-1 antagonists, BW 5117 and FR17113 was effective in inhibiting effects of relapse plasma, suggesting a non-canonical activation of PAR-1 in SRNS. The phosphorylation of VASP, JNK and TRPC6 was effective in inhibiting effects of relapse plasma, suggesting a non-canonical activation of PAR-1 in SRNS. The phosphorylation of VASP, JNK and TRPC6 was effective in inhibiting effects of relapse plasma, suggesting a non-canonical activation of PAR-1 in SRNS. The phosphorylation of VASP, JNK and TRPC6 was effective in inhibiting effects of relapse plasma, suggesting a non-canonical activation of PAR-1 in SRNS.

Conclusions: We propose that the SRNS circulating factor acts as a pro-fibrotic effector that can activate PAR-1 leading to increased podocyte injury. A greater understanding of these signalling pathways will lead to the identification of novel therapeutic targets for this disease.

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PO1990

TRPC6 Is a Key Mediator of a PAR-1 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 post-transplant recurrence of idiopathic nephrotic syndrome (FSGS). 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-1Sve,1) led to proteinuria, sclerosis and death at 42 days. It was found that the signalling


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response to PAR-1 agonist treatment of podocytes in vitro was also present in the kidney and in vivo, as seen in the podocyte dysmorphisms. Changes in the podocyte tropomyosin isoforms after injury might be linked to changing podocyte shape and the FPE phenomenon.

Methods: To test our hypothesis, we used RT-PCR and RNAseq (Illumina and Pacbio) to identify the whole array of Tpm isoforms that are enriched in podocyte and in injured human nephropathy glomeruli. Using different mouse models for podocyte injury (i.e., Cd2ap KO, Lamb2 KO, Co4a3s K0 & AdrNephropathy (AdrN)), we identified a change in Tpm isoforms in the glomeruli isolated from these mice.

Results: RNAseq results from WT glomeruli show a different pattern of Tpm cytoskeletal components than the injured glomeruli, with the most significant changes occurring in Tpm 1.7 & Tpm 3.4. Pacbio 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 treated from podocyte-specific translating-ribosome-affinity-purification ("TRAP") mice. This system 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 isoform changes in regulating podocyte shape in health and injury conditions.

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PO1993

IRE1α Is Essential for Podocyte Proteostasis and Mitochondrial Health
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Background: Glomerular epithelial cell (GEC)/podocyte proteostasis is disrupted in glomerular diseases. To maintain proteostasis, the endoplasmic reticulum (ER) orchestrates the unfolded protein response (UPR), which includes upregulation of chaperones and clearance of misfolded proteins via autophagy. Inositol requiring enzyme-1 alpha (IRE1alpha) and PERK are the sensors of the UPR, which eliminates misfolded proteins when ER is stressed. This study characterizes the mechanisms by which IRE1α regulates proteostasis in GECs.

Methods: Mice with podocyte-specific deletion of IRE1α (IRE1α KO) were produced by breeding IRE1α flox/flox mice with mice expressing podocin-Cre recombinase. Nephropathy was induced with a single injection of adriamycin (ADR). GECs were cultured from glomeruli of IRE1α flox/flox and IRE1α KO mice and were treated by deletion 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 induction was blunted in ADR-treated IRE1α KO animals, evidenced by reduced LC3-I and 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 4μC 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. IRE1α KO mice and IRE1α KO glomeruli were smaller, 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 damage are compromised by IRE1α deletion. IRE1α deletion is cytoprotective 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 misense NPHS2 mutations reported to result in misfolding and mis Trafficking of the encoded slit-diaphragm protein, Podocin. Studies have overexpressed mutated protein in podocytes and mouse podocytes to identify how the disease is caused. This is the first in vivo model to identify how mutations in the endogenous NPHS2 locus as well as a control wild type (WT) line. These include the sequence variants c.274G>T, c.535C>T and c.530G>A leading to the protein changes G92C, P118L and R168H respectively. Control and mutant lines were used to generate...

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kidney organoids containing all nephron segments. Podocin localisation was assessed by electron microscope analysis and tubular injury was assessed by tissue injury. We also found that the previously reported knockdown of OASIS CKO mice was protected from LPS-mediated tubular injury. DNA damage was assessed by Comet assay. However, this difference was not statistically significant.

Results: We discovered that in addition to K+ and Na+, the APOL1 channel is permeable to Ca2+. The RRVs led to an influx of Ca2+ and Na+, which increased the plasma membrane, where they localized prior to cation flux. Reduction of Ca2+ and Na+ in the media inhibited RRV-mediated cell death. We also found that the previously reported high Ca2+ channels were a consequence of perforated podocytes. 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 membranous 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 C-terminally His-tagged fragment consisting of the first 5 domains of human PLA2R was expressed in Escherichia coli and affinity purified 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 regions of IgG heavy (VH) and light (VL) chains were cloned through a single-cell isolate B cells with antigen-specific 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 as rIgG in Expi293 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 attenuate glomerular injury.

Results: 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 a constitutively active Gaα15 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±37 ng/mg creatinine) vs. 127±25 [vehicle] vs. 127±25 (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.
Conclusions: These data suggest that: 1. Pharmacologic blockade NPRC may be a useful strategy for treating 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 (SYNPO2L) and AKT/mTOR signaling (CAVIN3, KIT). KIT SYNO2L 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 (AP39), 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 beneficial effects in vitro 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 yzogen precursor, prothrombin (PT). We hypothesized that circulating PT would directly modulate both podocyte function and in situ survival in a rat model of nephritic syndrome.

Methods: Purumycin amninosulfonic acid (PAS)-induced proteinuria was treated with: 1) PT antiserum oligonucleotide to induce hypoprothrombinaemia (LoPT), 2) Serial i.v. PT infusions to sustain hyperprothrombinaemia (HiPT), or 3) sham (PAN only) controls (Con; n=12/group). Ongoing podocyte injury was a known critical determinant of glomerular disease progression. Recent research suggests thrombin exerts beneficial effects in vitro 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 yzogen precursor, prothrombin (PT). We hypothesized that circulating PT would directly modulate both podocyte function and in situ survival in a rat model of nephritic syndrome.

Results: Circulating plasma PT levels (Figure A) modulated podocyte function (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 (proteinauria) 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 therapeutic target to slow glomerular disease progression toward chronic kidney disease.

Funding: NIDDK Support

PO2001
Exosomal Long Non-Coding RNA-G21515 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 29.71±6.06 years and urinary protein was 1.00±0.62±1.00 g/24h in these IgAN patients. lncRNA-G21515 was significantly down-regulated in IgAN patients. The predicted target genes of lncRNA-G21515 are FCGRs, which encode family of Fc gamma receptors (FcrRs). S was observed in 12 IgAN patients (66.7%) and was positively correlated with lncRNA-G21515 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-G21515 was higher in S1 group than in S0 group (11.26(7.92,20.38) vs 7.04(3.93,11.00), P=0.025). The AUC of lncRNA-G21515 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-G21515 relative expression (Fold change). In addition, patients with higher lncRNA-G21515 relative expression had more severe podocyte injury.

Conclusions: Exosomal lncRNA-G21515 was down-regulated in IgAN patients, but positively correlated with S change. Exosomal lncRNA-G21515 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 mechanism. The relationship of these systems in podocyte has not well been understood.

Methods: In this study, we generated podocyte-specific proteasome impaired mice (Rplt3pKO) by deletion of Rplt3, which is essential for construction of 26S proteasome, using Cre-loxP system. Albuminuria and number of sclerotic glomeruli increased in the Rplt3pKO mice compared with Rplt3control mice. Oxidative stress and podocytes apoptosis were related to podocyte injury. To evaluated autophagic activity, LC3 dots

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in podocytes were evaluated after administration of chloroquine, inhibitor of autophagic flux. In cell culture experiments, cultured podocytes were treated with bortezomib (BTZ), proteasome inhibitor, which lead to podocyte apoptosis. The expression of LC3 was evaluated in podocytes after administration of bortezomib in the presence of 6E4/peptatinA, inhibitor of autophagic flux.

Results: In vivo, after administration of chloroquine, LC3 dots decreased in podocytes of Rpt3pdKO mice compared with RptCtrol mice. In vitro, the expression of LC3 decreased and the accumulation of p62 increased in cultured podocytes after treatment of BTZ in the presence of 6E4/peptatinA. These results indicated autophagic activity was stimulated in both proteasome inhibition and pULLK, which is a downstream of mTOR signal, was phosphorylated in podocytes with proteasome impairment, suggested that suppression of autophagic activity was associated with mTOR activation. Pre-treatment of rapamycin, inhibitor of mTOR, ameliorated podocyte apoptosis induced by BTZ in vivo and in vitro, the number of sclerotic glomeruli decreased in Rpt3pdKO mice with rapamycin administration compared with in RptCtrol pdKO mice without rapamycin administration.

Conclusions: Impairment of proteasome suppressed autophagic activity associated with mTOR activation in podocytes. Activation of autophagy have the protective effect on podocyte injury due to proteasome impairment.

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 truncated 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 IGFIIR, EGFR, TGFβ2. These candidates are being developed as WT1 responsive reporters.

Conclusions: Previous reports suggested NPHS1 promoter reporters as a model system to investigate mutant WT1 function. However, the transcriptional effect of WT1 was subsequently not cell specific. Future work to establish a robust WT1 reporter is ongoing using cloned IGFIIR, EGFR, TGFβ2 promoters.

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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 pre-analytical and analyzable 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 various kidney diseases.

Methods: We examined the impact of operator bias and sample size on FPW measurement in electron micrographs from nephrotic (NS) and non-nephrotic (N) cases, including primary focal segmental glomerulosclerosis (FSGS) and minimal change disease (MCD), and other glomerular lesions effecting the podocyte. FPW was measured for each individual FP between the midpoints of flanking filtration slits and the geometric mean 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 a MCD vs. 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

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PO2005

Glomerular 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 controls 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 (NRE1 and PPARy). 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 gene sets for cell transcriptional 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 pathology hallmarkled 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 amionucleoside (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 phallolid. Cell images were taken with using Opera High-content Screening (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 podocyte 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 of 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 podocyte-specific, actin microfilament component. Nucleation of actin monomers is the rate limiting step in actin polymerization. There are two distinct nucleators for actin nucleus in podocytes, Arp2/3 complex and formin, which mediate branch and linear actin filament formations, respectively. Our previous study 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 activities in nucleus, 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, co-immunoprecipitation were performed to test FNBP1L essentiality and mechanism.

Results: FNBP1L was specifically expressed in podocytes in glomeruli, and its expression was decreased in purinycin aminonucleosides-treated in podocytes. When FNBP1L was knocked down, we found that the expression of WT1, SYNPO and CD2AP were 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 nucleus 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 nucleus in podocytes coloaded with INF2 and affected its localization in cytoplasm and its actin nucleus. Consistently, the reduction of FNBP1L impaired the interaction between N-WASP and Arp2/3 complex and mis-localized INF2 in the cytoplasm.

Conclusions: FNBP1L may regulate branched and linear actin filament productions. This was supported by regulation Arp2/3 complex and INF2 actin nucleus 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 podocytepathies.

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PO2008

Role of AT1e in Radiation-Induced Nephrotoxicity
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Background: Argininylation increases actin polymerization and supports cellular morphology. However, the effect of radiation therapy (RT) on argininylation is not known. This study investigated the impact of RT on arginyltansferease 1 (ATE1) and its role in podocyte morphology and kidney function.

Methods: Human podocytes were irradiated with 4 Gy, and preceeded by rituximab mAb (100 μg/ml) or IgG (100 μg/ml) treatment, 30 min before RT. Additionally, 8-8-week-old C57BL/6 male and female mice were subjected to either (i) 1x14 Gy bilateral kidney-only RT (ii) lethal-dose total body irradiation (TBI 10.5 Gy) and rescued by strain-donor hematopoietic stem cell transplantation (HSCT) or (iii) untreated (sham-RT control). Functional, histopathological, and biochemical changes were studied at baseline and 10 weeks post RT

Results: In podocytes, RT (4 Gy) produced time-dependent downregulation of ezrin (30%) and AT1e (50%) and a significant increase in apoptosis at 4h (p<0.001). Rituximab pretreatment protected from ezrin relocalization and AT1e 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<0.01). 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 (50%) and TBI (70%) compared to control. Podocyte numbers of ezrin microtubular structures associated with podocyte infolding, coining a podocyte infolding glomerulopathy (PIG). Here, we test this hypothesis.

PO2009

PO2010

Podocyte Infolding Glomerulopathy: New Disease or Pattern of Injury?
Sri Vibhavari Guntupalli, Suzanne G. Martin. St. Vincent Hospital, Worcester, MA.

Introduction: Occasional podocyte infolding is reported in membranous nephropathy, but global and diffuse infolding is rare. Whether this is a new disease entity or a pattern of podocyte injury may influence therapy.

Case Description: 52 year-old-male 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 infolding 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 PLAZR. Serum PLAZR 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) persist 8 months after starting treatment.

Discussion: In 1985, Dales and Wallace [1] described massive deposits of spherular organelles in the subepithelial space of glomerular capillary walls in a patient with membranous nephropathy. In 2008, Jh et al [2] studied 25 Japanese patients with microspheres and microtubular structures associated with podocyte infolding, coming the term “podocyte infolding glomerulopathy.” Rare cases are reported in India, Latin America and Europe. It is unknown 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 yet understood. Response to therapy and prognosis are not well-described. 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 infolding glomerulopathy is a separate disease entity not responsive to immunosuppression.

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Funding: NIDDK Support
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-2/9 activity in the culture media of HGEC.

Conclusions: Testican-2 is a circulating protein that is synthesized in the human podocyte. Podocyte-testican2 promotes angiogenesis in cultured HGEC, which may be mediated by upregulating MMP-2/9 activity and increased endothelial cell migration.

Funding: NIDDK Support

PO2012
Mitochondrial Quality Control Mechanisms in Renal Cortical Mitochondria 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 triggers 1) mitochondrial fission or fusion, 2) increased fatty acid metabolism, and/or 3) mitophagy as quality control mechanisms.

Methods: Rats receiving i.p. injection of streptozotocin (STZ, 65 mg/kg) or vehicle (3) mitophagy as quality control mechanisms.

Results: During the normoalbuminuric stage of DM, renal cortical mitochondria undergo increased fatty metabolism, as well as enhanced fission and mitophagy that are blunted by TLM in association with its antioxidant effect and, thus, are likely quality control mechanisms triggered by oxidative damage.

PO2013
Indoxyl Sulfate Modulates Expression of Myosin Heavy Chain Isoforms and induces Sarcopenic Phenotype in Mouse

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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 protein.

Results: IS reduced exercise tolerance and was associated with increased muscle weight and decreased cross-sectional area.

Conclusions: IS induces direct sarcopenic effect on mouse skeletal muscle and predominantly decreases on fast-twitch muscle fibres. In the future, we will further investigate the molecular mechanism of uremic toxin induced sarcopenia.

PO2014
Lnc-Gm43360 Regulates TCMK-1 Senescence by the miR-141/Sirt1 Pathway

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Background: Aging is a complex process, which will lead to the gradual decline of physiological functions of all organ systems. 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 reduction 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. Lnc-Gm43360 negatively regulates miR-141 expression and positively regulates 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 senescence by miR-141/Sirt1 pathway.

PO2015
Modifed Lipoproteins Modulate Renal Lymphatic Vessel Vasodynamics via NKCC1 on Lymphatic Endothelial Cells

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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 isoleucylglutamides (IsoGLu) which modify lipoproteins (apoA1), we examined whether apoA1 modified with IsoGLu (apoA1-IsoGLu) modulates renal lymphatic vessel contractility via NKCC1.

Methods: Paroxysmic nephropathy (PAN) 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 apoA1 or IsoGLu-apoA1 on the NKCC1 signaling pathway were assessed in LECs.

Results: PAN rats had significantly higher renal lymph flow which contained significantly more isoGLU vs Cont. Ex vivo studies showed renal collecting lymphatic vessels from PAN were more dilated than Cont. Immunostaining 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
Maki Murakoshi, Tomohito Gohda, Yusuke Suzuki. Department of Nephrology, Juntendo University Faculty of Medicine, Tokyo, Japan.

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 vacuolization in the proximal tubule, but KO-HFD mice did not. Immunohistochemical analysis showed that vacuolar membranes were clearly positive for a lysosomal marker, LAMP-1, suggesting impairment in lysosomal function. The expression of megalin 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 mProx 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.

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: Cy5+/ rats (CKD) and normal littermates (NL) consumed an autoclaved grain-based diet containing 0.7% 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 26-wk-old (n=10 rats/group). DNA was extracted fromecal and fecal samples collected at euthanasia, the V4 region of the 16s rRNA gene was sequenced via Illumina MiSeq, and data were analyzed using QIIME2 and LEfSe.

Results: Intestinal microbial a-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 Bilophila in NL rats and greater Allipotri in CKD. Both of these taxa have been shown 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

PO2018

Effect of High Fiber or Probiotics-Enriched Diets on Kidney Injury in Mice Model of Bilateral Ischemia Reperfusion
Shirin Pourafshar, Nabin Poudel, Nataliya Skrypnyk, Junlan Yao, Mark D. Okusa. University of Virginia Health System, Charlottesville, VA.

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 57BL/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 resumed 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). In the HF group, the IR increased serum creatinine compared to sham (P<0.05). However, NGAL and KIM1 were lower in HF and P compared to C, respectively (p<0.005). 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: We examined the association between dietary intake of fat subtypes (SFA, PUFA, monounsaturated fatty acids [MUFA]) ascertained by 24-hour dietary recall with mortality in continuous NHANES adult participants (1999-2014) stratified by absence vs. presence of kidney dysfunction (eGFRs ≤60 vs. >60ml/min/1.72m², respectively). Dietary fat intake was estimated as a proportion (%) of total energy intake, and associations with all-cause mortality were estimated using adjusted Cox models.

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 death risk (ref: lowest tertile) (HRs [95%CI] 1.09 [1.04,1.15]), whereas those with the highest tertile of PUFA intake had better survival (HR [95%CI] 0.82 [0.76, 0.90]). In participants with kidney dysfunction, those in the second and third highest tertiles of SFA intake had significantly higher mortality risk and trended towards higher mortality, respectively: HRs (95%CI)s 1.21 (1.04, 1.41) and 1.33 (0.97, 1.82), 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 multivariable 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 (Table). 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

PO2022

Impact of Participation in Food Assistance Programs Among NHANES Dialysis Patients from 2001-2016

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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 study 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

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a marker of nutrition status. The analyses were adjusted for demographics, BMI, diabetes, hypertension, and hyperlipidemia.

Results: A total of 1,565 dialysis patients were analyzed across all NHANES cohorts. Dialysis patients receiving food assistance were more likely to receive less calories and protein while on dialysis. Food assistance participation was significantly more likely to report lower 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 noninstitutionalized 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 creatinine.

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.

PO2023
Tanushree Banerjee,1 Deidra C. Crews,1 Charles E. McCulloch,1 Nilka Rios Burrows,2 Karen R. Siegel,1 Rajiv Saran,3 Yuto Han,3 Neil R. Powe.1
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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 for all 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. Log binomial regression model was used to estimate adjusted risk ratios (RR) for the association of food insecurity and racial/ethnic groups.

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 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 lower 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 noninstitutionalized 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 creatinine.

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.

PO2024
Approach to Nutritional Protein Intake in Hemodialysis Patients with Hyperphosphatemia: Associations with Mortality in the DOPPS
Sugaru Yamamoto1, Brian Bieber,2 Hirota Komaiba,3 Hiroki Kitabayashi,3 Takanoobu Nomura,4 Alex Cases,3 Christian Combe,5 Ronald L. Pisoni,6 Bruce M. Robinson,7 Masafumi Fukagawa.8 Arbor Research Collaborative for Health, Ann Arbor, MI; 2Research Institute for Contemporary Medical Science, Tokyo, Japan; 3Kyorin University Co., Ltd., Tokyo, Japan; 4Tokai University School of Medicine, Isehara, Japan; 5Universitat de Barcelona, Barcelona, Spain; 6Université de Bordeaux, Bordeaux, France.

Background: Pts 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/decrease 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 protein intake recommendation increased 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

PO2025
Dietary Acid Load Is Associated with the Risk of Mortality and Kidney Replacement Therapy in Diabetic CKD Patients but Not in Non-Diabetics
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Background: Dietary acid load (DAL) may be related to CKD progression but results are still conflicting. In addition, no studies have evaluated the association of DAL with mortality in CKD. The aim of this study was to evaluate two estimates of DAL, PRAL (potential renal acid load) and NEAP (net-endogenous acid production), in relation to events of mortality and kidney replacement therapy (KRT) in CKD.

Methods: Baseline clinical and dietary data (food frequency questionnaire) from the PROGREDIR Cohort (n=454), a CKD cohort based on Sao Paulo, Brazil, composed predominantly of older people with CKD G3 and G4 was used in this analysis. PRAL and NEAP were computed using previously validated formulas, and those with missing values were excluded (n=11). Events of death (n=190) and KRT (n=62) were ascertained after a median follow-up time of 6 years. Uni and multivariable Cox proportional hazards and Coxnet M. Risk models were computed.

Results: Mean age was 68 ± 12, mean eGFR was 38 ± 15 mL/min/1.73m², 63% were male and 56% were diabetic. Mean intake of PRAL and NEAP was 4.1 ± 18.5 and 51.9 ± 17.4 mEq/d, respectively. Initially, neither PRAL nor NEAP were associated with mortality or KRT. However, after stratification for diabetes, both estimates were positively related to the risk of KRT and death in diabetics only, even after adjustments (Table). Competing risk analysis were consistent with the Cox findings. By entering interaction terms between diabetes and DAL estimates, which were significant, both PRAL and NEAP showed an inverse association with the risk of clinical events.

Conclusions: Our results suggest the existence of a relevant interaction between PRAL/NEAP and diabetes: whereas DAL estimates were associated with mortality and KRT in diabetics, this association was not observed in non-diabetes.

Funding: Government Support - Non-U.S.
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 *University of California Irvine, Orange, CA; 1University 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: We performed a cross-sectional study of HD patients at four Southern California facilities. Patients were randomized to one of two smoking intervention groups: a standard intervention or one focusing on dietary changes. Dietary data was collected using a 3-day food record. Results were analyzed by race/ethnicity to identify differences in estimated P content and P type across groups.

Results: There were 102 patients in each group, with an average age of 63 years. The majority of patients were white (72%) and male (60%). The mean estimated P content was significantly lower in the standard group compared to the dietary intervention group (1927 ± 1127 vs. 2383 ± 1369 mg/day, p < 0.001). There were no significant differences in estimated P type across groups (26% vs. 27% animal-based P, p = 0.72).

Conclusions: Dietary interventions focusing on dietary changes can significantly reduce estimated dietary P content in HD patients, with no significant effect on estimated P type.

Funding: NOCR:016858

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.

PO2026

Mediterranean Diet and the Risk of CKD: A Systematic Review and Meta-Analysis

Panupong Hansrivit1, Sharad Oli,2 Resha Khanal,1 Nasroolah Ghahramani,1 Chane Li,3 Morancy Shang,3 Saleh, Kingsley Morancy,1 Mirza,1 Morancy Shang,4 UPM-P, Paris; Harrisburg, PA; 2Pou州 State College of Medicine, Hershey, PA; 3Mayo Clinic Minnesota, Rochester, MN; 4University of Mississippi Medical Center, Jackson, MS; 5Maimonides Medical Center, Brooklyn, NY.

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. The study criteria were set based on the definition of the CKD per the National Kidney Foundation. The results were stratified by median dietary adherence as 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 1,999 ± 258.0 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; F 26.5%). By excluding kidney transplant patients, the adjusted OR for CKD was 0.901 (95% CI, 0.868-0.935; I² 9.4%). Both findings remained significant on sensitivity analysis. No publication bias was detected. The incidence of CKD was 0.028 events per person-year (95% CI, 0.012-0.044). From meta-regression analysis, male sex was associated with higher incidence of CKD in an adjusted model. There was no significant association between age, black race, eGFR, and total daily energy intake vs. CKD incidence.

Conclusions: Adherence to Mediterranean diet by a 1-point increment of MDS was associated with 10% lower risk of CKD. However, this only applies to healthy patients, the pooled adjusted OR for CKD was 0.901 (95% CI, 0.868-0.935; I² 9.4%).

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 a lack of research 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 7-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 $30k, and 10 (33%) were employed. 64.5% (20) were interested in learning more about PBE; 35% had never heard of it. 22% (7) reported consuming animal protein 2-3x/week, and 77.9 ± 5.2, p<0.05), and higher systolic and diastolic BP (144.3 ± 8.2 vs. 133.9 ± 10.7, p<0.05) than those who did not eat plant-based foods had a higher BMI than those who consumed plants. From meta-regression analysis, male sex was associated with higher incidence of CKD in an adjusted model. There was no significant association between age, black race, eGFR, and total daily energy intake vs. CKD incidence.

Conclusions: Adherence to Mediterranean diet by a 1-point increment of MDS was associated with 10% lower risk of CKD. However, this only applies to healthy patients, the pooled adjusted OR for CKD was 0.901 (95% CI, 0.868-0.935; I² 9.4%). Both findings remained significant on sensitivity analysis. No publication bias was detected. The incidence of CKD was 0.028 events per person-year (95% CI, 0.012-0.044). From meta-regression analysis, male sex was associated with higher incidence of CKD in an adjusted model. There was no significant association between age, black race, eGFR, and total daily energy intake vs. CKD incidence.

Conclusions: Adherence to Mediterranean diet by a 1-point increment of MDS was associated with 10% lower risk of CKD. However, this only applies to healthy patients, the pooled adjusted OR for CKD was 0.901 (95% CI, 0.868-0.935; I² 9.4%).

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.

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Methods: We recruited 20 subjects (55±12 years, BMI 40.7±16.6 kg/m², 45% male, 65% >70 DM, 50% CVD) 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 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

<table>
<thead>
<tr>
<th>Variable (mm Hg)</th>
<th>0M</th>
<th>1M</th>
<th>2M</th>
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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,2 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 (MDH) patients (pts). We assessed GLIM (Global Leadership Initiative on Malnutrition) evaluated agreement and survival prediction of GLIM vs. SGA and MIS in MDH pts.

Methods: We investigated two cohorts, MHD Italy (121 adult pts from Italy; 67±16y, 65% men, BMI 25±5 kg/m² and MHD Brazil (169 elderly (age>60 y) pts from Brazil; 71±7y, 66% men, BMI 25±4 kg/m²), followed for 40 (27; 46) and 17 (12; 31) months (median and 25% 65%; 70%). Respectively, GLIM comprises: 1. Screening and 2. Confirming malnutrition by phenotypic and etiologic criteria. For 1., presence of >1 criteria from protein energy intake ≤ 5 and 8 was considered inadequate.}

Conclusions: Malnutrition was present in 38.8% by GLIM, 25.6% by SGA and 29.7% by MIS. There was a low agreement between SGA and MIS (κ = 0.43), and between SGA and MIS (κ = 0.38). The long-term benefits and cost-effectiveness of this approach also needs to be evaluated.

Funding: Commercial Support - Renal Research Institute

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 dietary fiber 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 (6%) 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.
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 addressed 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 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 Qui-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 dose ranged from 3 to 14 scoops (20-30g/scoop). 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 exposure and lifetime impact of protein supplements was not considered and may be relevant.

Continuous Intraluminal Amino Acid Infusion from the Start of Dialysis Is Better to Avoid Catabolism Under the High-Volume Pre-Dilution Online Hemodiafiltration

Motoko PO2034
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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 the high-volume pre-dilution on-line HDF (HVPO-HDF). The optimal administration method of amino acid infusion under the HVPO-HDF was analyzed.

Methods: The subjects were 10 patients receiving HVPO-HDF (7 males, 4 diabetics, mean age: 77.2±5.5 years). We compared the pre- and post-dialysis plasma amino acids levels and the total amino acids amount in the waste fluid when the amino acid 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 replacement fluid flow rate was 600 mL/min. The replacement fluid volume was 90 mL/min and total replacement fluid volume was 400 mL/min.

Results: In pre-dialysis plasma levels of total amino acid (TAA), Group A and Group B showed the same level (2477 ± 267 mmol/mL and 2622±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 almost equal (900±81 mg/dL and 880±1204 mg of TAA, 880±5712 mg of EAA and 454±6453 mg of EAA, 402±644 mg and 434±862 mg of NEAA, respectively). In Group A, post-dialysis plasma levels of amino acids were significantly lower than in Group B (2066±636 mmol/mL of TAA, 946±193 mmol/mL and 220±439 mmol/mL of EAA, 1120±193 mmol/mL and 1577±260 mmol/mL of NEAA, respectively, p < 0.01).

Conclusions: We analyzed 175,392 US veterans who received care between 2004 and 2006, with available serum LDL and albuminuria (UCAR) data. All UCAR measurements until the end of follow-up (2014) were used to ascertain UCAR slopes using mixed effects modeling. The relationships between LDL and faster UCAR slope (a 0.1 mg/dL/year) stratified by baseline albuminuria stage (A1-A3) were estimated using logistic models adjusted for baseline demographics, comorbidities, prescription of statins and non-statins, BMI, albumin, HDL, triglycerides, eGFR, and UCAR.

Results: Assessment of abnormal serum albuminuria (UCAR) was considered as a marker of kidney disease progression. Prior studies showed abnormal albuminuria levels may predict the progression of renal function decline; however, associations of low-density lipoprotein cholesterol (LDL) with UCAR change is unclear. Therefore, we sought to investigate the association of LDL and UCAR slope across albuminuria stages. We analyzed 175,392 US veterans who received care between 2004 and 2006, with available serum LDL and albuminuria (UCAR) data. All UCAR measurements until the end of follow-up (2014) were used to ascertain UCAR slopes using mixed effects modeling. The relationships between LDL and faster UCAR slope (a 0.1 mg/dL/year) stratified by baseline albuminuria stage (A1-A3) were estimated using logistic models adjusted for baseline demographics, comorbidities, prescription of statins and non-statins, BMI, albumin, HDL, triglycerides, eGFR, and UCAR.

Results: Cohort mean age was 65±11 and included 3% females, 14% African-Americans, and 87% diabetics. The median [IQR] of serum LDL level and eGFR were 97 [75,119] mg/dL and 73 [58,88] mL/min/1.73m2. To further study the relationship with LDL by age, we performed age-stratified analysis and found similar results. The odds ratio of faster UACR slope for serum LDL levels of 5.0 mg/dL in the age group of 20-39 years was 1.67 (95% CI: 1.14, 2.43), and 1.67 for serum LDL levels of 5.0 mg/dL in the age group of 40-49 years, and 1.86 for serum LDL levels of 5.0 mg/dL in the age group of 50-59 years. The odds ratio of faster UACR slope for serum LDL levels of 5.0 mg/dL was 1.64 (95% CI: 1.14, 2.37) in the age group of 60-69 years, and 1.83 for serum LDL levels of 5.0 mg/dL in the age group of 70-79 years. The odds ratio of faster UACR slope for serum LDL levels of 5.0 mg/dL was 1.69 (95% CI: 1.15, 2.48) in the age group of 80 years or older. These findings suggest a strong association between LDL and faster progression of albuminuria.
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

PO2037
Lipidomic Markers for Cognitive Impairment in Maintenance Hemodialysis Patients
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Background: Cognitive impairment (CI) was relatively common in maintenance hemodialysis patients. The pathophysiology of CI in this particular population was not well understood. Whether the classic lipid components that affect cognitive outcome in general population have similar effect in dialysis patients is not clear. In this study, we tried to get a better understanding of the pathogenesis CI in hemodialysis patients by lipidomic analysis and find potential lipid markers to predict cognitive decline.

Methods: From July 2013 to July 2019, we followed up the cognitive evaluation results of the hemodialysis patients in our dialysis center. The cognitive function was evaluated by the MMSE and MoCA at baseline and follow-up period. Plasma and hemocytes of enrolled patients were collected at 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 performed on an Exion LC-system coupled with a QTRAP 6500 PLUS system (Sciex).

Results: At the baseline, plasma from 21 patients and hemocytes from 65 patients were collected for lipidomic analyses. 539 lipids were detected in plasma and 237 lipids were detected in hemocytes. In individuals with plasma lipid files data, 10/21 suffered MMSE scores decrement and 16/21 showed MoCA decrement. In patients with hemocytes lipids files date, 29/65 of them suffered MMSE scores decrement and 43/65 showed MoCA decrement. Compared with retained MMSE scores group, decreased MMSE scores group presented higher level of plasma PA 32:1, PA 38:5, CE-17:1, and lower level of plasma DAG 40:6(18:0/22:6), PE 36:4(18:1/18:3). There was no significant difference in erythrocytes lipids between the two groups. Compared with retained MoCA scores group, decreased MoCA scores group presented higher level of plasma LacCer d18:1/18:0, LPE 18:2, G3M d18:1/20:1, PE 36:3(18:1/18:2), LPE 18:1, lower level of plasma PI 38:5(18:0/20:5), and higher level of erythrocytes GM3 d18:0/20:0 (Fold change >1.5 or <1/1.5, P value <0.05).

Conclusions: The pathogenesis of CI in dialysis patients may closely relate with vascular injury. Lipid analysis may contribute to a new approach to predict the risk of cognitive decline in hemodialysis patients.

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
Marcelo Lopes,1 Eiichiro Kanda,2 Brian Bieber,1 Kazukihito Tsuuryu,2 Hideki Hirakata,1 Angelo Karaboyas,1 Stefan H. Jacobsson,1 Indranil Dasgupta,1 Bruce M. Robinson,1 Roberto Pecos-Filho,1 DOPPS ‘Arbor Research Collaborative for Health, Ann Arbor, MI; 2Kawasaki I Daigaaku, Kurashiki, Japan; 3Nara-ken, Nara, Japan; 4Fukao Renal Clinic, Fukaoa, Japan; 5Karolinska Institute, Stockholm, Sweden; 6University of Warwick Warwick Medical School, Coventry, United Kingdom.

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; >10mg/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-Brody Instrumental Activities of Daily Living Scale (score ranges from 0 to 8) less than 11. We investigated the association between combinations of MIC (+/-) 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-/ High FS 57%, MIC-/ Low FS 24%, MIC+/High FS 9%, and MIC+/Low FS 10%. Patients with MIC+/high 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+/ high 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+/high 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-Amlose 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 Escalghado,1 Bruna Pavia,1 Bengt Lindholm,2 Peter Bergman,2 Peter Stenvinkel.1 1 Federal University Fluminense, Rio de Janeiro, Brazil; 2Karolinska Institute, 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 (H6-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 bacterial taxa.

Results: Thirty-one participants finished the study, 15 in RS group (53.3 %); 56.0±7.5 yrs; 50.0±3.6 months on HD and BMI 26.1±5.0 kg/m^2 and 16 in the placebo group (31.2%); 53.5±11.4 yrs; 44.3±2.6 months on HD and BMI 26.6±5.2 kg/m^2. 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=0.061] 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.
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

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Background: Contamination of contaminated water is a risk factor for infectious diarrhea and according to estimates of the World Health Organization the most often reported cause of death in children and the elderly. Our organization “Easy Water for Everyone (EWfE)” uses a membrane filtration device with repurposed hemodialyzers and we hereby present our remarkable public health effects (Raimann for EWfE, 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. In addition to this, we also tested the association of age on the estimate, and conducted a subset analyses in those younger than 15 years. 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 ROC and Bland-Altman plots. We evaluated the model as a diagnostic tool for sarcopenia using ROC and Bland-Altman plots. We evaluated the model as a diagnostic tool for sarcopenia using ROC and Bland-Altman plots. We evaluated the model as a diagnostic tool for sarcopenia using ROC and Bland-Altman plots. We evaluated the model as a diagnostic tool for sarcopenia using ROC and Bland-Altman plots.

Results: BCM yielded the following equation: ASM (kg) = −1.838 + 0.395 × total body water (L) + 0.105 × body weight (kg) + 1.231 × male sex − 0.026 × age (years) (R² = 0.914, standard error of estimate = 1.35 kg). In the validation group, Bland-Altman reliability analysis showed no significant bias of 0.098 kg and limits of agreement of 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

Indoxyl Sulfate Reduces the Inducibility of NLRP3 Inflammasome 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 monocyte cell-derived macrophages, with or without indoxyl 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 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 indoxyl sulfate probably constitutes 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 Jiuanzuan 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 gender (33.2% in men vs. 11.0% in women, P<0.001). The prevalence of hyperuricemia increased from 19.2% 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 (P=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, polycythemia secondary to chronic exposure to high altitude may also contribute to the hyperuricemia.

Fig 1 Prevalence of hyperuricemia and serum uric acid level in different age group (Left: Prevalence of hyperuricemia, Right: serum uric acid level). *P<0.001
Changes in the Gut Microbiota After a Controlled Feeding Study in Individuals with CKD and Healthy Controls

Annabel Birute,1 Gretchen Wiese,2 Tzu-Wen L. Cross,2 Riya Thakkar,2 Stephen R. Lindemann,2 Elizabeth Stremske,2 Ranjani N. Moorthi,1 Kelly Swanson,1 Sharon M. Moe,1 Kathleen M. Hill Gallant.1,2 Indiana University School of Medicine, Indianapolis, IN; 3Purdue University, West Lafayette, IN; 4University of Illinois System, Urbana, IL

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, GFR 29-55mL/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 QIME2 and LEfSe.

Results: Fecal microbial diversity did not differ between patients with CKD or matched controls and was not affected due to the dietary intervention. At baseline, control individuals had a relative higher abundance of Bifidobacteria and an unclassified genus within Coriobacteriaceae, while CKD patients had a higher relative abundance of Lachnospiraceae. After receiving a week of controlled meals, CKD patients had a higher relative abundance of Anaerotruncus 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 Lachnospiraceae and higher Bacteroides and Holdemansia. Meanwhile, healthy controls had a lower relative abundance of Anaeroanaerobias and Clostridium, while controls had a higher relative abundance of Parabacteroides and Sutterella. Changes in the Gut Microbiota After a Controlled Feeding Study in Individuals with CKD and Healthy Controls

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), 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 ± 13.0ml/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 matched patients with IS and PGC1α between the groups of patients. In the HD group was observed a positive linear correlation between TFAM and NRF1 (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.

Dysbiosis of Gut Microbiota in Adult Idiopathic Membranous Nephropathy with Nephrotic Syndrome

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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 158 individuals were recruited for this study. Of these, 80 were CKD–3–5 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. The results indicated that the nephrotic syndrome (NS) patients had a significantly different alpha and beta diversity compared with the CKD–3–5 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, Megasphaera, Akkermansia, and the butyrate-producing bacteria Lachnospiraceae, Roseburia, and Fusobacterium were more abundant in the controls (LDA score > 3) than the CKD–3–5 and NS patients. Compared with the healthy controls, we found that Parabacteroides was increased in CKD–3–5 and NS patients. In addition, Oscillibacter 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 Myroides 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.

The Alter of Gut Microbiota in Dialysis Patients and Its Influence on the Prognosis for ESRD Patients

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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 fscal 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 Lachnospiraceae, Klebsiella, Akkermansia and Roseburia. HD could repair the abnormal changes of these flora in pre-dialysis patients. We could not found any bacteria difference 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 Bacteroides 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 restore the relative abundance of beneficial bacteria and reduced some potential pathogen bacteria. Some gut microbiota were associated with prognosis in all of ESRD patients and peritonitis in PD patients.
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 low 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). We evaluate the effect of the ONS with and without exercise during the HD sessions for 6 months in the quality and quantity of MM in adult HD patients.

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 Theraband 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). According to the data distribution Student t test or Mann-Whitney test were used to analyze the data.

Results: Twenty-three patients complete the study. Both groups improved their weight (ONS: baseline, 53.5 ± 4.9kg; final, 54.3 ± 4.9kg; p = 0.020 and ONS + EX: baseline, 57.2 ± 9.2kg; final: 59.9 ± 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% LIT; final: 53.5 ± 4.9% LIT). The EX group had improvements in the 6MWT: HGS and in the SPPB (baseline: 383 ± 58m, final: 425 ± 44m; p = 0.000; baseline: 22.6 ± 8.8kg, final: 24.8 ± 8kg, p = 0.000 and baseline: 10.2 ± 1.1, final: 10.8 ± 1.4, p = 0.801, respectively) with decreases in the intramuscular lipid infiltration (baseline: 53.1 ± 4.5% LIT; final: 50.0 ± 3.8% LIT).

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

PO2049
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 associated with mitochondrial function and physical performance, critical components of protein-energy wasting observed in patients with CKD.

Methods: In a cross-sectional study, we evaluated 63 participants [20 with CKD stage 3-5, 20 with CKD stage 5 on maintenance hemodialysis (MHD), and 20 controls with no history of CKD]. Mitochondrial function was evaluated using 31P magnetic resonance spectroscopy to evaluate the phosphocreatine (PCr) recovery after exercise. A longer PCR recovery results in a greater time constant tau (τ), which indicates worsening mitochondrial function. Physical performance was measured using the six-minute walk test. BCAA levels were measured in plasma samples using nuclear magnetic resonance. Linear regression analysis was used to evaluate association and adjusting by age, race, sex, and body mass index (BMI).

Results: Groups were similar in terms of gender, BMI, and history of diabetes and hypertension. Patients on MHD were younger than patients with CKD stage 3-4 (p<0.05, r=0.67 and p<0.05, r=-0.54, respectively). The EX group had improvements in the 6MWT: HGS and in the SPPB (baseline: 383 ± 58m, final: 425 ± 44m; p = 0.000; baseline: 22.6 ± 8.8kg, final: 24.8 ± 8kg, p = 0.000 and baseline: 10.2 ± 1.1, final: 10.8 ± 1.4, p = 0.801, respectively) with decreases in the intramuscular lipid infiltration (baseline: 53.5 ± 4.9% LIT; final: 50.0 ± 3.8% LIT).

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
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-1β) 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

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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 50 ng/ml, 1,25-dihydroxyvitamin D (1,25D) was 55 pg/ml. 24-hour urine sodium was 145 mmol, urine ammonia was 30 meq, urine citrate was 590 mg, and urine magnesium was 102 mg. 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).

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

Time to Hyperkalemia Recurrence in 1 Year Among 103,155 US Veterans

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Background: Elevated serum potassium (sK) is commonly asymptomatic, but in a subset of patients, hyperkalemia (HK) is associated with worse outcomes and frequent recurrence. Whether the initial HK event was captured during a hospitalization may be associated with time to recurrence. Further characterizing time to recurrence in inpatient (INPT) and outpatient (OPT) settings may improve HK monitoring and treatment.

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

Underline represents presenting author.
Methods: Among 3,958,837 US veterans that had a sK between 2004-2006, there were 589,019 that had an index 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 85,940/53,757 (16%) of patients with index INPT and OPT events, 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/1.73 m². In patients with HK recurrence, 50% (n=51,675) 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 workforce 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
Intention to treat (A) and as-treated (B) analyses: change moderate to vigorous physical activity (MVPA) in EIM vs mHealth

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-Symptom Burden (FACT-SB) and Leicester Uremic Symptom (LUS) Scale. Quality of life using SF-36 questionnaire, functional capacity using Duke Activity Status Index, Physical Fatigue Scale (FACIT-F) and Leicester Uremic Symptom Scale, Quality of life Symptom burden was assessed using Functional Assessment of Chronic Illness Therapy-Overall Well being (FACT-G), Functional Assessment of Chronic Illness Therapy-Physical Well being (FACT-P), Functional Assessment of Chronic Illness Therapy-Spiritual Well being (FACT-S) and Leicester Uremic Symptom Scale, Quality of life

Results: At baseline, SF-36 and FACIT-F scores were similar. At baseline, FACIT-F significantly correlated positively with physical activity (r = 0.35, p<0.05). 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 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 ALMIFMI deficits (mean Z-score -0.31 at 24 months, p=0.02 vs controls). Fat gains were disproportionately_visitual 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

PO2060
Changes in Body Composition, Muscle Strength, and Fat Distribution Following Renal Transplantation

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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 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 ALMIFMI deficits (mean Z-score -0.31 at 24 months, p=0.02 vs controls). Fat gains were disproportionately_visitual 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
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 ATPmax (-0.12 m/s, p<0.01 and -0.19 m/s, p<0.01, respectively). Accelerometry counts per minute (r=58, p<0.01) was more strongly correlated with ATPmax than HAP scores (r=46, p<0.01) with no interaction by CKD status (p=9). Accelerometry counts explained 43% of the difference in ATPmax between CKD and controls and HAP scores 15% after adjustment.

Conclusions: Objective PA was more strongly associated with ATPmax and explained more of the differences in ATPmax between CKD and controls than self-reported PA. Further studies should demonstrate if exercise interventions can improve muscle ATPmax in CKD.

Funding: NIDDK Support, Private Foundation Support

Figure 1. Association of ATPmax with log transformed acceleration counts

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
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). 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 mmol/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 28.5±1. The mean eGFR was 39±7.5 ml/min per 1.73m² in CKD and 98±15 in non-CKD. The mean ATPmax was 0.67±0.185 mM/sec and mean FACT-F score was 49±11.5. CKD was associated with increased fatigue (mean difference: 7.6, 95% CI [1.8, 13.5], p=.025) compared to non-CKD after adjustment. Of those with CKD each 1 SD (standard deviation) greater ATPmax was associated with a 5.4-point (95% CI [1.03, 9.7]), p=.017) reduction in fatigue after adjustment. Further adjustment for MA attenuated the estimated association by 38% (3.3 points, 95% CI [-1.1, 7.7], p=.134). Of those with CKD, participants with MA (n=15) had a 10. points greater fatigue (95% CI [1.8,18.1], p=.018) after adjustment compared to those without MA (n=21).

Conclusions: 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
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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 blood pressure (SBP) and diastolic blood pressure (DBP), and time to first cardiovascular event (CVD event) during follow-up (2013-2018). Outcomes of interest were cardiovascular disease and kidney disease progression, defined as ≥50% eGFR decline or ESRD. Cox proportional-hazards regression models were used to test the association between BP and adverse outcomes. Covariate adjustment was made for age, sex, race/ethnicity, marital status, education, smoking, and body mass index.

Results: Of the 317 participants, 48% were female, 29% had diabetes, and mean age was 28±3yrs. Of those with CKD, 30.7% had CKD stage 3, 14% had CKD stage 4, and 5.5% had CKD stage 5. Median SBP was 120 (IQR: 110-130) mmHg and median DBP was 70 (IQR: 60-75) mmHg. In adjusted models, a baseline SBP ≥130 was significantly associated with CVD events (HR: 3.32, 95% CI: 1.34-7.8) and CKD progression (HR: 1.63, 95%CI: 1.02-2.59) compared with SBP<120. Every 10 mmHg 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 uric acid/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. 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, 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, 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; adjustment was 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 ≥300-299 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
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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, and to examine the association between UACR and ACEi/ARB use.

Results: Among 7,377 adults with HTN, 83.4% had UACR 0-29 mg/g, 13.5% had UACR ≥300-299 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

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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 rates, 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

Rate ratio for each outcome based on generalized linear model with Poisson errors. Composite CV outcome was the 1st occurrence of any 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 for eGFR. We analysed repeated measures data at 10 second intervals over the entire observation period using sequential neural networks with the categorical outcomes of coincident CKD, and incident mortality. Follow up was approximately 10 yrs. Python v 3.77 and TensorFlow v2.0.0 were used for the analysis.

Results: N=4388 TILDA participants were included, N=2013 were male, mean age was 62 (8) yrs, 647 had CKD. 178 died over follow up. Figure 1. A demonstrates profiles coincident CKD, AUC = 0.81(resampled model: which included an input variable weight at time x was estimated based on propensity score to either be—or not be—anaemia at time t. Weighted survival probability and weighted hazard ratio were estimated.

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

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PO2069
Risk of Mortality, ESKD, and Hospitalization Among Medicare Beneficiaries with Pulmonary Hypertension and CKD

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Background: Pulmonary hypertension (PH) is highly prevalent among patients with non-dialysis dependent CKD (~20%). We studied the risks of mortality, ESKD, cardiovascular (CV) and non-CV hospitalizations among those diagnosed with both PH and CKD.

Methods: Patients with PH (based on 2 claims within 2 years) were identified from a Medicare 5% sample (1995-2016). For each PH patient we randomly selected 5 participants diagnosed with the same CKD stage as the PH patient but without a PH diagnosis. We used Cox proportional hazards models to assess the association between PH and mortality, adjusting for age, sex, race, and comorbidities. We considered death as a competing event in Fine-Gray models to assess the association between PH and ESKD.

Results: We studied 41,478 patients with PH and CKD and 207,390 CKD stage-matched patients without diagnosed PH. Over 59% of the study population were >80 years, 12% were African American, 47% had diagnosed diabetes and 46% had COPD. The presence of diagnosed PH (vs. no PH diagnosis) was associated with increased risk of mortality, ESKD, and CV and non-CV hospitalizations at 1-, 3-, and 5-year follow-up (Table 1). Diabetes modified these associations with higher risk of all outcomes noted among those without diabetes.

Conclusions: Among older Medicare beneficiaries diagnosed with CKD, the presence of PH increased risk of mortality, ESKD, and hospitalization. Mechanistic understanding of these associations, especially the increased risk of ESKD, requires additional study.

Funding: NIDDK Support

Table 1. Associations of PH with mortality, ESKD, and cardiovascular and non-CV hospitalization in those with PH and CKD

PO2070
A Marginal Structural Model to Estimate Causal Effect of Time-Dependent Anemia Status on Renal and Cardiovascular Outcomes Among Community-Dwelling Japanese Subjects at Beginning of Impaired Renal Function

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Background: We investigated whether anemia increases the risk of renal and cardiovascular (CV) outcomes considering the changes of anemia status over time, using a marginal structural model.

Methods: We retrospectively analyzed data from a Japanese database (IMDC) consists of annual health checkup data linked to medical and pharmacy claims for over 3 million of beneficiaries. Subjects with consequent eGFR values of ≥60 and then <60 mL/min/1.73 m 2 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-specific hemoglobin value according to the Japanese guidelines. Renal outcomes (composite of ≥30% eGFR decline over 3 years, eGFR <15 mL/min/1.73m2, SCR doubling, initiation of chronic dialysis and kidney transplantation), CV outcomes (myocardial infarction, stroke, unstable angina and heart failure) and mortality was assessed. In order to incorporate dynamic change of anemia status and covariates during the follow-up, a time-dependent standardized inverse probability weight at time x was estimated based on propensity score to either be— or not be—anemia at time x. Weighted survival probability and weighted hazard ratio were estimated.

Results: 32,870 subjects were enrolled in the study cohort (median age 52, 73% male) and 4.2% of subjects had anemia at the baseline. Anemia treatment was rarely provided even in the anemia group (3.9%). During the average of 4.1-year of follow-up period, 210 renal outcomes and 1039 CV outcomes occurred. In 91% of the cases with the renal outcomes, eGFR decline occurred first. The weighted hazard ratios (95% confidence intervals) for renal outcomes, CV outcomes and mortality were 2.6 (1.7-3.8), 1.6 (1.2-2.2), and 2.8 (1.8-4.3), respectively.
PO2077
Estimation of Sodium Consumption by Novel Formulas Derived from 12-Hour Urine Collection
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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<0.007). 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 correlation of spot urine equations from 12-hour urine collection and 12-hour nighttime urine collection can accurately predict 24-hour urine sodium excretion.

Funding: Government Support - Non-U.S.

PO2073
Cardiac Structure and Function and Long-Term Risk of ESKD in African Americans: The Atherosclerosis Risk in Communities (ARIC) Study
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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 [1.3-5.38] 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 for atrial fibrillation (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, SSB, coronary artery disease, CHF, cGFR (CKD-EPI), proteinuria, ACEi- ARB, beta-blocker and diuretic use.

Results: Median sMg was 2.0 mEq/L (25th-75th percentile 1.9 to 2.1 mEq/L). Higher sMg at baseline was associated with lower SBP (2.63 mmHg; 95% CI 0.25 to 4.05, per 1 mEq/L) and lower DBP (-2.75 mmHg; 95% CI -4.16 to -1.34, per 1 mEq/L) (Fig 1A, 1B). Higher sMg was associated with a lower risk of AHA-defined HTN at baseline (aOR 0.25, 95% CI 0.12-0.55, per 1 mEq/L), a lower risk of sub optimally controlled BP (aOR 0.22, 95% CI 0.10-0.53, per 1 mEq/L) but not with a higher risk of CRIC-defined HTN (aOR 0.77, 95% CI 0.50-1.20, per 1 mEq/L). 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 mEq/L).

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.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
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Results: Mean age was 57.5 years, 55.2% were male and 40.4% were black. In the overall population, MPO was associated with a 15% higher risk of AFib hospitalization (aHR 1.15, 95% CI 1.05-1.27, per 1 SD log transformed MPO). The association of MPO with future AFib hospitalization was predominantly noted in those with a prior history of AFib (n=650; P-interaction<0.001), such that there was a 16% higher risk in those with baseline AFib (aHR 1.16, 95% CI 1.01-1.34, per 1 SD log transformed MPO) (Fig 1A), while there was no significant association for those without baseline AFib (aHR 1.11, 95% CI 0.97-1.28, per 1 SD log transformed MPO) (Fig 1B).

Conclusions: In patients with CKD, higher MPO was associated with an increased risk of hospitalization due to AFib, which appeared to be restricted to those with a prior AFib diagnosis. Whether therapies targeting MPO activity and oxidative stress in this population reduce AFib hospitalizations remains to be tested.

PO2075
The Association Between Pre-Donation Hypertension and Early Post-Donation Systolic Blood Pressure Among Older Living Kidney Donors
Fawaz Al Ammary, Abimereki Muzzaalic, 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 aimed 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, 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 2.43 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 1.39, 95% CI 1.07-1.82, p<0.001) and 50% higher odds of having 6-month postdonation systolic BP >140 mmHg (aOR 1.50, 95% CI 1.18-1.90, 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 predonation 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 ≥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 69.6% [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.
**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**

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**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) vs. adult ABPM criteria (aHTN) for the diagnosis of HTN and detection of LVH in adolescents.

**Methods:** ABPM and ECHO reports from adolescents age 13-21 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 ≥120/80 mmHg, sleep BP ≥110/70 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 >51 gm/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 (kappa 0.39, 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 either by 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 >51 gm/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 >51 gm/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 >51 gm/m² (0.63, p=0.07).

**Conclusion:** There is good concordance of HTN and aHTN 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)**


**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 medication (Group 1), subjects with psychiatric diagnosis & on SSRIs/SNRIs (Group 2) and subjects with psychiatric diagnosis & on no medications (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:** Of 475 subjects met inclusion criteria-Group 1=135, Group2=232, and Group3=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 (122.7±11.0 vs 117.5±11.0, p<0.0001) and nighttime diastolic BP (62.2±6.3 vs 56.2±6.2, p<0.0001). There was no difference in the prevalence of early signs of kidney dysfunction over weight and obese adolescents by examining routine labs including creatinine for hyperfiltration and albuminuria.

**Conclusions:** Obesity is a potentially modifiable risk factor for the development and progression of kidney disease in children. The aims of this study were to assess this variation by using ABPM.

**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. The aims of this study were to assess this variation by using ABPM.

**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 and outcomes by subgroups were examined using standard statistical software. 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).

**Conclusion:** Obesity 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 # UL1-TR001105, The Sackler 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**

Qiongjing Yuan,1 Hui Xu,1 Jinwei Wang,1 on behalf of the C-STRIDE study group.1 Guangzhou Hospital Central South University, Changhai, China; 2 Peking 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 3.42-5.09) years, lower incidence rate of ESRD events was observed with increases in 24h U Mg (Figure 1). Higher incidence rate of CVD events was seen with increase in 24 h U Mg (Figure 2). After adjustment for demographic and traditional ESRD risk factors, 24h U Mg 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.
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 related 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 (±6.9), mean LA reservoir strain was 24% (±9.1%). There were 61 events: 40 hospitalizations and 21 deaths. In the adjusted model, HR (95%CI) per SD LA volume index was 1.4(1.0, 1.9); LA reservoir strain was 1.5(1.1, 2.1); LA reservoir strain and LV global longitudinal strain had a c-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
Anoosh Moin, Craig B. Langman. Ann and Robert H Lurie Children’s Hospital of Chicago, Chicago, IL.

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. Children of 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

Table 1 Association of 24h UMg with CVD events among pre-dialysis CKD patients

<table>
<thead>
<tr>
<th>UMg (mg/dL)</th>
<th>Total (n=49)</th>
<th>Model 1</th>
<th>Model 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total CVD</td>
<td>HR (95% CI)</td>
<td>1 (0.6-1)</td>
<td>1 (0.6-1)</td>
</tr>
<tr>
<td>&lt;95%</td>
<td>1.00 (0.58-1.67)</td>
<td>1.00 (0.58-1.67)</td>
<td>1.00 (0.58-1.67)</td>
</tr>
<tr>
<td>≥95%</td>
<td>1.00 (0.58-1.67)</td>
<td>1.00 (0.58-1.67)</td>
<td>1.00 (0.58-1.67)</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

Conclusion: Although non-dipping is 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.

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

Underline represents presenting author.
Proportion of children who are appropriately diagnosed

PO2085

Associations of Blood Pressure Variability with Cardiovascular Events, Death, and ESKD in Patients with CKD

L. Parker Gregg,1,2 Susan Hedaya,1 Hui Yang,1,2 Peter N. Van Buren,1,2 Sankar D. Navaneethan,3,4 Salim S. Virani,1,2 Wolfgang C. Winkelmayer,5 Carlos A. Alvarez,1,2 University of Texas Southwestern Medical Center at Dallas, Dallas, TX; 3VA North Texas Health Care System, Dallas, TX; 4Baylor College of Medicine, Houston, TX; 5Michael E DeBakey VA Medical Center, Houston, TX; 6Texas Tech University Health Sciences Center School of Pharmacy, Dallas, TX, US, Dallas, TX.

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 matched 1:1 for initiation of a loop or thiazide diuretic vs. other antihypertensive class as 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 393 (244-752) days, there were 7,326 CV events, 16,376 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.

Conclusions: 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

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

Underline represents presenting author.
abnormalities. Left ventricular mass index (LVMI), relative wall thickness (RWT) and ejection fraction were normal. Left ventricle was dilated in 1 patient. On beta-2 nanograms/mL, complement C3, C4, C1q, proteinaemia, use of steroids and antihypertensive do not differ significantly between the patients with and without BP abnormalities.

**Conclusions:** Masked HTN and blunted nocturnal dipping is common in adolescents with SLF and can be missed if ABPM is not applied in clinical practice. Additional studies between the patients with and without BP abnormalities.

ABPM has been shown to correlate with target organ damage and provides a more reliable assessment of blood pressure (BP) control compared to clinic BP. Exercise stress testing (EST) is not recommend by the AAP for the evaluation of hypertension although anecdotal, it is used frequently by pediatric cardiologists. Despite this, reports in adults show an association between exaggerated exercise systolic blood pressure (EESP) and cardiovascular mortality and morbidity, masked hypertension, and target organ damage. We report 2 pediatric patients with hypertension and evidence of target organ damage, but with a discrepancy between their ABPM and EST BP results.

**Case Description:** See table below.

**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 181mmHg as the threshold for CVE and ACM. We also examined the interactions of diuretic use with the treatment on CVE and ACM. We also examined the interactions of diuretic use with the treatment on CVE and ACM. We also examined the interactions of diuretic use with the treatment on CVE and ACM.

**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 1/2.0 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 (dihydropyridines) and beta-blockers.

**Conclusions:** Impedance cardiology is a simple, noninvasive method for evaluating underlying hemodynamic drivers of HTN. Hypertension management is more effective when guided by hemodynamic state.
Participants on diuretics over time.

**PO2091**

**Abstract Withdrawn**

**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:** In persons with low baseline diastolic blood pressure (DBP) and previous stroke, intensive systolic blood pressure (SBP) lowering might decrease cerebral perfusion increase risk for recurrent stroke.

**Methods:** SPS3 was a 2x2 factorial RCT that examined the effects of intensities versus standard (<130 vs. 130-149 mmHg) SBP control and combination versus aspirin alone antplatelet 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 63±11 yrs, 63% male and 15% black. Mean baseline SBP was 143±19 mmHg and DBP was 78±11 mmHg. There were 267 strokes over 10725 person-years of follow-up. In spline regression models, those with lower baseline SBP were at higher risk for stroke (Fig1, panel A) but stroke incidence was lower in intensive vs. standard SBP arm all three baseline DBP tertiles (Fig1, panel B). In a spline regression model, there was no evidence that intensive SBP lowering increased the risk of stroke in those with low baseline DBP (Fig 2). Repeating the analysis with a cardiovascular composite (MI, CHF, stroke, or cardiovascular death) table similar results.

**Conclusions:** While observational analysis suggested higher risk of recurrent stroke with low baseline SBP, intensive SBP lowering did not increase recurrent stroke risk in those with low baseline DBP and previous stroke.

**Funding:** NIDDK Support

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**PO2093**

The Influence of Baseline Diastolic Blood Pressure on the Effects of Blood Pressure Lowering on Death and ESKD Outcome

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**Background:** Intensive systolic blood pressure (SBP) lowering decreased the risk of death in SPRINT. However, there are concerns in those with low baseline diastolic blood pressure (DBP) that intensive SBP lowering might adversely affect kidney perfusion and increase the risk for death/ESKD.

**Methods:** The African-American Study of Kidney Disease and Hypertension (AASK) trial examined the effects of two different BP goals (mean arterial pressure (MAP) = 92 vs 102-109) in African American men and women (N=1094) with kidney disease but no diabetes. We investigated whether the effects of BP intervention on the risk of death/ESKD was modified by baseline DBP.

**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 SBP (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

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Figure 1. Mean follow-up SBP, DBP and MAP by BP arm in baseline DBP tertiles.
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 appears to have a largely beneficial direct effect and a small deleterious indirect effect on death/ESKD in CKD.

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 NH2 Support - NHLBI, Veterans Affairs Support
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 = -0.163; 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 inflammatory 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 hyperaldosteronism, with unilateral causes of PA being potentially cured with an adrenal resection. 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 the CKD-EPI equation. Statistical comparison utilized the student’s t-test, Chi-square test, and Wilcoxon rank-sum test.

Results: Of 250 patients included, mean age was 56.6 years (±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 (4.5 ± 4.5 AHM vs 7.3 ± 4.5 AHM, 22% vs. 35%, p=0.002) and 1 year (2.6 ± 2.3 AHM vs 4.8 ± 4.3 AHM, 40% vs. 58%, p=0.002) postoperatively.

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

Anna M. Zemek1, Alexander Hilepas2, Martin Herl1, Waileed Ali3, Benjamin A. Roddy1, George L. Bakris,3 1Department of Medicine, Division of Nephrology, Rush University Medical Center, Chicago, IL; 2Department of Medicine, Rush University Medical Center, Chicago, IL; 3Department of Medicine, Comprehensive Hypertension Center, University of Chicago Medicine, Chicago, IL; 4Department Transplant Surgery, Rush University Medical Center, Chicago, IL.

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 rHTN 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 and no more than a 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)

Mrunalini 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 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 migraines presented for management of uncontrolled severe HTN. Her HTN became increasingly resistant following use of pheniramine and febrifuramine for two years and a recent hysterectomy, with persistently elevated blood pressure (BP) up to 250/100 mmHg. Her medications included: hyalurazine, lopressor, procardia, demadex, accupril, 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 posterior communicating artery and right anterior choroidal artery. She was diagnosed with a cervical ICA dissection, CKD stage 3, heart failure, and severe aortic stenosis. The patient continues to have RfHTN despite maximal medical therapy and has now developed complications including a cervical ICA dissection, CKD stage 3, heart failure, and severe aortic stenosis.

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.

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 protocols 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 Lianat,1 Elias Basil,1 Jonathan J. Taliercio,1 Ali Mehdi,1 Remy Daou,2 Susana Arriagin,1 Victoria Konig,1 Jesse D. Schold,1 Serge C. Harb,1 Per Wierup,1 Sevag Demirjan,1 Georges Nakhoul,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.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
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 pressors (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). (Table 1)

**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>
<th>Stage 3 (N=495)</th>
<th>Stage 4-5 (N=294)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>p-value: b=Kruskal-Wallis test, c=Pearson’s chi-square test</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with kidney disease</td>
<td>N</td>
<td>Stage 3 (N=495)</td>
<td>Stage 4-5 (N=294)</td>
</tr>
<tr>
<td>1+</td>
<td>57.7</td>
<td>50.0 (11.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2</td>
<td>46.4</td>
<td>38.0 (13.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>3</td>
<td>32.7</td>
<td>26.2 (15.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>4</td>
<td>20.9</td>
<td>15.3 (12.6)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Presented as Median [P25, P75] or N (column %).

**PO2104**

**Cardiovascular Events and Mortality in Adults with Kidney Failure after Major Noncardiac Surgery**

Tyrone Harrison,1 Paul E. Ronksley,1 James Wick,1 Shannon M. Ruzycki,1 Matthew T. James,1 Deirdre Mccaughhey,1 Kelly B. Zarnke,1 Brenda Hemmelgarn.2,1 University of Calgary Cammung School of Medicine, Calgary, AB, Canada; 1University of Alberta Faculty of Medicine and Dentistry, Edmonton, AB, Canada.

**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; 590 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. Compared to CKD 3 patients, CKD 4/5 patients required longer intubation (33% more than 2 days compared to 20%, P=0.003), more pressors (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 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). (Table 1)

**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.

**PO2105**

**Race Differences in Cardiovascular Events After Percutaneous Coronary Intervention-Induced AKI**

Joseph Lunvera,1 Robert M. Clare,2 Karen Chisswell,2 Julia J. Scialla,2 Patrick H. Pun,2,1 Kevin L. Thomas,3,1 Monique Starks,2,1 Clarissa J. Diamantidis.1 1Duke University School of Medicine, Durham, NC; 2Duke Clinical Research Institute, Durham, NC; 3University of Virginia School of Medicine, Charlottesville, VA.

**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 6699 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 2.01]. 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 Death in Adults with CKD: Findings from the Chronic Renal Insufficiency Cohort (CRIC) Study
Mary Hannan,1 Ana C. Ricardo,1 Julia Brown,1 Eunice Carmona,1 Zahraa Hajiri,2 Natalie Meza,1 Jinsong Chen,1 Mildy R. Saunders,2 James P. Lash,1 1Department of Medicine and 2Department of Urology, University 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 1-2 criteria, and non-frailty as meeting zero criteria. Cox proportional hazards models were used to evaluate associations with atherothrombotic events, incident heart failure, and death.

Results: Baseline age was 57.5 years, 45.5% were female, mean eGFR was 46.9mL/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 atherothrombotic 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 atherothrombotic events compared to non-frail individuals (Table).

Conclusions: 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

<table>
<thead>
<tr>
<th>Frailty Status</th>
<th>All-Cause Death</th>
<th>Cardiovascular Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-frail</td>
<td>0.80</td>
<td>0.79</td>
</tr>
<tr>
<td>Pre-frail</td>
<td>1.26</td>
<td>1.26</td>
</tr>
<tr>
<td>Frail</td>
<td>1.40</td>
<td>1.32</td>
</tr>
</tbody>
</table>

*Adjusted for clinical site, age, sex, race/ethnicity, education, marital status, smoking, BMI, systolic BP, diabetes mellitus, cardiovascular disease, LDL cholesterol, HDL cholesterol, ACE/ARB, aspirin, statin, baseline eGFR, and proteinuria

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 preventive 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=1167), ischaemic stroke (n=1802), and intracerebral haemorrhage (n=209), 1267 (40%) had CKD. CKD was independently associated with greater risk of ischaemic 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 mainly 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 ischaemic stroke; adjusted OR=4.06, 2.04-8.06; p=0.001 for initial NIHSS). Among patients with ischaemic 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 year) 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.

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 82.4 yrs; 45.4% female). During a median follow-up of 7.5 yrs and compared with non-normalized BP, normalized BP was associated with an increased risk of cardiovascular death (HR, 1.79; 95% CI, 1.23-2.61) and all-cause mortality (HR, 1.48; 95% CI, 1.15-1.90). 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

<table>
<thead>
<tr>
<th>Cardiovascular death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-normalized BP</td>
</tr>
<tr>
<td>Normalized BP</td>
</tr>
</tbody>
</table>

*Adjusted for clinical site, age, sex, race/ethnicity, education, marital status, smoking, BMI, systolic BP, diabetes mellitus, cardiovascular disease, LDL cholesterol, HDL cholesterol, ACE/ARB, aspirin, statin, baseline eGFR, and proteinuria

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.

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 GFR (RR 0.75, 95% CI 0.55 to 1.02; participants = 14777; studies = 4; 12%, p ≥ 0.53), but a significant difference between rise in serum potassium level (RR 0.90, 95% CI 0.84 to 0.96; participants = 14334; studies = 4; 12% 66%), and elevation of serum creatinine level (RR 0.86, 95% CI 0.78 to 0.95; participants = 1470; studies = 3; 12% 72%).

Conclusions: In HF patients, sacubitril-valsartan shows possible reduction of risks for renal impairment, and definite reduction of risks for both increasing serum creatinine and hyperkalemia, as compared to ACEi and ARBs.

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

467
Non-increase of serum creatinine

Non-increase in serum potassium

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 Hua He,2 Charlton C. Starke,2 Yajun Guo,3 Siyi Geng,2 Chunjian Chen,2 Erin Mahone,2 Jodie R. Laurent,2 Christina L. Wiggins,2 Praktiti Mehta,2 Paige R. Pielert,2 Vecchi Batuman,1 L. Lee Hamm,1 Jiang He.2
1Tulane University School of Medicine, New Orleans, LA; 2Tulane 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 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 84.2% for ABI and 44.8%, 93.3%, 54.2%, and 99.5% for TBI, respectively. AUCs for ABI and TBI were 0.71 and 0.73, 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 a higher 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 Fishbane,2 Pablo E. Pergola,3 Lynda Szczez,4 Tyson T. Lee,4 Dustin J. Little,4 Kin-Hung P. Yu,4 Washington University School of Medicine in Saint Louis, Washington University in Saint Louis School of Medicine, Saint Louis, MO; 2Northwell Health, Great Neck, NY; 3Renal Associates PA, San Antonio, TX; 4FibroGen Inc, San Francisco, CA; 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, roxadustat-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 III or IV 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 least-squares mean (LSM) [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.

PO2113
Roxadustat Lowers Low-Density Lipoprotein Cholesterol in Patients with Anemia of CKD
Simon D. Rogier1, Mohamed A. El-Shalawy2, Carol A. Pollock2, Rosa H. Jimenez3, Robert Leon3, Maksym Pola3, Kin-Hung P. Yu4, Renal Research, Gosford, NSW, Australia; 2The University of Sydney, Sydney, NSW, Australia; 3FibroGen Inc, San Francisco, CA; 4AstraZeneca, Warsaw, Poland; 5University 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=1948) and a 14.2% increase in the placebo group (n=1430). The LSM treatment difference was statistically significant (p<0.0001). In the patients with DD-ID group, there was a 18.5% 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-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).
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>Mean Change</th>
<th>NDD-NDD</th>
<th>DD</th>
<th>ID-DD</th>
</tr>
</thead>
<tbody>
<tr>
<td>NDD-NDD</td>
<td>120.1</td>
<td>-17.1 (1.29)</td>
<td>122.5</td>
<td>163/162</td>
<td>123.2</td>
</tr>
<tr>
<td>DD</td>
<td>119.9</td>
<td>-17.0 (2.17)</td>
<td>127.2</td>
<td>160/160</td>
<td>126.6</td>
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<tr>
<td>ID-DD</td>
<td>120.0</td>
<td>-17.2 (2.63)</td>
<td>127.6</td>
<td>160/160</td>
<td>126.8</td>
</tr>
</tbody>
</table>

Roxadustat is an oral hypoxia–inducible factor prolyl hydroxylase inhibitor that stimulates erythropoiesis, which can affect blood pressure (BP). We assessed 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=3880), including incident-dialysis-dependent (ID-DD; on dialysis for ≤ 90 days) patients and NDD patients (data censored after dialysis initiation) were included. Mean change from baseline (CFB) in mean arterial pressure (MAP) averaged over Weeks 20–28 (NDD-NDD, SDD) and over weeks 10–12 (ID-DD); time to first exacerbation of hypertension (SBP ≥ 170 mmHg or DBP ≥ 110 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 significantly reduced among patients with eGFR≥60 compared to placebo (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.

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-PAD and NDD-CKD patients and epoetin alfa in DD-CKD patients.

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

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 57±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 15–30). Rivaroxaban reduced primary endpoint events with no heterogeneity by eGFR above or below 60 (most CV death 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

No Adverse Effects of Veverimer on Volume Status or Blood Pressure in Patients with CKD and Metabolic Acidosis

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Background: Current American Heart Association guidelines recommend sodium bicarbonate (NaHCO₃) for treatment of metabolic acidosis in dialysis patients. Veverimer would not increase BP, weight or induce volume overload. In Phase 3 randomized, blinded placebo-controlled trials in acidic patients (pts) with CKD (baseline mean eGFR 29 mL/min/1.73 m²), veverimer significantly increased serum bicarbonate (L/S mean ± 4.7 μEq/L at Week 52) with safety profile similar to placebo (Wesson et al. Lancet, 2019).

Funding: Commercial Support - Fibrogen, Inc.; AstraZeneca plc; Astellas Pharma Inc.
Methods: We analyzed parameters related to volume status in these Phase 3 trials. 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). Conclusion: 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.

Poster

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 patients and 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 at 24 months (Figure). CKD-D patients were 22.7% (-33.3%, -11.4%) less likely to receive high-intensity statins. There was a steady and similar increase in proportional achievement 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.

PO2118

Cardiovascular Determinants of Physical Function in Patients with ESKD on Hemodialysis

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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. Conclusion: 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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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 examine the relationship 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: 2355 patients underwent 6615 patient-years follow-up (pyru), 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 pyru. 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.

The first event was MACE in 571 patients (24.2%), ESKF in 299 patients (12.6%) 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.

Introduction: Laboratory data provide clues to the etiology of resistant hypertension. We present one such case where in a prescriptive diagnosis of Liddle’s syndrome was made, and appropriate therapy initiated. Yet the hypertension failed to be controlled despite multiple antihypertensive regimens.

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 hypertension 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 Asians. It presents with features suggestive of mineralocorticoid excess. The differential diagnoses are Liddle’s syndrome, Crhousos 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.

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, 1.934; 95% confidence interval, 1.185-3.157; P = 0.008) and high ACI-low RDW (adjusted hazard ratio, 1.921; 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 = 0.002).

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.

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 medications in addition to amiloride should be a clue to the misdiagnosis.
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 blood pressure measurement in ipsilateral affected arm as not being risk factor for lymphedema.

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. 132±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 and 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 prospectively recruited and underwent transthoracic 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 (65.8±12.2yrs, 63% male) were recruited and followed for a mean period of 3.9±2.7years. 56 patients developed the composite endpoint. On log rank tests, impaired LAs (Figure 1), older age, lower eGFR, anaemia, 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 creatine and thus has the potential to be a ‘biomarker’ for identification of high-risk patients, enabling early initiation of therapy.

Deformed stent (arrow) with severe in-stent restenosis
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 structure 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 prothrombogenic 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.

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±12.03, 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 -69.3] in T1, 0 [0-47.2] in T2 and 6.4 [0-64.7] in T3. (p=0.088) Multivariate analysis showed that preventing excessive weight gain might help prevent cardiovascular complications in CKD.

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.

Funding: Government Support - Non-U.S.
Macrophase Neutrophil Gelatinase-Associated Lipocalin Has a Critical Role in Aldosterone-Induced Renal Fibrosis via the CCL5/IL4 Pathway

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Background: Neutrophil Gelatinase-Associated Lipocalin (NGAL) (or lipocalin 2) is a matrix metalloproteinase inhibitor 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 infection in a CKD mouse model protects from proteinuria and renal lesions. We hypothesized that NGAL produced from macrophages promotes expression of chemotacticant molecules involved in renal lesions induced by mineralocorticoid excess.

Methods: The role of Lcn2 was analyzed using full Lcn2 knock out mice (NGAL KO) challenged with uni-Nephrectomy, Aldosterone 200 mg/kg/day. Salt 1% (NAS model) during 6 weeks. Assessment of CCL5/IL4 in kidney fibrosis were studied using macrophage administration (50 mg/kg in chow diet) or by injections of anti-IL4 antibody (600 mg/kg week).

Results: NAS induced a significant increase in the expression (relative values, meansSEM, 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 (3.38±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, CD86 and CCL5  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. Macrophages isolated from Lcn2 KO or WT mice were co-treated with aldosterone (10µM) and NaCl (40mM). In WT macrophages, expression of CCL5 (2.81±0.30) and the CCL5 chemokine (2.48±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 Th2 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, a-SMA and fibronectin.

Conclusions: NGAL produced by macrophages plays a critical role in renal interstitial fibrosis through the CCL5/IL4 pathway in mice exposed to mineralocorticoid excess.

PO2130
Water Intake and Blood Pressure in Children: Results from the SPA Project

Gianluigi Ardissino, Michela Perrone, Silvia A. Ghiglia, Patrizia Salicci, Francesca Tel, Valentina Capone, Maria Cristina Mancuso, Sandra Piantanida, Silvia Di michele. SPA Project 'Pediatric Nephrology, Dialysis and Transplantation, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milano, Italy; 'Pediatric Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy; 'Pediatric Department, Vittore Buzzi Children's Hospital, University of Milano, Milano, Italy; 'Polo Materno Infantile - Ospedale F. del Ponte, Varese, Italy; 'UOC Pediatría Ospedale di Pescara, Pescara, Italy.

Background: Sodium (Na) intake is involved in the development of hypertension (HTP); to reduce Na is important in the treatment of HTP, 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 years old (IQR: 3.5-6.2) 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, perhaps 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.

PO2131
Altered Tryptophan Catabolism via the Kynurenine Pathway Associates with CKD-Accelerated Atherosclerosis

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Background: Non-traditional risk factors like inflammation and oxidative stress play an essential role in the increased cardiovascular disease risk prevalent in chronic kidney disease (CKD). Tryptophan catabolism by the kynurenine pathway (KP) is linked to atherosclerosis and renal function in both clinical studies and experimental models. However, the role of KP in the pathogenesis of CKD accelerated atherosclerosis is unknown.

Methods: 9-week old 5/6 nephrectomized (CKD) and sham-operated (CON) LDLr−/− mice were placed on a high-fat/high-cholesterol diet (HFD) for 16 weeks. KP metabolites were measured using targeted mass spectrometry in the plasma, urine and tissues. Expression and activity of Indolamine 2,3 dioxygenase (IDO1) - first step of the KP were quantified by immunoblotting, immunohistochemistry, and kynurenine to tryptophan ratio (KTR) in aortic tissue in both groups.

Results: CKD mice demonstrate increased KP metabolites compared to sham-operated mice (CON) both at baseline and after exposure to HFD for 16 weeks. Exposure to HFD for 16 weeks increases most KP metabolites in both CON and CKD mice, except for levels of tryptophan and 3-hydroxy antranilic acid that decrease with HFD exposure. 3-hydroxy kynurenine and kynurenine acid increase with HFD exposure in CKD mice, whereas these levels tended to decrease in controls. Hepatic tissue in the CKD mice fed HFD reveals no changes in KP metabolites except increased quinolinic acid, whereas the splenic tissue and renal tissue reveals low tryptophan levels and higher KTR, kynurenine acid, and antranilic acid. These changes in the HFD fed CKD mice are likely due to a combination of increased synthesis in specific tissues and reduced clearance. IDO expression and activity were also increased in atherosclerotic lesions of CKD mice on HFD for 16 weeks compared to control mice with intact renal function.

Conclusions: In summary, KP metabolites are altered both in the circulation, tissues, and arterial wall of the CKD atherosclerosis model implicating KP in the pathogenesis of atherosclerosis in CKD.

Funding: Other NIH Support - NHLBI

PO2132
Male Sex Hormones Drive an Increase in Renal Necrosis in Spontaneously Hypertensive Rats (SHR)

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Background: We recently published that maturation in male SHR increases necrosis which contributes to the development of hypertension. Maturation in male SHR is associated with both increases in sex hormones and blood pressure (BP). Testosterone has been shown to induce renal tubular cell necrosis in vitro. This study tested the hypothesis that male sex hormones drive maturation-induced increases in renal necrosis in male SHR.

Methods: At 4 wks of age, male SHR were randomly assigned to one of three groups: sham, gonadectomy (ORX), or treatment with the BP lowering drugs hydrochlorothiazide (HCTZ; 55mg/kg/day) and reserpine (Res; 4.5 mg/kg/day) in drinking water to prevent age-related increases in BP (n=6). At 8 wks of age, telemeters were implanted in a subset of rats (n=3-4/group). Rats were allowed 1 wk of recovery, then BP was continuously recorded. All rats were euthanized at 13 wks of age. Renal necrosis was quantified using FACs analysis of 7AAD+ cells. Data are expressed as mean ± standard error. Kidneys were isolated from additional untreated 5 and 15 wk old male SHR (pre- and post-maturation) and processed for Western blot analysis of key proteins mediating necrosis, receptor-interacting protein kinase 3 (RIP-3) and high mobility group box 1 (HMGB-1).

Results: H2O was significantly lower in ORX and HCTZ/Res-treated SHR compared to sham (mean arterial BP (mmHg): Sham = 139±2, HCTZ/Res = 117±3; ORX = 126±2; p<0.002). As expected, renal necrosis was greatest in sham control (renal necrosis

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

Underline represents presenting author.
expressed as % total gated kidney cells: Sham = 46±3.0%. ORX significantly decreased renal CD81 and increased NCC in Hypertensive nephropathy compared to normal nephroi, with no evident altered vs. sham despite having the lowest BP (ORX = 4.4±0.9; HCTZ/Res = 3.5±0.3; p<0.003). To begin to gain insight into the mechanisms mediates maturation-induced increases in nephrosis, RIP3 and HMGB1 protein expression were measured in 5 and 15 wk old normal blood pressure, decreased kidney function, as well as decreased KLF2 expression of glomerular endothelial cells 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.

**Conclusions:** We established 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 ofafferent 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 nephropathy.

**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 (RSNA). The presence of the SP receptor NK-1 on renal immune cells was assessed by FACS.

**Results:** IRA: capsaicin decreased RSNA from 62.4±5.1 mV*sec to 21.6±1.5 mV*sec (p<0.003) in controls, a response impaired in nephritis. Suppressed RSNA in nephritic rats and enhanced SP was revealed transiently after systemic administration of a neurokinin 1 (NK1-R) blocker. NK-1 receptors occurred mainly on CD11+ dendritic cells (DCs). An enhanced frequency of CD11c+CD11c+ cell, NK-1 receptor+ macrophages and DCs were assessed in nephritis. Administration of the NK-1 antagonist aprepitant during nephritis reduced CD11c+CD11c+ cell, macrophage infiltration, renal expression of chemokines and markers of sclerosis.

**Conclusions:** Hence, SP promoted renal inflammation by weakening sympatheticnhibitory mechanisms while at the same time substance SP released intrarenally from afferent nerve fibers aggravated immunological processes i.e. by the recruitment of DCs.

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

**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 ofafferent 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 nephropathy.

**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 (RSNA). The presence of the SP receptor NK-1 on renal immune cells was assessed by FACS.

**Results:** IRA: capsaicin decreased RSNA from 62.4±5.1 mV*sec to 21.6±1.5 mV*sec (p<0.003) in controls, a response impaired in nephritis. Suppressed RSNA in nephritic rats and enhanced SP was revealed transiently after systemic administration of a neurokinin 1 (NK1-R) blocker. NK-1 receptors occurred mainly on CD11+ dendritic cells (DCs). An enhanced frequency of CD11c+CD11c+ cell, NK-1 receptor+ macrophages and DCs were assessed in nephritis. Administration of the NK-1 antagonist aprepitant during nephritis reduced CD11c+CD11c+ cell, macrophage infiltration, renal expression of chemokines and markers of sclerosis.

**Conclusions:** Hence, SP promoted renal inflammation by weakening sympatheticnhibitory mechanisms while at the same time substance SP released intrarenally from afferent nerve fibers aggravated immunological processes i.e. by the recruitment of DCs.

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

**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 death. 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 and observing adhesion of cells and cell death. We established the appropriate culture environment by confirming the pressure and survival rate applied to endothelial cells according to rotational force and observing adhesion of cells and cell death.

**Results:** The survival rate of human primary glomerular endothelial cells was maintained at a pressure of up to 4mHg and decreased from above. After the application of 4mHg pressure for 48hr in human primary glomerular endothelial cells, expression of KLF2 mRNA was decreased, while eSMA 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.

**Conclusions:** Hence, SP promoted renal inflammation by weakening sympatheticnhibitory mechanisms while at the same time substance SP released intrarenally from afferent nerve fibers aggravated immunological processes i.e. by the recruitment of DCs.

**Funding:** Government Support - Non-U.S.
Substance P: Differential Influences on Action Potential Production in Afferent Neurons of the Kidney? Kristina Rodionova,1 Tilmann Ditting,1,2 Christian Ott,2,3 Roland E. Schmieder,4 Mario Schiffer,2 Kerstin U. Amann,1 Roland Veelken,1,2,3 Friedländer-Alexander- Universität Erlangen-Nürnberg, Erlangen, Germany; 2Paracelsus Medizinische Privatuniversität, Nürnberg, Germany.

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 Th11-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 proteins (pH 6) with and without exposure to SP (0.5 μm) or CGRP (0.5 μm). Neuronal classification as tonic (high AP generation under 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/60 of stimulation with pH6). The co-injection of renal NKA and SP decreased the number of action potentials in tonic neurons (15.2±2.1 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/60 vs. 16.9±2.3 APs/60, p≤0.05, mean±SE). Addition of SP did not affect phasic neurons. Co-stimulation with CGRPP 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 potential via a TRPV1-dependent mechanism in acid-sensitive renal afferents could be demonstrated. Afferent nerve fibers are like respond very specific in different conditions while influencing sympathic nerve activity and putatively renal physiology or pathology (proinflammatory actions of SP).

Funding: Government Support - Non-U.S.
MO, month old; NS, 0.6% NaCl; HS, 4% NaCl; *p<0.05 vs. respective NS group; †p<0.05 vs. respective 3 MO group; ‡p<0.05 vs. respective 8 MO group.

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-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 (AgtII, 1000 ng/kg/min subcutaneously) in WT mice a canagliflozin (Can), 15mg/kg/day in drinking water for 4 weeks.

Results: In human kidney samples (N=183 patients), SGLT2 mRNA was significantly correlated with Agt (r=0.55, p<0.001), Renin (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+ Canal than WT+Cana. 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 ameliorate 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 alters blood pressure (BP) in angiotensin-II independent hypertension induced by 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, final body weight and blood pressure was lower in mutant sPRR mice (final body weight 24.9 ± 2.5 vs control 28.0 ± 2.5 g; systolic BP 110 ± 5 vs control 121 ± 6 mm Hg). Percentage decrease in body weight was similar between sPRR and control mice (4.1 ± 0.8% vs control 3.1 ± 1.6%). In the renal cortex, sPRR mice had lower BUN, creatinine, and albuminuria compared to controls (Table 1). Mutant sPRR mice had lower fractional glucose excretion than controls (0.6 ± 0.1% vs control 1.2 ± 0.2%). 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

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

Underlines represent presenting author.
**PO2145**

**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 Cyclopodrine 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 SD rats were subjected to continuous infusion of Ang 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, and 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±9.0 mmHg, n=4), and serum Mg was elevated in HMD group (NMD: 1.6±0.19 mg/dL vs HMD: 2.4±0.09 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±0.10±1.5% vs HMD: 1.1±0.10%, n=4). Positive area of claudin-16 immunostaining in HMD was greater than NMD (NMD: 1.5±0.13% vs HMD: 1.7±0.01%, 15%, 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.

**PO2146**

**Pharmacological Sympathetic Denervation of the Kidney with Angiotensin II Receptor Blockade?**

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**Background:** A putative interaction between angiotensin II (Ang II) and the renal sympathetic nervous system has been described. We tested the hypothesis that the angiotensin II receptor inhibitor candesartan mimicks a functional renal sympathetic denervation.

**Methods:** Measurement of arterial blood pressure (MAP), heart rate (HR), renal sympathetic nerve activity (RSNA), glomerular filtration (GFR), renal plasma flow (RPF), urine volume and urinary sodium. To assess neural control of volume homeostasis, 21 days after the induction of congestive heart failure (CHF) via myocardial infarction rats underwent volume expansion (0.9% NaCl, 10% body weight) to decrease RSNA. CHF rat and controls with or without renal denervation (DNX) or pretreated with the angiotensin II type 1 receptor antagonist candesartan (0.5 ug iv) were studied.

**Results:** CHF rats excreted only 68±5% of the volume load in 90 min. CHF rats pretreated with candesartan or after DNX excreted from 92% to 103% like controls. Decrease of RSNA induced by volume expansion were impaired in CHF rats but unaffected by candesartan point to an intrarenal drug effect. GFR and RPF were not significantly different in controls or CHF rendering more hemodynamic effects on sodium and water excretion unlikely. 0.5 mg candesartan did not inhibit the pressor response to i.v. Ang II as compared to higher blood pressure lowering doses.

**Conclusions:** The prominent function of increased RSNA – retaining salt and water - could no longer be observed after renal ANG II receptor blockade in CHF rats mimicking renal nerve ablation. Since inhibitors of the renin-angiotensin system are nowadays standard treatment of patients with CHF and hypertension, the role of efficient sympathetic denervation in these patients needs further meticulous scrutiny.

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

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**PO2147**

**Extracellular Volume, Peripheral Resistance, and Cardiac Index May Be Altered in Early CKD**

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**Background:** It is unknown if extracellular volume (ECV), cardiac index (CI), and peripheral resistance are altered in early stages of chronic kidney disease (CKD) before significant decline in glomerular filtration rate (GFR) or if these can be identified by routine laboratory measures.

**Methods:** A total of 21 participants, including 13 with CKD stages 1-3 and 8 non-CKD controls, were prospectively recruited from outpatient clinics. CKD stage 3 was defined as an estimated GFR (eGFR) of 30-59 ml/min/1.73 m² and stage 1-2 as an albuminuria-to-creatinine ratio >30 mg/g and eGFR ≥60. ECV was measured using bioimpedance spectroscopy and normalized to total body weight. CI and total peripheral resistance index (TPRI) were measured using non-invasive cardiac output monitoring. Measurements were compared using Fisher exact tests, Student’s t tests, and Pearson correlations.

**Results:** Participants with CKD had a mean (SD) age of 65.4 (12.9) years vs 59.5 (13.5) years for controls, P=0.36. Mean eGFR in the CKD group was 47.0 (17.9) mL/min/1.73 m². In the CKD group there were 8 (61.5%) with diabetes, vs 3 (7.7%) controls, P=0.39. Mean systolic blood pressure was 159.2 (22.3) in the CKD group vs 143.1 (26.2) in the control group, P=0.17. Edema was present in 9 (69.2%) of the CKD group vs. 2 (25.0%) controls, P=0.08. Mean (SD) ECV/weight was marginally higher in the CKD group vs controls (74.2±7.6 mmHg vs HMD: 94.2±7.6 mmHg, P=0.06). The CKD group had higher b-type natriuretic peptide (BNP), 182.8 (236.0) vs 33.5 (35.4) pg/mL, P=0.04, lower CI, 2.4 (0.4) vs 3.0 (0.5), P=0.04, and higher TPRI, 3800.4 (645.7) vs 2980.8 (265.3) dyn.s.cm⁻⁵, P=0.001. Log-transformed BNP correlated with CI, r=-0.77, P=0.002, and TPRI, r=-0.50, P=0.04 (Table). ECV/weight did not correlate strongly with CI, r=0.27, P=0.29, and TPRI, r=0.25, P=0.42.

**Conclusions:** In this hypothesis-generating study, patients with CKD had higher TPRI and lower CI than non-CKD controls. CI and TPRI correlated with BNP but not systolic blood pressure. BNP, an easily measured and universally available test, may be used as a correlate for CI and TPRI in patients with early stage CKD. These findings need to be confirmed in larger cohorts.

**Funding:** Veterans Affairs Support.
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 disease (CKD) is a major pathway for progression to end-stage kidney disease. Although AKI 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. We used an acute model of AKI, and then nephrons 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 kidney 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). Exsudates (3 mg/kg/day; a non-steroidal MR antagonist [MRA]), or vehicle were administrated 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 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.

Funding: Government Support - Non-U.S.
OR=1.20, 95% CI=0.99-1.45; p=0.07). Similarly, although patients with CKD had a lower prevalence of small vessel disease (8.8 vs 13.6%; p=0.01), undetermined (26.1 vs 39.4%; p=0.001), and other aetiology (1.0 vs 3.6%; p=0.001) subtypes, these associations were also lost after adjustment (Adjusted OR=0.81, 0.67-0.97; p=0.03).

Conclusions: There were no independent positive associations between CKD and specific TOAST subtypes which suggests that renal-specific risk factors are unlikely to play an important role in the aetiology of particular subtypes. Future studies of stroke and CKD should report subtype-specific analyses to gain further insights into potential mechanisms.
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.

**Funding:** NIDDK Support

### PO2158

**Title:** Fibroblast Growth Factor 23 Induces Ventricular Arrhythmias and Prolongs QTc Interval in Mice In Vivo Mediated Through FGF Receptor 4

**Authors:** Julian Vallejo, Derek Wang, Jonah M. Graves, Christian Faul, Michael J. Wacker.

**Institution:** Department of Biomedical Sciences, School of Medicine, University of Missouri-Kansas City, Kansas City, MO; Division of Nephrology, Department of Medicine, The University of Alabama at Birmingham, Birmingham, AL.

**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 (FGFR4). 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 FGFR4.

**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 and without pretreatment with an FGFR4-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 PVC/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 28.0 ± 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. FGFR4 blockade abrogated the QTc prolonging effects of FGF23 (n=8).

**Conclusions:** We conclude that FGF23/FGFR4 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

**Title:** Use of Immune Checkpoint Inhibitors in ESKD

**Authors:** Rirmi Wanchoe, Jia Hwei Ng, Jamie S. Hirsch, Rushang Parikh, Yurin Khanin, Kenzar D. Jhaeveri. Northwell Health, Great Neck, NY.

**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 a minimum of one IESKD 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 inhibition alone. Eight patients were receiving proton pump inhibitors. 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 survived from this event. The remaining patients tolerated the ICIs well, without significant complication or side effect. No dose adjustments were required. In regards to cancer status, the cancer did not progress in 3 patients but progressed in the remaining five. 4 patients died. Literature review revealed total of 26 patients mostly receiving HD (92%). Interestingly, 27% of these patients were on dialysis as a result of a rejected kidney transplant due to ICI therapy, and then continued to receive ICI. Over 80% of the patients had either partial or complete response to treatment. Aside from the kidney transplant rejection preceding death, a minimal number of patients had a grade 2, 3, or 4 adverse immunotherapy related event (15%).

**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.

### PO2160

**Title:** AKI as a Risk Factor for Mortality in Oncological Patients Receiving Immunotherapy

**Authors:** Clara García-Carro, Mónica Bolufer, Roxana Bury, Eva Muñoz, Enriqueta Clara Bury, Alejandro Gabaldon, María Jose Cearreas, Daniel Serrón, Maria Jose Soler.

**Institution:** 1Hospital Vall d’Hebron, Nephrology Department, Barcelona, Spain; 2Hospital Vall d’Hebron, Oncology Department, Barcelona, Spain; 3Hospital Vall d’Hebron, Pathology Department, Barcelona, Spain.

**Background:** Checkpoint inhibitors (CIPI) are used to treat cancer by promoting immune-mediated elimination of tumor. CPI-association AKI (CPI-AKI) is an adverse effect and its incidence is 13-29%. The effect of CPI-AKI on patient survival is unknown. Our main goal was to evaluate if CPI-AKI is a risk factor for mortality in patients with cancer under immunotherapy.

**Methods:** We evaluated data of all patients under CPI at our centre between March 2018-May 2019 and followed-up until April 2020. We divided them into 2 groups according the development of CPI-AKI. Kaplan-Meier and Cox survival analysis comparing patients who developed CPI-AKI with those who did not were performed.

**Results:** 821 patients received CPI during the study period. Mean age was 62.03 years and 59.2% men. Malignancies: lung 30.3%, urogenital 20.5%, melanoma 10.8%. CPI treatment: 54.34% patients received anti-PD1, 28% anti-PDLL1, 1.16% antiCTLA4, 4.4% other drug. 11.7% two CPI. Mean baseline creatinine was 0.85±0.30 mg/dl. 125 patients (15.2%) developed CPI-AKI. 790 patients completed follow up and were included in the survival analysis, including all with CPI-AKI. Mean time of follow up 13.2months. 50.8% patients had died at the end of follow up, mean time after starting CPI 8.60 months. There were no differences in age/gender or basal creatinine between patients who died and those who survived. In patients who developed CPI-AKI, mortality was 70.40% vs 47.27% as compared with non-CPI-AKI (p<0.0001). Cox survival analysis including age/ gender, malignancy and type of CPI identified CPI-AKI as a risk factor for mortality (HR 1.597, 95%CI 1.258-2.028, p<0.001) as well as malignance (melanoma HR 1.897, 95% CI 1.290-2.793, lung HR 1.272, 95% CI 1.010-1.602 and urogenital HR 1.543, 95% CI 1.178-2.041, p<0.001) and CPI (PD1 HR 2.160, 95% CI 1.458-3.205, PDL1 HR 1.887, 95% CI 1.523-2.384 and 2 drugs HR 2.049, 95% CI 1.279-3.279, p=0.005).

**Conclusions:** In a study including more than 800 patients with advanced cancer receiving immunotherapy, CPI-AKI incidence was 15.2%. More than 50% of patients died during a mean follow up of 13 months. CPI-AKI development was a risk factor for mortality in our series. As far as we know, this is the first time that the association between AKI and mortality in patients receiving immunotherapy is described.

### PO2161

**Title:** A Single-Center Cohort Study of Nephrotoxicity due to Immune Checkpoint Inhibitors

**Authors:** Craig T. Irwin, Jennifer Panic, Fahad A. Lodhi, Joshua T. Lee, Sabri E. Elkhidir, Connie M. Folz, Soumya Pulipati, Adam M. Bissonnette, Zefi Fatima, Rebecca Blonsky, Chady A. Leon, Siddhartha Kattamanchi. Marshfield Clinic Health System, Marshfield, WI.

**Background:** Previous studies and case reports have demonstrated an increased risk of nephrotoxicity in patients receiving immune checkpoint inhibitors (CIPIs) compared to clinical trials. The primary objective of this study was to contribute to the existing data regarding the frequency, causes of, and risk factors for CPI-induced AKI.

**Methods:** This was a retrospective cohort study of patients receiving at least one dose of a CPI at a health system in Central Wisconsin from 2013 to 2019. Baseline serum creatinine, defined as the average of all values obtained within 6 months of the CPI start date, was compared to the baseline creatinine measured during CPI therapy and through 60 days after the last CPI dose. Patients developing an AKI of at least three day duration were further assessed to determine the likely cause of AKI, with the incidence of potentially CPI-induced AKI being our primary outcome.

**Results:** Of a total of 936 patients, 7 at least one dose of a CPI at MCHS during the study period. After applying exclusion criteria, a total of 910 patients were included in the analysis. A total of 8.4% of patients (76 of 910) were on dual CPI therapy (ipilimumab...
and nivolumab). The incidence of AKI of any duration was 36.6% (333 of 910 patients), with 2.6% (24 of 910 AKI (defined as 3 days or longer or not re-measured) occurring 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 received concurrent bevacizumab. 164 patients (26%) experienced AKI in the first 12 months after initiation of CPI use; 51% of these patients were male, and 90% were White. In the first year of 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 hyponatremia were due to endocrinopathies. CTLA4 inhibitors were associated with a higher risk of grade 3 or 4 hyponatremia 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%).

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)

Harish Shanthanu Seethapathy, Nilasha Rusibamayila, Donald F. Chute, Meghan Lee, Jan A. Stroehblm, Nilasha Rusibamayila, Donald F. Chute, Kerry Reynolds, Meghan E. Sise. Massachusetts General Hospital, Boston, MA; Northwell Health, Great Neck, NY.

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 hypercalcemia 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. The predictors of severe electrolyte abnormalities were determined using a multivariable logistic regression model.

Results: We analyzed 2438 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 following treatment, 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 hyponatremia were due to endocrinopathies. CTLA4 inhibitors were associated with a higher risk of grade 3 or 4 hyponatremia 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%).

Funding: Other NIH Support - National Institutes of Health through Cancer Center Support Grant

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

Underline represents presenting author.

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PO2165

ImmuneCheckpointInhibitor–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 AIN 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, glomerular lesion, ICI class, 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 RCC group (10.8 months) vs no RCC 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 findings regarding statin use, a drug with widespread use.

PO2166

Statin Use, Renal Cell Carcinoma, and Combination Immunotherapy: 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 RCC group (10.8 months) vs no RCC 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(ICIs) 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 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/infucinib). 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 patients#1 and #2 were further stained by indirect IF for acid-base transporters in α-IC(c4 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-kid) were not reduced. This suggests a more targeted reduction in α-IC in patients with AIN secondary to ICI with and without dRTA in the future will be useful.

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. Stroehbahn,2 Harish Shanthanu Seethapathy,3 Nifasha Rusibamalya,2 Keagan S. Casey,2 Shrutti Gupta,2 David E. Leaf,1 Matthew Frigaard,2 Meghan E. Sise.1 Massachusetts General Hospital, Boston, MA;2 Brigham and Women’s Hospital, Boston, MA.
Background: CAR-T therapy uses genetically engineered T cells to target tumor antigens. It is associated with 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 nphrictic 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 were 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 transaminisits within 4-6 weeks of starting dabrafenib. The majority improved with intravenous hydration and discontinuation of the drug. One patient with persistent 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 population.
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 56% 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.
Methods: We have performed 28 treatments of hemodialysis with High cut off filters (HD-HCO). The HD-HCO protocol includes daily dialysis session of 6 hours during the first 6 days to subsequently switch to dialysis every other day until free light chains levels below 500 mg / L, or until the recovery of renal function allows the independence of dialysis. All these patients have a chemotherapy regimen based on Bortezomib (250 mg of the drug is given 3 times a week) and Dexamethasone (28) treatments of hemodialysis (a retrospective analysis of the 28 treatments that are performed with HD-HCO after 8 years of experience (July 2011 to May 2019) to demonstrate the presence of the same complications as the conventional HD.

Results: Loss of albumin is one of the main drawbacks of the technique. Our patients have had changes in albumin levels due to the fact that our protocol includes the infusion of 2 vials of 20% albumin of 50 ml. at the end of each HD-HCO session. Another concern is intradialytic complications. We have reviewed this topic and our results show that patients in HD-HCO do not present a greater number of complications than those who dialyze with HD-C. The total number of sessions was 291. 21 patients developed hypotension (7%). The number of sessions in which the patient presented fever was 6 (2%), coagulation of the circuit occurred in 23 sessions (7.7%). The catheter dysfunction (when it does not allow to reach 250 ml/min of blood flow) in 26 sessions (8.7%) and only 13 times the replacement of the catheter (4.26%) was necessary, consequently, in those who required a greater number of dialysis sessions. In only 1 case (patient who required 27 sessions) to place a permanent Tesio catheter was necessary. Figure 1

Conclusions: Our findings indicate that the HD-HCO has the same safety profile as the conventional HD. There is no serious infectious complications in our patients despite the fact that all of them are immunosuppressed patients (AKI secondary to Multiple Myeloma in patients treated with chemotherapy).

PO2172
Acute Myeloid Leukemia Worsens Sepsis-Induced AKI
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Background: Patients with hematologic malignancies are at high risk for acute kidney injury (AKI), which is associated with high morbidity and mortality. Sepsis is the main cause of AKI in ICU patients with hematologic malignancies. However, the contributions that host or cancer cells make to systemic inflammation during sepsis-induced AKI is not known.

Methods: We created a mouse xenograft model of acute myelogenous leukemia (AML) associated sepsis AKI. Human leukemia HL-60 cells were injected into the tail vein of 6 week-old male NOD/SCID/IL-2Rγ-/- (NSG) mice. After engraftment 2 weeks later, coelomic ligation and puncture (CLP) was performed to induce sepsis (n=8-12 per group). Tumor engraftment in the bone marrow (BM) and blood tumor burden were measured by flow cytometry of human CD33 and human CD45 double positive cells. Multiple organ damage, and both mouse and human systemic cytokines were evaluated at 24 h after CLP or sham surgery.

Results: AML infused sepsis-induced AKI. Both BUN and LDH were significantly higher in AML+CLP than CLP alone (AML+CLP vs vehicle+CLP, BUN 74.5±25.4 vs 42.7±25.3 mg/dL, LDH 3,969±1,720 vs 1,863±661 mg/dL, p<0.05). CLP dramatically increased the percentage of circulating leukemia cells (pre CLP vs post CLP, 2.2±1.3 % vs 20.6±13.3 %, p<0.05). Tumor burden in either BM or blood did not correlate with AKI severity. Systemic mouse IL-6 in AML+CLP at 24 hours after CLP was significantly higher than CLP alone (45.9±2.4 vs 15.1±2.4 ng/mL, p<0.05). Systemic human IL-6 in AML+CLP was higher, but not significantly, than vehicle+CLP. There was no correlation between human cytokines and severity of AKI, although human cytokines (IL-6 and TNFa) significantly correlated with tumor burden in both BM and blood at 24 hours after CLP.

Conclusions: We established a clinically relevant mouse xenograft model of human leukemia associated sepsis AKI. Leukemia intensifies sepsis-induced AKI, and sepsis increased the numbers of circulating AML cells. Systemic cytokines derived from the human leukemias correlates with tumor burden, but not with the severity of cytokines-induced AKI. Whereas malignant cells do not produce circulating cytokines that directly drive the systemic immune response to subsequent sepsis-induced AKI, cell-cell interactions in the BM niche may impact systemic inflammation indirectly, possibly through mouse IL-6.

Funding: NIDDK Support

PO2173
Acute Acquired Fanconi Syndrome (FS) in Multiple Myeloma (MM) After Autologous Hematopoietic Stem Cell Transplantation (HCT): A Case Series
Janina Paula T. Sy-Go, Nelson Leung, Mayo Clinic Minnesota, Rochester, MN.

Background: Proximal tubular dysfunction can occur in patients with MM. The main clinical presentation is electrolyte abnormalities indicative of FS. The objective of the study was to describe and identify the rate and clinical predictors of developing acute acquired FS in adult patients with MM after autologous HCT.

Methods: We identified 2515 adult MM patients who underwent autologous HCT at 28 treating centers. Conventional dialysis (CM) from December 31, 2018. 45 without research authorization were excluded. 13 patients were identified after searching for “Fanconi,” “Fanconii,” and “Fanconi’s” in the EMR. 6 patients did not have FS. 4 patients were diagnosed with FS prior to HCT. The remaining 3 patients (0.12% of cohort) were clinically diagnosed to have FS based on features suggestive of FS- hypokalemia, hypophosphatemia, hypouricemia, proximal renal tubular acidosis, and normoglycemia.

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

PO2174
Hyponatremia Is Common After Indwelling Catheter Drainage of Malignant Ascites
Shruti Gupta,1 Maria Clarissa Tio,2 Emily D. Gutowski,2 Michael S. Stecker,3 Ashish Verma,2 Shveta S. Motwani,2 David B. Mount2,1 Gearoid M. McMahon,4 Sushrut S. Waikar1,4 Brigham and Women's Hospital, Boston, MA; 2Harvard Medical School, Boston, MA; 3Dana-Farber/Children's Hospital Cancer Center, Boston, MA; 4Boston Medical Center, Boston, MA.

Background: Indwelling peritoneal catheters (IPCs) are frequently used to drain tense, symptomatic, malignancy-related ascites. Large-volume drainage may lead to hyponatremia due to massive salt depletion. To date, no studies have examined the epidemiology of hyponatremia after IPC placement.

Methods: We retrospectively reviewed the charts of 461 patients who had IPCs placed between 2006 and 2016 at a tertiary care hospital. Among the 309 patients with labs available pre- and post-catheter, we studied the incidence of hyponatremia and its risk factors. We also examined the management of hyponatremia and its association with mortality.

Results: The overall incidence of hyponatremia post-IPC placement was 85%, of whom 8% had severe hyponatremia with a serum sodium (sNa) <120 meq/L. The mean decline in sNa pre- versus post-catheter was 5 mEq/L (+/- 5.1) and fell by a 10 meq/L among 52 patients (16.8%). Patients with hyponatremia prior to catheter placement had an 8-fold (95% CI, 2.9-21.7) higher adjusted odds of having persistent hyponatremia post-catheter (Table 1). Patients with hepatitis pancreatic-biliary malignancies and lower BMI also had a higher adjusted odds of hyponatremia. Hyponatremia was either unrecognized or untreated in 61% of patients. Patients who had sNa ≤120 meq/L had shorter median survival compared with those with a post-IPC sNa <120 meq/L (8 versus 17 days, log-rank p value = 0.03 (Figure 1)).

Conclusions: Though IPC placement is often a palliative measure, severe hyponatremia is common, and severe hyponatremia may be associated with shorter survival. These patients may warrant closer monitoring post-catheter placement.

Funding: Other NIH Support - NIDCD F32DC017342

Table 1: Predictors of Hyponatremia Post-IPC

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariable Analysis</th>
<th>Multivariable Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>OR (95% CI)</td>
<td>0.98 (0.96-1.0)</td>
</tr>
<tr>
<td>Hyponatremia-Biliary Cancer</td>
<td>OR (95% CI)</td>
<td>2.42 (1.05-5.6)</td>
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<tr>
<td>BMI (kg/m2)</td>
<td>OR (95% CI)</td>
<td>5.09 (1.5-17.5)</td>
</tr>
<tr>
<td>IPD (vs. HDP)</td>
<td>OR (95% CI)</td>
<td>7.87 (3.1-20)</td>
</tr>
</tbody>
</table>

Figure 1: Survival After IPC

Survival After IPC
PO2175
Seleznio-Associated Hyponatremia: Single-Center Real-World Data
Omar Mamlok,1 Kenar D. Jhaveri,2 Jaya Kala.3 1University of Texas MD Anderson Cancer Center, Houston, TX; 2Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY; 3University of Texas John P and Katherine G McGovern Medical School, Houston, TX.

Background: 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, diarrhea, poor solute intake, or pseudo-hyponatremia from high M protein level.

Methods: We retrospectively reviewed the medical records of all relapsed MM patients at our cancer institute. The study was approved by the institutional review board. We reviewed data relevant to hyponatremia in patients' clinical presentation, medication history, comorbid conditions, physical examination, and laboratory review.

Results: Hyponatremia was seen in 13/17 patients within 5 weeks of therapy, 8 of whom required hospitalized. Three of these hospitalized patients had grade 3 hyponatremia (serum sodium 120 to ≤130 meq/l) with severe symptoms including fall and altered mental status. Both groups of patients received antiepileptics, anti-depressants 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. Nephropathy was consulted on only 4 out of 13 patients. These patients with selinexor 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 gastrointestinal 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.

PO2176
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 CAJAN, 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. This retrospective study evaluated whether anti-emetics modify the risk of AKI.

Methods: The medical records of acute adult cancer patients who received CIS between Jan 1, 2010 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. Fisher’s exact test was used for univariable associations between categorical values and logistic regression analyzed multivariable associations with AKI at p<0.05.

Results: Of ~8700 patients, 6889 met search criteria. A total of 3,381 (56.3%) patients received antiemetics. AKI developed after cisplatin in 1,666 (24.2 %) patients. Of those with AKI (n=1666), patients who received any antiemetic represented 52.6% (n=877), while patients with no documented antieumetic use represented 47.4% (n=789). Of patients without AKI (n=5223), patients who received any antiemetic represented 57.5% (n=3004), while patients who did not have documented antiemetic use represented 42.5% (n=2219). (P<0.001). Patients who received antieumetics also received a higher cumulative dose of CIS (360 vs 330 mg/m², P<0.001). By univariate analysis older age, male gender, black race, and cumulative CIS dose were associated with higher risk for AKI (OR=0.001). After adjusting for these variables, use of any antieumetic was protective for AKI (OR 0.84, 95% CI: 0.75, 0.94; P<0.001).

Conclusions: Our study confirms the high rate of AKI in patients receiving CIS. While anti-emetic use appears to be associated with a lower rate of AKI, additional analyses will be needed to determine risk or benefit profiles of specific agents and/or class of agents given recent data demonstrating inhibition of kidney transporters with certain anti-emetics. Dissecting out other important covariates such as requirements for anti-emetics based on higher cumulative CIS will be necessary in prospective randomized controlled studies.

Funding: NIDDK Support

Figure 1. Kaplan–Meier analysis

PO2177
Acute Kidney Disease After Microvascular Radical Cystectomy for Bladder Cancer Is Associated with CKD
Shengnan Ge, Ying Tang, Junzhe Chen, Sha Fu, Qiyuan Huang, Wenzuan Yu, Anping Xu. Sun Yat-Sen University Sun Yat-Sen Memorial Hospital, Guangzhou, China.

Background: Acute kidney disease (AKD) 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 microvascular 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=0.024), robotic RC (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 microvascular RC. The high incidence of AKD may be related to the microvascular RC and resulted in higher risk of new-onset CKD compared with No-AKD. This persistent or repetitive injury is significantly associated with CKD.Hence, interventions for AKD are needed to improve outcomes.

PO2178
Comparative Analysis of Characteristics and Survival Outcomes of Clear Cell and Sarcomatoid Subtypes of Renal Cell Carcinoma: Results from the SEER Database 2000-2017
Dona Attia,1 Tapas Ranjan Behera,2 Sara A. Attia.1 Taussig Cancer Institute, Cleveland, OH; 2Northeastern University, Boston, MA; 3Cleveland Clinic, Cleveland, OH.

Background: Renal cell carcinoma (RCC) accounts for more than 90% of kidney cancers. Clear cell RCC (ccRCC) is the commonest type, while sarcomatoid RCC (sRCC) is rare and constitutes 5% of all RCCs. sRCC is known for aggressive clinical course and poor prognosis. In this study, we sought to compare the epidemiological features and survival trends of ccRCC with sRCC, using SEER dataset 2000-2017.

Methods: The Surveillance, Epidemiology and End Results (SEER) database was used to identify all adult patients (a18 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 (66.3±13.7 for ccRCC vs 62.9±12 for sRCC), the female-ratio (1.71 vs 2.31), and being caucasian race more affected (79% vs 82%), sRCC had a significantly worse prognosis in univariate analysis with median overall survival of 7 months vs 30 months for ccRCC. Caucasian male patients were more affected in both types. But neither sex nor race significantly affected survival in sRCC (P 0.814, 0.794 respectively), however, black americans have worse outcomes in ccRCC (HR 1.123[1.083-1.163], P < 0.001). On multivariate
regression analysis, advanced stage, high histological grade, and older age 65+years (HR 1.002, 95%CI [1.000–1.004], P = 0.0001) 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
Ashish Verma,1 Sonu Subudhi,2 Ankit B. Patel,1 Maria Clarissa Tio,1 Sushrut S. Waikar,1 1Brigham and Women’s Hospital, Boston, MA; 2Massachusetts General Hospital, Boston, MA; 1Boston University Medical Campus, Boston, MA.

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 (mEq/L) – (serum chloride (mEq/L) + serum bicarbonate (mEq/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 caloric intake, hemoglobin, cancer diagnosis, eGFR and urine albumin to creatinine ratio.

Results: This study included total 39,137 participants [mean (SD) age, 46.83(19.25) years, 20,162(51.5%) 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
Indro P. Efebera,1 Teresa Chua,2 Hugo Ferreira,2 Ana M. Paiva,2 José M. Costa,2 1Hospital Amato Lusitano, Castelo Branco, Portugal; 2Instituto Portugues de Oncologia do Porto Francisco Gentil EPE, Porto, Portugal.

Background: Patients with haematological malignancies (HM) 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 HM 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 16 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 1.156 – 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 0.63; 95% CI:0.42 – 0.95; p=0.07).

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 from AKI After Hematopoietic Stem Cell Transplant: A Systematic Review and Meta-Analysis
Karthik Kovuru,1 Swetha Rani Kanduri,1 Wisit Cheungpasitporn,2 Charat Thongprayoon,2 Juan A. Medaura,1 Kianoush Kashani,2 1University of Mississippi Medical Center, Jackson, MS; 2Mayo Clinic Rochester, Rochester, MN.

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 transplant (HSCT).

Methods: Ovid MEDLINE, EMBASE, and the Cochrane Databases were systematically 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 Bummag, Michael Ozga, Isabelle Ayoub, Salem Almaani, Nidhi Sharma, Yvonne A. Efereba, 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 hematologic 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 VPGF/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 VPGF/CR as hematological response PFS and OS were similar for patients having PR and SD as renal response respectively (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 VPGF 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

<table>
<thead>
<tr>
<th>AT DIAGNOSIS</th>
<th>Partial Response (n=1)</th>
<th>Stable Disease (n=1)</th>
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<tbody>
<tr>
<td>Median SC (mg/dl)</td>
<td>1.0 (0.9, 1.1)</td>
<td>2.0 (2.0, 2.0)</td>
</tr>
<tr>
<td>Median 24-hr Proteinuria (g/24hr)</td>
<td>3.0 (3.0, 3.0)</td>
<td>5.0 (5.0, 5.0)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>1 YR POST TRANSPLANT</th>
<th>Partial Response (n=1)</th>
<th>Stable Disease (n=1)</th>
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<td>Median SC (mg/dl)</td>
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<tr>
<td>Median 24-hr Proteinuria (g/24hr)</td>
<td>3.0 (3.0, 3.0)</td>
<td>5.0 (5.0, 5.0)</td>
</tr>
</tbody>
</table>

Median Serum Creatinine prior to ASCT in PR group was 1.2 mg/dl and 2.0 mg/dl in SD group.

P20183

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. 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 have 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 with no significant reduction in incidence with reduction in MTX dose. Given the retrospective nature of the data and the many complexities to dosing in future dosing with no significant reduction in incidence with reduction in MTX dose.

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

<table>
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<tr>
<th>No dose reduction</th>
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<th>AKI N2</th>
<th>AKI N3</th>
<th>Total</th>
</tr>
</thead>
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<tr>
<td>No dose reduction</td>
<td>156 (46.8%)</td>
<td>57 (28.9%)</td>
<td>72 (39.1%)</td>
<td>285 (98.8%)</td>
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<tr>
<td>Dose reduction</td>
<td>101 (30.8%)</td>
<td>30 (7.9%)</td>
<td>32 (17.6%)</td>
<td>163 (51.2%)</td>
</tr>
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</table>

P20184

Nephrology and Hematology Referral Trends in CKD Patients with Monoclonal Gamopathy 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 gamopathy (MG) in the setting of CKD raises the possibility of monoclonal gamopathy of renal significance (MGRS) which would require a nephrology or hematology referral. However, rate and factors that affect specialty referral in population 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 (RG) and 180 (30.2%) 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, acute 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.

P20185

Efficacy of Early Use of Double Filter-Based Extracorporeal Treatment Combined with Chemotherapy in Acute Myeloma Kidney Disease

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Background: Before the introduction of modern chemotherrapy, less than 25% of patients with AKI and Multiple Myeloma (MM) who required dialysis recovered sufficient renal function to no longer be on dialysis, with an overall survival of less than 1 year. Although impaired renal function has been a marker of poor prognosis there are may other factors involved in determining patient survival. We aimed to investigate the factors related to renal recovery and to an higher survival rate in MM patients.

Methods: A monocentric retrospective study was carried out enrolling 23 patients with biopsy-proven acute myeloma kidney and sFLC levels >1000 mg/l. Patients received Bortezomib-based chemotherapy and extracorporeal treatment for sFLC removal. For each session 2 dialyzers of the same kind were used and the dialytic dose was only related to the sFLC removal. The dialyzers had high absorptive properties: PMMA (poly(methylmethacrylate), Filtreytor BK-F 2.1 m2 cut-off 20 kDa); PEGA (poly ester polymer alloy; FDX or FYD 210-GW 2.1 m2, cut-off undisclosed).

Results: The factors that have been found to be significantly and independently associated with higher survival rate were: baseline serum albumin, reduction of sFLC at day 12 and day 30, reduction of sFLC at day 30 above 50%, number of session and dialysis independence.

Conclusions: Our analysis highlights the importance of the early treatment for removal of sFLC in AKI for MM. In fact the variable associated with higher survival rate are the reduction of sFLC at day 12 and day 30 and number of session. These results indicate that the early removal of sFLC can guarantee a better outcome. Baseline serum albumin is also associated with survival rate and it demonstrates that it still carries a prognostic value in the population with AKI. This finding suggests the importance of albumin-sparing extracorporeal treatments. In fact alternative techniques, as HD-HCO, have been proposed for sFLC removal but they present high costs and albumin leakage.
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.

PO2187
Diffuse Background Monoclonal Light Chain Staining in Kidney Biopsies, Without Electron Dense Deposits: Is It Relevant?

YO Salem, J Am Soc Nephrol 31: 2020

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Background: The management of diffuse background monoclonal light chain staining is challenging in renal biopsy. Large experience indicates that diffuse background monoclonal light chain staining in the biopsy report, but by itself, should not be classified as MGRS. It does warrant a thorough hematologic work-up and may 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.

PO2188
Immune Checkpoint Inhibitor-Induced p-ANCA Multigranulat Vasculitis
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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 ICi use 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). Urimysis revealed >180 RBCs and 17 WBCs per high power field with a urine to protein ratio of creatinine (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 no evidence of endocarditis with vegetation seen on echocardiogram; however, with negative blood cultures the etiology was attributed to autoimmune (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 multigranulat involvement of her vasculitis including the heart valves. Aggressive treatment with steroids, plasmapheresis, and rituximab has proven effective without hindering her tumor response.

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 (ICPI), with acute tubulointerstitial nephritis (AIN) as the foremost common pathologic finding. Risk of AKI is higher with use of proton pump inhibitors (PPIs) and dual ICPI use. Glomerular disease with ICPI is infrequently found on kidney biopsy. We report a case of concomitant IgA nephropathy and AIN associated with dual ICPI blockade.

Case Description: A 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. Admission 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 eosinophils. His urinalysis had >50 RBCs and 5 WBCs per high power field and 24-hour urine protein was 5085mg. His serum complement levels were normal. Kidney biopsy showed moderate AIN and an exudative and mesangial glomerulonephritis with dominant IgA deposits. The patient was started on prednisone 60mg daily and PPI was stopped. No additional doses of immunotherapy were administered. His serum creatinine improved to 1.6mg/dl after 1 week, with plan for outpatient steroid taper. At 10mg prednisone daily, his creatinine increased to 4.5mg/dl prompting pulse steroids due to concern for ongoing interstitial inflammation versus worsening IgA nephropathy. One week later 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 ICPI therapy. Risk of AKI in this patient was higher given use of PPI and dual ICPI 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
Hypercalcemia 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 case of AKI due to hypercalcemia 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 pruritis. Workup was significant for sCa 12.8 mg/dl and Scr 3.6 mg/dl. Hypercalcemia was suspected to be malignancy related from bone metastasis or humoral stimulation. He received fluids, calcitonin and Zoledronic acid. Further investigations showed a suppressed iPTH-6.3 pg/ml, normal PTrP, low TSH 0.04 uU/ml, free T4 1.91, normal 25-OH vitamin D, 1,25dihydroxy vitamin D 7.6 pg/ml and normal androgens. 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, hyperthyroidism, nonmalignant diffuse lymphadenopathy, and 1.25 dihydroxvitamin D induced hypercalcemia are suggested of immune related adverse effects rather than disease progression. Patient was started on prednisone 1mg/kg/d. Hypercalcemia, AKI, pruritis and inflammatory arthritis resolved.

Repeat 1.25 dihydroxvitamin D and CRP levels were back to normal.

Discussion: Hypercalcemia related to checkpoint inhibitors was previously described in setting of increased PTrP. Our patient had hypercalcemia 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 hypernatremia, and a non-anion gap metabolic acidosis (NAGMA). (Na: 120 mmol/L, Cl: 89 mmol/L, K: 3.8 mmol/L, HCO3: 20 mmol/L and Creatinine 6.7 mg/dL). Urine anion gap was positive at 8meq/L, urine osmolar gap was low at 57 mosm/kg and urine pH was 6.0. Subsequent laboratory work up was notable for AM cortisol of 1.0 ug/dL, serum ACTH 1.4 pg/mL and DHEA 12 ng/dl. Other pituitary hormones including LH, TSH, FSH, prolactin and insulin were normal. Histopathology revealed grade II chronic active T-cell mediated rejection (TCMR). With GIS. After a multidisciplinary discussion, he underwent transplant nephrectomy.

Discussion: Recent studies have shown that acute interstitial nephritis is the most common type of Pembrolizumab associated nephrotoxicity. We report a novel case of Pembrolizumab toxicity, where distal RTA concurrently manifests with secondary AI. Rapid resolution of both these conditions upon initiation of steroids suggests that they are both immune mediated adverse effects associated with Pembrolizumab.

PO2193
Immune Checkpoint Inhibitor Therapy-Related Graft Intolerance Syndrome in a Failed Kidney Transplant Recipient on Hemodialysis
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Introduction: Immune checkpoint blockers (ICBs) are monoclonal antibodies against inhibitory receptors on T-cells resulting in anti-cancer activity. The use of ICBs among kidney transplant (KT) recipients and cancer is controversial, as ICBs can lead to immune tolerance and is associated with a higher risk of rejection in functioning allografts. In failed allografts, the effects of ICBs 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 urethelial 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 GIS. 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 a multidisciplinary discussion, he underwent transplant nephrectomy.

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 is usually related to allograft rejection or acute cellular rejection. In our case, GIS developed after ICPI initiation. 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
Crescentic Glomerulonephritis and Phospholipid 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 Crescentic 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: Nephropathy was confirmed for AKI and hematuria in a 67-year-old male smoker with lung adenocarcinoma. He started on pembrolizumab and pemetrexed 8 months ago, last dose 3 weeks prior to consult. He developed thrust irrigation from local irradiation, and pantophobia was initiated. No NSAIDs, herbal medications or iodinated contrast exposure. Prior to treatment, baseline Creatinine (Cr) was 1.1 mg/dl, and urinalysis was negative for proteinuria. NIH SLE criteria was 11/12, 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. PET-CT showed diffuse cGN.[Glomeruli: necrosis (2/38), cellular crescents (10/38), and fibrocellular crescents (18/38)]. Protein:creatinine ratio (UPC) was 1.52g/l. Complements were normal. Serology workup was negative. PET-CT showed diffuse cGN.[Glomeruli: necrosis (2/38), cellular crescents (10/38), and fibrocellular crescents (18/38)].
PO2195
Diffuse Large B-Cell Lymphoma Presenting with Light Chain Cast Nephropathy: A Case Report
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Introduction: Light chain cast nephropathy is caused by filtration of excessive amounts of free light chains into the renal tubules, leading to acute kidney injury (AKI). The most associated cell lineage is multiple myeloma (MM). Non-associated cases of cast nephropathy associated with diffuse large B-cell lymphoma (DLBCL) were reported.

Case Description: A 55-year-old previously healthy man presented with foamy urine for 3 months and exercise intolerance. Physical exam showed pale conjunctiva, multiple neck masses, and no edema. His serum creatine (Scr) was 7.6 and 15.2 mg/dL initially and on admission 4 weeks later, whereas baseline Scr had been normal one year ago. His hemoglobin level was 7.9 g/dL, and white blood cell count was 8750/mumL without esophagitis. No active urine sediments were found. A UPCR was 7250 mg/g, and a UPCR 300 mg/mumL. Ultrasound showed decreased kidney sizes (R 9.0, 4.7 cm). Immuno-electrophoresis detected monoclonal λ light chain in both his serum and urine, and a serum λ free light chain level was 8830 μg/mL, with a k-to-λ ratio of 0.0024. Following a diagnosis of DLBCL (Lugano stage IV) by neck mass biopsy, a renal biopsy disclosed diffuse aggregation of amorphous eosinophilic proteinaceous casts in the tubules, with a normal glomerular compartment and mild arteriosclerosis, findings consistent with IgG-λ light chain cast nephropathy. He was treated with 4 courses of R-CHOP, hemodialysis, and a short course of plasmapheresis, thereby spiking his creatinine to 2830 μg/mL after 4 months. His complete response for DLBCL was achieved 6 months later but he remained on hemodialysis.

Discussion: This is, in the literature, the first adult DBLCL patient presenting with proteinuria and renal deterioration proven to be light chain cast nephropathy. Standard lymphoma treatments were given, and based on limited evidence, plasmapheresis was given to reduce the light chain load (Median serum free light chain level was 6590 mg/mL in MM patients as reported by Bridoux in JAMA 2017). Decreasing plasma light chain concentration leading to improvement in AKI has been reported for MM. However, this case remained dialysis-dependent despite a decline in light chain levels. To conclude, we provide a unique case of DLBCL with cast nephropathy. Clinicians could take this entity into consideration and treatment may be tailored for better outcomes.

PO2196
A Case of Mixed Cryoglobulinemia Type II with Monoclonal Gammopathy in a Patient with Chronic Hepatitis B
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Introduction: Non-Hepatitis C related mixed cryoglobulinemia Type II (MCT2) is rare. Causes include lymphoproliferative disorders, chronic infections like Hepatitis B and autoimmunity.

Case Description: A 68-year-old Chinese male presented with livedo reticularis and autoimmunity. He was a chronic hepatitis B carrier with chronic hepatitis B infection. His liver function tests were within normal limits and HBsAg was positive. He was treated with interferon therapy for hepatitis B 15 years ago. The patient presented with headache, fatigue, arthralgia, myalgia, rash, and Raynaud's phenomenon. He was diagnosed with MCT2 by a minor criterion of non-HCV-related mixed cryoglobulinemia (MCT2). He was treated with oral prednisolone 10 mg/day for 4 months. After 4 months, his clinical symptoms and laboratory parameters improved. The patient was maintained on chemotherapy and hemodialysis, and he died 8 months after renal biopsy.

Discussion: A 54-year-old Chinese man presented with a 4-year history of multiple myeloma, proteinuria and hematuria. He had Monoclonal IgAλ, plus free λ spike in both serum and urine. He was treated with chemotherapy. His serum creatinine was normal until 11 months before admission, and he was on hemodialysis for 3 months before admission. Renal biopsy showed diffuse amyloid casts in the tubular lumen, and he had no obvious amyloid deposits in other kidney compartments and no sign of extra-renal amyloidosis. The amyloid fibrils formed around mononuclear cells which were IgM kappa positive. The patient was treated with chemotherapy and hemodialysis, and he died 8 months after renal biopsy.

Case 2: A 58-year-old Chinese man presented with a one-and-a-half-year history of proteinuria and slowly rising serum creatinine. He had Monoclonal IgDλ spike in both serum and urine. Amyloid casts were observed in the tubular lumens and in the centre of some casts were mononuclear cells. There were no amyloid deposits in other kidney compartment and no sign of systemic amyloidosis. The patient also had fine granular deposits along the tubular basement membrane with linear staining along tubular basement membrane suggestive of IgA to IgM amyloid. He was treated with chemotherapy and achieved very good partial remission (VGPR). After twenty-seven months of follow-up, the patient still had no sign of systemic amyloidosis.

Discussion: These 2 cases of MCT2 with cast nephropathy have different pathologic characteristics from the usual myeloma casts and tubular epithelial cells may play important roles in the pathogenesis.

PO2197
Myeloma Cast Nephropathy with Diffuse Amyloid Casts: Two Case Reports and Literature Review
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Introduction: Multiple myeloma (MM) is a plasma cell derived hematologic malignant disease. The malignant proliferating plasma cells can secrete massive monoclonal immunoglobulins which can cause various pathologic types of renal injury. Myeloma cast nephropathy (MCN) is the most common pathologic lesion with the worst renal prognosis. Rarely, the free light chains in the protein casts can form amyloid fibrils. Here, we report two rare cases of myeloma cast nephropathy with diffuse amyloid casts.

Case Description: Case 1: A 54-year-old Chinese man presented with a 4-year history of multiple myeloma, proteinuria and hematuria. He had Monoclonal IgAλ, plus free λ spike in both serum and urine. He was treated with chemotherapy. His serum creatinine was normal until 11 months before admission, and he was on hemodialysis for 3 months before admission. Renal biopsy showed diffuse amyloid casts in the tubular lumen, and he had no obvious amyloid deposits in other kidney compartments and no sign of extra-renal amyloidosis. The amyloid fibrils formed around mononuclear cells which were IgM kappa positive. The patient was treated with chemotherapy and hemodialysis, and he died 8 months after renal biopsy.

Case 2: A 58-year-old Chinese man presented with a one-and-a-half-year history of proteinuria and slowly rising serum creatinine. He had Monoclonal IgDλ spike in both serum and urine. Amyloid casts were observed in the tubular lumens and in the centre of some casts were mononuclear cells. There were no amyloid deposits in other kidney compartment and no sign of systemic amyloidosis. The patient also had fine granular deposits along the tubular basement membrane with linear staining along tubular basement membrane suggestive of IgA to IgM amyloid. He was treated with chemotherapy and achieved very good partial remission (VGPR). After twenty-seven months of follow-up, the patient still had no sign of systemic amyloidosis.

Discussion: These 2 cases of MYC with diffuse amyloid casts have different pathologic characteristics from the usual myeloma casts and tubular epithelial cells may play important roles in the pathogenesis.

PO2198
Masked Light Chain Proximal Tubulopathy (LCTP) and Focal Segmental Glomerulosclerosis (FSGS) in Multiple Myeloma (MM)
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Introduction: Patients with MM often do not have a myeloma-defining disease, and delayed recognition/treatment of a monoclonal gamopathy of renal significance (MGRS) may confer worse renal outcome. Here we report 3 patients with “masked” LCTP (one also had FSGS) and a 4th patient with both FSGS and LCTP. None had crystalline deposits. All 4 patients had a history of untreated, smoldering MM and the initial kidney biopsy interpretation in 3 of the cases reported no evidence of MGRS. Treatment of the underlying MM resulted in improvement of renal parameters in all, suggesting MM as the etiology for the renal disease.

Case Description: 75 y/o, worsening renal function (WRF), albuminuria and monoclonal proteinuria (MP). Biopsy: FSGS. Initial immunofluorescence (IF) was negative. Re-examination after prostate digestion 6 months later: LCTP. Therapy for MM resulted in decreasing freem light chains (FLCs), decreasing renal function, and decreased albuminuria and MP 72 y/o, WRF and albuminuria. Biopsy: FSGS and LCTP attributed to MM. Therapy for MM resulted in decrease in FLCs, stabilization of renal function and decreased albuminuria. 75 y/o, WRF and heavy MP. Biopsy: diabetic nephropathy with interstitial inflammation. IF was negative. Following autologous stem cell transplant for progression to symptomatic MM, there was a striking improvement in FLCs, renal function and MP 73 y/o, WRF, heavy MP and Fanconi’s syndrome. Biopsy: mild glomerulomegaly and focal sparse lysocytic infiltrates. Initial IF was negative. Re-examination after prostate digestion 6 months later: LCTP. Therapy for MM resulted in decreasing FLCs, improvement of renal function and improvement in renal markers. The patient remained asymptomatic.

Discussion: FSGS has been rarely linked to MM. In view of the connection between treatment of the MM and improvement of the renal parameters, FSGS must be considered as an additional MM-related MGRS. The presence of monoclonal light chains (LCs) in the tubular epithelial cells (TECs) should raise the possibility of this diagnosis. Because monoclonal LCs deposits in TECs may not be detectable by standard IF techniques (“masked” LCTPs), paraffin IF after prostate digestion should always be performed in the setting of the underlying lymphoproliferative disease causing monoclonal gamopathy of renal significance (MGRS). Early treatment of MCT2 is not established, although immunosuppression consisting of corticosteroids with Rituximab or cyclophosphamide is required in severe renal involvement. We demonstrated a favourable outcome with Bortezomib-based clone directed therapy after achieving a non-sustained response with Rituximab/prednisolone. Long-term monitoring of the underlying low grade non-Hodgkin’s lymphoma (NHL) is necessary.
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: a 68-year-old man with widely metastatic mCRPC despite multiple lines of therapy and secondary chronic hydropnephrosis with bilateral nephrostomy tubes. He received 3 rounds of 225Ac-PSMA617 in 2-month intervals. Baseline serum creatinine was 1.6 mg/dL (GFR 44 mL/min/1.73m²) and it increased up to 3.3 mg/dL (GFR 18 mL/min/1.73m²) after 225Ac-PSMA617 therapy. A kidney 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 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 proteinuria leading to cessation of treatment. Baseline serum creatinine at initiation of TRNT was 1.0 mg/dL (GFR 82 mL/min/1.73m²). He subsequently developed progressive CKD and serum creatinine was 1.7 mg/dL (GFR 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 nuclides 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 was re-evaluated after exposure, therapy 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 of ~2.5mg/dL from ~1mg/dL. The patients reported occasional frothy urin 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. Cytologic atypia of the tubular epithelium was consistent with karyomegaly interstitial nephritis (KIN), previously documented in cases of ifosfamide toxicity. In these cases, 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. Subsequent therapy and ongoing 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 Inhibitor 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 activated 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, calcitomin and phytodiolinates 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 phytodiolinates, probencid and calcitomin, serum phosphorus levels remained within normal limits.

Discussion: FGFR-induced hyperphosphatemia has a similar clinical presentation as hyperphosphatemic familial tumoral calcinosus (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, calcitomin) and alendronate. Phytodiolinates (vitamin K) interfere with matrix Gla protein, a tissue inhibitor of calcification.
PO204
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 (< 8.8 mg/dL) also noted. After clarification, the blood tube that had result of hyperkalemia is sodium heparin (green top) tube. We restated 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 leukapheresis 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 anticogulated 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.

PO2203
Attack of the Clones: Leukemia and Myeloma
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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 may be 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 y/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, CD-20 positive subepithelial hump-shaped deposits and abundant glomerular neutrophils suggesting crescentic glomerulonephritis. At the same time, we also found focal lymphocyte infiltration, light chain amyloidosis. At the same time, we also found focal lymphocyte infiltration, which are confirmed of nodal marginal zone B-cell lymphoma and three different types of cast nephropathy present simultaneously in patient with multiple myeloma.

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 gammapathy of renal significance. Early diagnosis with renal bone marrow biopsy and subsequent treatment with immunosuppressive therapy is crucial.

PO2206
Breast Cancer-Associated Podocytopathy

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.

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

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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 g of normal serum creatinine and albumin. A kidney sonogram was unremarkable. Further workup was negative for infectious, autoimmune, vasculitis and anti-glomerular basement membrane (GBM) antibodies. The patient was started on Lisinopril 10mg, however proteinuria worsened to 12.6 gms 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-proteinuriac 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 cancer hospital.

Case Description: For two consecutive months all patients admitted in ICU at Basavatarama 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%), amongst whom either it 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%) and 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; 68.18%) of RRT followed by CRRT/CVVHD (N=8; 34.78%). Regional citrate anticoagulation was commonest anticoagulation used (62.5%). 46% patients recovered their renal functions but creatinine did not reach baseline for 11% of patients. 29% patients with AKI died and a 14% of patients lost to follow up. CRRT was associated with better survival (n=4; 50%) followed by SLED (n=4; 26.66%).

Discussion: Incidence of AKI was higher among patients in oncological ICU with half of them required RRT. Commonest etiology of AKI was sepsis where shock state was observed in majority of patients. Although SLED was used more frequently, outcomes were better with CRRT/CVVHD.
Discussion: Narsoplimab is a human monoclonal antibody that inhibits mannann-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 pathway can ameliorates proteinuria induced kidney injury. However she did not improve in her platelet count, LDH and C5b9 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%), membranoproliferative GN (MPGN; 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 necrosis/interstitial nephritis (ATIN) with myoglobin casts (2 cases; 8.3%); AT/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 reports, 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 AT/ATIN 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 tumour 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 involvement affecting multiple organ systems. We report a case of ECD with bone

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 artery 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 & Bow 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 perivascular lymphoid aggregates of monoclonal CD 20+ 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 chemotherapy and remained on maintenance dependent. The 2nd case was a 73-yr old male with incidental finding 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 different 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. Cystatin C is mainly excreted by glomerular filtration and is partly secreted via tubular secretion as MATE, as compared to creatinine. As MATE is not expressed in high abundance in the kidney, selpercatinib, can reduce cystatin C clearance leading to an incorrect diagnosis of drug related kidney injury. Cystatin C is an alternative marker that is freely filtered, completely reabsorbed and not affected by renal function and proteinuria. It is therefore not affected by transporter inhibitors and may be a better marker of kidney injury in patients receiving Selpercatinib. We present a patient on Selpercatinib with significant difference in kidney function by creatinine and cystatin C.

Case Description: 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 one year of therapy with no change from baseline and with no significant proteinuria. Renal sonogram showed right side hydronephrosis which prompted placement of ureteral stent. Creatinine did not improve with persistent hydronephrosis prompting conversion to a nephroureterostomy tube one year later. Creatinine remained elevated at 1.9mg/dl despite resolving hydronephrosis. Cystatin C levels were measured and showed significant discrepancy with serum creatinine as shown in Table below. This finding highlighted that although the patient did have chronic kidney disease, the extent was less than estimated by solely creatinine.

Discussion: This case highlights the benefit of checking both creatinine and cystatin C in patients on selpercatinib. Despite urological intervention, the persistence in elevated
PO2214

ALECT 2 and Hepatocellular Carcinoma: An Intriguing Association

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Introduction: Amyloidosis derived from leucocyte 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 gammapathy of undetermined significance was admitted for constipation and distended abdomen. Creatinine on admission was 5mg/dl and he was initiated on dialysis. Imaging revealed cirrhosis, ascites and two liver masses involving the portal vein. Alpha fetoprotein was 7123ng/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 and liver with sparing of the heart. We report a case of hepatocellular carcinoma (HCC) in a patient with ALECT2.

PO2216

Eculizumab for Treatment and Prevention of Recurrent Gemcitabine-Induced Atypical Hemolytic Uremic Syndrome After Gemcitabine Rechallenge: A Case Report

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Introduction: Atypical hemolytic uremic syndrome (aHUS) is a rare side effect of gemcitabine. Here, we report a case of gemcitabine-induced aHUS successfully treated with eculizumab, with subsequent use of eculizumab to prevent recurrence of aHUS after reinitiating gemcitabine.

Case Description: A 29-year-old male with intrahepatic cholangiocarcinoma on gemcitabine and cisplatin was admitted with AKI. On presentation, he was newly hypertensive to 162/108 mmHg and edematous. His labs were notable for a serum creatinine (Scr) of 1.19 mg/dL (baseline 0.6 mg/dL), hemoglobin 8.8 g/dL (baseline of 12.6 g/dL) with reticulocytosis, platelet count 190 K/uL, LDH 635 U/L, haptoglobin <10 mg/dL, schistocytes on blood smear, and a normal ADAMS13 level. Urine studies revealed hematuria, proteinuria, and granular casts. Gemcitabine and cisplatin were discontinued, yet his SCR continued to rise to 2.12 mg/dL, LDH to 1222 U/L and platelet count fell to 77 K/uL. Eculizumab was initiated and his creatinine improved to 1.14 mg/dL, and his LDH, platelet count, and haptoglobin normalized. Eculizumab was stopped after 2 months without subsequent recurrence. He was reinitiated on dose-reduced gemcitabine and cisplatin due to progression of his cancer despite multiple alternative chemotherapy regimens. Eculizumab was reinitiated concurrently with gemcitabine and continued bweekly. His blood pressure, Scr, haptoglobin, LDH and platelet count remained stable. Unfortunately, he died due to cancer progression 3 months later. Figure 1 summarizes his treatment and laboratory course.

Discussion: We report a case of successfully utilizing eculizumab to prevent recurrence of gemcitabine-induced aHUS after gemcitabine reinitiation, which has not been previously reported to our knowledge. There are scarce reports of gemcitabine reinitiation without eculizumab, most of which resulted in recurrent renal toxicity. There may be utility in the use of eculizumab in patients who need to reinitiate gemcitabine. Larger studies evaluating this approach are warranted.

PO2217

A Case of Lupus Nephritis Improved by Molecular Targeted Drug Therapy for Multiple Intrapulmonary Metastasis of ROS-1 Gene-Positive Lung Cancer

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Introduction: Systemic lupus erythematosus is a multisystemic disease associated with genetic, environmental and epigenetic factors. The effect of tyrosine kinase inhibitors has only been reported in SLE model mice for imatinib. Here we report a case in which lupus nephritis was improved by a molecular targeted drug for multiple intrapulmonary metastases of ROS-1 gene-positive lung cancer.

Case Description: Thirty-one-year-old woman, who was diagnosed with SLE at the age of 14 years, had been treated with immunosuppressive agents including corticosteroids, cyclophosphamide and mycophenolate mofetil, with frequent relapses. At the age of 30 years, she was admitted to our hospital due to development of systemic erythema, which was diagnosed as drug-induced eruption with increased SLE activities. She was treated with prednisolone (PSL) 50 mg/day and remission was achieved for
SLE, however, during the systemic screening, lung adenocarcinoma was accidentally detected, and thoracoscopic right middle lobeectomy 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 and 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 inhibitors may be effective for lupus nephritis.

**PO2218**

**Paraneoplastic Minimal Change Disease Associated with High-Grade Neuroendocrine Tumour**

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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 neuroendocrine tumor (NET) were reported. Here we report a 47-year-old patient with duodenal NET with nephrotic 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 creatinine of 3.9 mg/dL, proteinuria of 4.3 g/day and Na 118 mmol/L. IV diuretics with albumin infusion initiated, which improved his kidney function. Serologies and proteinuria workup - 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 tumor burden, but MCD should be kept on the differential as well. Like membranous nephropathy, remission of MCD 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 prior presenting to our renal clinic for acute kidney injury (AKI). She had 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 patient had slight segmental wrinkling of capillaries and glomerular basement membranes, and segmental podocyte swelling. She also had leptomeningeal involvement. Treatment included dexamethasone, systemic and intrafleural doxorubicin, methotrexate, and cytarabine. SCr returned to baseline, however, her course was complicated by severe mucositis, neutropenic fever, gastrointestinal hemorrhage and refractory shock. The patient was stabilized and opted to return home with hospice.

**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 inhibiting 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.

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

Underline represents presenting author.
Discussion: Even in EBV recipient-positive patients, there is still a risk to develop PTLD and hence consider prophylactic PTLD which resolved spontaneously when withdrawing Belatacept. This suggests that overly aggressive immune suppression, rather than induction of dysregulated proliferation, was the culprit. The fact that the patient did not show an acute increase in EBV RNA, and EBV by ISH on core biopsy of the spleen was negative, suggests that pre-transplant serosering based on EBV seropositivity may not be sufficient to predict risk for developing PTLD. The patient had complete resolution of AMS and B symptoms with discontinuation of Belatacept, with no subsequent recurrence of PTLD after switching to sirolimus/mycophenolate.

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 R2 with locking frequency was fit to Chopra model. The fits provided regional values of transverse relaxation rates R2obs, R1obs at infinite spin-lock frequency (R1∞), and an exchange rate-weighted parameter S1. Since cortex and outer stripe of outer medulla (OSOM) were clearly identified with T1-weighted image, even with UUO kidneys, these regions were selected for analysis. Paraffin tissue sections were stained using picrosirius red or anti-collagen I antibody. Histological scores for tubular dilation and fibrosis, based on conventional image 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 UO day 5, while tubulointerstitial fibrosis was mild at this stage. Both histological changes became more evident with progression and fibrosis showed larger increases from day 5 to day 15 (tubular dilation ~25% increase, fibrosis ~3 fold increase). Relaxation rates R2obs, R1obs and S1 were progressively dropped (25-50%) in UUO kidneys. Interestingly, R1obs showed the highest sensitivity to tubular dilation, while S1 showed the highest correlation with renal fibrosis.

Conclusions: Relaxation parameters showed high detectability to tubular dilation and overall changes in UUO progression. S1 best detected fibrotic changes. This would be because it depends mainly on the average exchange rate between water and collagen fibres, which is shifted relative to water as amides to collagen triple helices and collagen 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 >105, 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/6 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>C/T mutations, 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: Glemorula had ~25% fewer total mtDNA mutations (p= 0.002) and specifically ~80% fewer oxidative lesions (G>C/T, A-G>C/G, G= 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 differential accumulation of reduced mutations in glomeruli of mtRNA gene mtRib1 but not mtRib2, 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 polymerease error, were significantly reduced.

Conclusions: These data suggest that renal mtDNA mutation is cell specific and that even in aged, accumulation of some mutations is tractable with therapeutic intervention.

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Underline represents original author.
PO2226
Integrated Analysis of the DNA Methyome, 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 intrinsic 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

PO2227
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.
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 extrosomal 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 just 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 extrosomal mRNAs with more than 2.0-fold relative to the control. BARD also changed expression of 15 renal miRNAs and 3 urinary extrosomal miRNAs. The correlation coefficients between renal and urinary extrosomal mRNAs as well as miRNAs were both less than 0.1. mRNAs 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, Actc19, Bsh51, Ep101, Hmox1, Pir, Slc4a11 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 mro-mir-877 was changed in both the kidney and urinary exosomes.

Conclusions: The correlation coefficients between renal and extrosomal 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.

PO2229

Urinary Excretion of Extracellular Vesicles in 24 Hours: Time Point Collection and Normalization Strategy
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Background: Urinary extracellular vesicles (uEVs) are an ideal source of biomarkers for kidney diseases. Despite the interest generated, little is known about collection time and normalization approach. The majority of the studies on uEVs focus on spot urine collection based on the assumption that it accurately reflects the renal function. However, the practice to collect spot urine does not allow for calculating and standardizing the uEV excretion rate and then assessing the renal function. Moreover, no research has been carried out yet to show the difference between spot urine and 24h collections. The aim of this study is to compare uEVs excreted in all 24 hour urine void as single spot and compare it with 24 hour collection.

Methods: Each single spot void urine was collected and 20% of the volume was used to create the 24 hours collection. uEVs were enriched by differential centrifugation. Transmission electron microscopy (TEM), western blot (WB), nanoparticle tracking analysis (NTA), tunable resistive pulse sensing (TRPS), imaging flow cytometry (iFC) and miRNA (miR16 and miR200b) quantitation by qPCR were used to quantify uEVs markers variation during the 24 hour. Creatinine, urinary osmolality and particle concentration (NTA, TRPS) were used to normalize the analytes.

Results: TEM showed a heterogeneous population of uEVs and WB confirmed the presence of EVs marker (TSG101, ALIX and CD9). RNA was extracted by a column-based method (miRNA extraction kit Qiagen) and cel-39 miRNA was spiked in each sample. A multiparametric detection of nephron markers podocalyxin (PODXL1), aquaporin-2 (AQP2) and uEv pan tetraspanins (CD9 + DC63 + CD81) was performed in imaging flow cytometry and imaging flow cytometry. Whereas the uEV composition of did not change across the 24 hours analysis, the quantity of uEVs and related markers (miRNA and proteins) fluctuated during the day depending on the hydration and excretion rate. Creatinine, urinary osmolality and particle count normalization failed to normalize “outliers".

Conclusions: In conclusion, this study represents the very first report which compares single void urine versus 24 hour uEV analysis. We concluded that the 24 hour collection is the preferred choice for a robust and rigorous assessment of uEVs and its associated markers.

PO2230

Ultra-Fast Clearing Protocol for 3D Optical Renal Pathology
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Background: Kidney pathology involves three separate microscopy workflows. Histology, typically carried out on paraffin-embedded sections, used to optically visualize large-scale renal morphology. Immunofluorescence, used for mapping presence of specific molecular variations, carried out on paraffin-embedded or fresh-frozen thin sections. To visualize renal ultrastructures, electron microscopy is applied, with elaborate preparation protocols on ultra-thin sections.

Methods: We have modified published protocols in order to simplify and speed up the workflow of routine optical kidney imaging. The presented protocol yields a slight swelling of a cleared sample, and increase effective resolution enough for 3-D confocal visualization of filtration barrier structures. The duration of the protocol is only 5 hours from harvesting the tissue until full image acquisition.

Results: Our simple and fast protocol can resolve footprint processes in mouse and human tissue using standard lab equipment and conventional 3-D confocal microscopy. Importantly, the protocol can be used to visualize various large-scale histopathological features as well as immune deposits in human patient material too. Compared to others, our tissue protocol is simpler and faster, and allow better 3-D in situ imaging capabilities.

Conclusions: We conclude that our simple and fast protocol, allow researchers and pathologists to use a single preparation and microscopy technique, to visualize both renal ultrastructure, histology and protein expression. Our protocol has the potential of, not just to complement, but also merging workflows used today while adding accessing to in situ depth information on all scales.

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pathophysiology. HFE-P 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-HFE-P and to test new treatments in a translational fashion.

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**PO2232**

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 far from the tumor of 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 γ variable region displayed classic V, D, J rearrangements but predominant VH1-24/DH2-15/HJ4 sequence, biased VH1 usage and less diversity than B cells derived IgG. Western blot and immunofluorescence staining demonstrated IgG immunoreactivity (including IgG4, Igκ and Igλ in HK-2, RP215, which specifically recognizes non-B cell-derived IgG, can identify the IgG γ in HK-2. The IgG γ 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.

**Funding:** Government Support - Non-U.S.
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 (HFHS) 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. HFHS mice gained weight in the first month but by 5 mo. of diet, SS-31+HFHS mice weighed significantly less relative to HFHS 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 48μg/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 60.0). HFHS untreated mice displayed more renal disease than RC mice (ACR: RC = 32.6 vs. HFHS = 243.2, p = 0.003), climbing significantly to an average of 519.8 μg/mg at 28-m.o. ACR increased in SS-31 HFHS mice but leveled off by 23-m.o. (5 mo. treat.), averaging 146.1 μg/mg with no significant increase by 28-m.o. By 9 mo. of treatment, ACR was significantly lower in HFHS/SS-31 treated mice than in the control group. Pre- and post-treatment quantification of podocyte by pS75 nuclear stain and PAS counter stain (n=4-7) showed that HFHS mice, regardless of treatment, had a 30% decrease in podocyte density relative to RC mice. Control HFHS mice tended to higher tuft volume (glomerular hypertrophy) than in SS-31 HFHS mice. However, results were not significant due to low 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 that extends to aging.

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Bacterial and Fungal Communities Entombed 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 25 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® MiSeq. 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 urine 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 stone. Bacterial and fungal bacterial sequences were most closely affiliated with Actinobacter and Curtobacterium. The brushite stone microbiome contained Capnocytophaga and Humibacter and the struvite stone microbiome included Pseudomonas and Staphylococcus.

Conclusions: This presentation firsts the 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, dissolution and recrystallization, similar to processes that have been documented in natural geologic stone growth.

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Targeting of Factor D in Cfh-/- Mice Does Not Relieve C3 Glomerulopathy 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 the 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 ecilizumab is unsuccessful in the majority of patients, consistent with the fact that C3G can lead to the terminal complement cascade while leaving upstream 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-/-;Cfd-/- progeny were backcrossed to C57BL/6 for 10 generations. Littermates of Cfh-/-, Cfd-/-;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-/-;Cfd-/- mouse to show that residual AP function is present in Cfh-/- mice. In addition, and FH and FI are not required for CFD to induce C3 deposition 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 CFD, may not completely suppress complement activation; substantial breakthrough through complement activation may then occur as even minuscule amounts of free FD become available.

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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 un dctectable C3 level. Circulating levels of C5 and properdin 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 membrane-bound C3b was mixed. Cell-surface C3 deposition was strongly positive when patient serum was supplemented with C3. In vitro control of C3 conversion 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=8; for A/G ratio and FGF-23). The development of epithelial-mesenchymal transition and the induction of senescence-related molecular signals and 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 atrosogen, Atrogxin1 and MuRF1, and phosphorylated AMP-activated protein kinase (AMPK), and the decreased muscular protein expressions of phosphorylated Akt, peroxisome proliferator-activated receptor-γ coactivator 1-α (PGC-1α), and mitochondrially encoded cytochrome c oxidase I (MT-CO1) in CKD mice (p<0.05, n=8). In mice treated with LIPUS, 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=8; for A/G ratio and FGF-23). The development of epithelial-mesenchymal transition and the induction of senescence-related molecular signals and 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 atrosogen, Atrogxin1 and MuRF1, and phosphorylated AMP-activated protein kinase (AMPK), and the decreased muscular protein expressions of phosphorylated Akt, peroxisome proliferator-activated receptor-γ coactivator 1-α (PGC-1α), and mitochondrially encoded cytochrome c oxidase I (MT-CO1) in CKD mice (p<0.05, n=8).

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, 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.

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), IL-10 (2), TNFα (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 kidneys (P<0.001 vs N). Trametinib blocked the increase in pERK in sham surgery and UNX kidneys and resulted in a significant decrease in p62. Phospho/total ERK (densitometry units) was 1.0 in N, 0 in SS+T (P<0.001 vs N) and 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

PO2241

Differential Role of NAD+ Deficiency in Acute and Chronic Kidney Disease
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Background: Nicotinamide adenine dinucleotide (NAD+) is a ubiquitous coenzyme involved in electron transport and a co-substrate for many dehydrogenase. NAD+ deficiency has been shown in acute kidney injury (AKI), but few is known about chronic kidney disease (CKD).

Methods: We studied the expression of key NAD+ biosynthesis enzymes in kidney biopsies from allograft patients during reperfusion, mimicking AKI, and in patients with CKD at different stages. We used ischemia-reperfusion injury (IRI) and ex vivo injection to model AKI, unilateral ureteral obstruction (UO) and tubulointerstitial fibrosis induced by proteinuria (POD-ATTAC) to investigate CKD in mice. Then we assessed the effect of a potent NAD+ replenishment therapy, the nicotinamide riboside (NR), in both AKI and CKD models.

Results: RNA-sequence analysis of human kidney allograft biopsies during reperfusion showed that the NAD+ de novo synthesis is impaired in the immediate post-transplantation period. This decrease in de novo NAD+ synthesis was confirmed in two mouse models of IRI where NR supplementation prevented plasma urea and creatinine elevation and tubular injury. In biopsies from CKD patients, the NAD+ de novo synthesis was impaired according to CKD stage, with better preservation of the salvage pathway (Figure 1). Similar alterations in gene expression were observed in UO and POD-ATTAC mouse models. NR supplementation did not prevent CKD progression in contrast to its efficacy in AKI.

Conclusions: Impairment of NAD+ synthesis seems to be a hallmark of AKI and CKD. An oral NR supplementation showed protective effects on AKI but had no effect on CKD mouse models. This study shows the dual role of NAD+ deficiency in AKI and CKD and the potential of NAD+ replenishment therapies as a preventive strategy for human AKI.

Funding: Private Foundation Support, Government Support - Non-U.S.

PO2242

Plasminogen Activator Inhibitor 1 (PAI-1) Induction During Kidney Injury Promotes Epithelial Dysfunction via TGF-β1 Receptor Signaling and Klotho Downregulation
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Background: Persistent PAI-1 induction is evident in several nephropathies in mice and humans. Although PAI-1 is an established CKD promoting factor, the precise role of PAI-1 in disease progression is unclear and, surprisingly, this fibrogenic response appears to be mediated by αvβ3-independent mechanisms. Expression of the anti-aging gene klotho is lost during renal injury, predisposing to CKD, and recombinant klotho administration in mice suppresses progressive fibrosis. Whether kidney tubular PAI-1 induction promotes maladaptive repair and orchestrates klotho downregulation is currently unknown.

Funding: Veterans Affairs Support, Other U.S. Government Support
Methods: To mimic sustained renal epithelial PAI-1 expression during renal injury, we stably expressed PAI-1 via lentiviral transduction in HK2 human kidney epithelial cells (CMV-PAI-1); western blotting confirmed PAI-1 overexpression relative to vector controls (CMV-Con). Double-transgenic cells engineered to express both PAI-1 and klotho were used to assess pathological interplay between PAI-1 and klotho in renal fibrosis.

Results: PAI-1 expressing HK-2 cells robustly upregulated pro-fibrotic factor expression/secretion (fibronectin and collagen-1) and exhibited deredifferentiation (loss of E-cadherin and increased vimentin expression), G2/M growth arrest and susceptibility to apoptosis, evident by increases in p73, p21 and p53 expression, caspase3 cleavage and annexin V positivity compared to the CMV-Con population. PAI-1-transductants had increased TGF-β receptor 1/2 levels and SMAD2/3 activation relative to vector controls. TGF-β1 receptor-1 kinase inhibition with SB431542 attenuated the PAI-1-driven fibrotic phenotype, independent of TGF-β-signaling pathway. Interestingly, sustained PAI-1 expression also downregulated klotho protein levels compared to controls. Rescue of klotho expression in CMV-PAI-1 cells attenuated fibrogenesis and reversed the proliferative arrest.

Conclusions: Persistent PAI-1 expression promotes a fibrotic maladaptive repair orchestrated, in part, via TGF-β1-receptor1/2 hyperactivity and klotho loss. Our studies identify not only a novel role for PAI-1 in renal tubular dysfunction but also in klotho deregulation in renal fibrosis.

Funding: Other NIH Support - Capital District Medical Research Institute; Friedman Foundation, Other U.S. Government Support, Private Foundation Support

PO2243
Percutaneous Renal Biopsy Using an 18-Gauge Automated Needle Is Not Optimal

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Background: As percutaneous renal biopsies (PRB) are increasingly performed with a 14, 16 and 18-gauge automated needles.

Methods: PRB of 592 native (N) and 1023 transplant (T) kidneys was performed by a nephrologist or a supervised nephrology fellow at Rush University Medical Center from 1/2002 to 12/2019 using real-time ultrasound guidance. Baseline clinical and laboratory data, biopsy sample data (number of cores, total glomeruli per biopsy (glomeruli on light and immunofluorescence + electron microscopy) and total glomerular per core and overall data (hematoma on renal US 1-hr post-PRB and complications requiring a transfusion or procedure post-PRB) were collected prospectively. PRB with N14g(n=337) vs N16g (n=255) and T16g (n=892) vs T18g (n=131) needles were compared. A P value of <0.05 was significant.

Results: PRB with an 18g needle yielded the lowest number of total glomeruli per biopsy (N14g vs N16g: 33±13 vs 29±12, P<0.01 and T16g vs T18g: 34±16 vs 21±11, P<0.001 and N16g vs T18g, P>0.001). PRBs with 18g needle were also less likely to have ≥20 total glomeruli per biopsy (N14g vs N16g: 85% vs 82%, P>0.4 and T16g vs T18g: 83% vs 46%, P<0.001). The number of cores per biopsy was: N14g:2.3±0.7, N16g: 2.2±0.6, T16g:2.8±0.7 and T18g: 2.2±0.6. Adjusting for the number of cores obtained, the total glomeruli per core was significantly less with 18g needle (N14g vs N16g: 15±8 vs 14±7, P<0.1 and T16g vs T18g: 15±6 vs 10±2, P=0.001 and N16g vs T18g, P<0.001). A hematoma by routine screening US 1-hr post-PRB was significantly higher for native (14g-35% vs 16g-29%, P=0.2), and transplant biopsies (16g-10% vs 18g-9%, P=0.9) irrespective of needle size. The complication rate for native (14g-8.8% vs 16g-7.1%, P>0.5), and transplant biopsies (16g-4.6% vs 18g-1.3%, P<0.02) as well as the transfusion rate for native (14g-7.7% vs 16g-5.8%, P=0.4), and transplant biopsies (16g-3.8% vs 18g-0.8%, P=0.1) were not significantly different irrespective of needle size.

Conclusions: The use of the smaller, 18g biopsy needle compromises the adequacy and thus, quality of the PRB while not enhancing safety.

PO2244
Deep Neural Network Facilitated Immunofluorescence Assessment of Glomerular Diseases: A Preliminary Report

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Background: Immunofluorescence (IF) tests of renal tissue are important in diagnosing glomerular diseases. Deep neural network were used to facilitate analysis of pathologic images recently, but not in IF assessment. We proposed a novel Convolutional Residual Dense Network (CR-DenseNet) to facilitate IF assessment of glomerular diseases.

Methods: A dataset with 614 IF images of glomeruli, including IgA Nephropathy, IgAN (n=319), Idiopathic Membranous Nephropathy, IMN (n=211) and Secondary Membranous Nephropathy, SMN (n=84) from Peking Union Medical College Hospital, PUMCH were used for training of CR-DenseNet. Additional 78 IF images from PUMCH (35 IgAN, 15 IMN and 28 SMN) and 98 IF images (36 IgAN, 34 IMN and 28 SMN) from other 3 hospitals were used for validation and human tests. These images were annotated by two nephropathologists independently. Convolutional residual dense blocks were introduced. Each of them consisted of a dense block with a convolutional skip connection connection. The number of filters in each dense block is 128, followed by a 1 × 1 convolution layer. In the output layer, the number of filters is the number of classes (2). The accuracy and F1 score were 80.0% to 84.6% and 0.762 to 0.880, respectively.

Conclusions: Our data showed that CR-DenseNet model were useful in IF assessment of typical glomerular diseases.

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>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>
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</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>34</td>
<td>63</td>
</tr>
</tbody>
</table>

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**PO2247**

The Spectrum of Biopsy-Proven Glomerular Diseases in Mexico: Experience at a Tertiary Hospital

Octavio R. Garcia-Flores, Belen Martinez-Vazquez, Virgilia Soto, Bernardo Moguel. Instituto Nacional de Cardiología Ignacio Chavez, Mexico, Mexico.

**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 alloagraft 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) 16.4%. The most frequent biopsy-proven diseases were secondary (59.1%) and primary (28.7%) glomerulonephritids (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 pacious 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.

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**PO2249**

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 metanalysis 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 specimens were obtained during pregnancy and 11 during the postpartum period. Proteinuria was present in 17 patients with a mean value of 3.5g/d. Hematruia 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.

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**PO2240**

Prevalence and Risk Factors Associated with Nephroclerosis 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 signatures and nephroclerosis and its association with clinical factors in patients undergoing nephrectomy for any cause at our institution.
Methods: Two nephropathologists evaluated the status of the renal parenchyma in 811 nephrectomy specimens. They assessed and either partial or radical nephrectomies 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 variables. 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 AS was 95%. The prevalence of nephrosclerosis was 88%. Lower pre-nephrectomy eGFR (adjusted odds ratio [OR] per 10 units decrease in eGFR, 0.04, 95% CI, 0.32-1.23) and age (adjusted OR per 10 years increase, 0.04, 95% CI, 1.04-2.39) 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 trained pathologists (NP). A total of 831 nephrectomies (449 nephrectomies for malignancy, 382 nephrectomies for non-malignancy) were included in the study. Reasons for nephrectomy 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 31 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 history of smoking. 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. 371 (45%) clinical diagnoses were reported including focal segmental glomerulosclerosis (FSGS) (157), mostly NOS variant (88%), diabetic glomerulosclerosis (57), interstitial nephritis (66), arteriopneumocerosis (39), pyelonephritis (36), acute tubular injury (10), chronic scarring glomerulonephritis (41), amyloidosis (1) and atheroembolic renal disease (31).

Conclusions: Pre-existing renal disease are frequently identified in nephrectomy specimens. FSGS was the most common diagnosis. A collaborative effort involving nephrologists, urologists and pathologists is warranted to improve the care of patients undergoing surgical nephrectomy.

PO2251

Kidney Filtration Markers in Human Saliva: Accuracy and Reproducibility of Novel Salivary Cystatin C Measurements

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Background: Invasive phlebotomy followed by laborious 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.

Methods: We developed novel Enhanced Enzyme and Immunoassay-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 triplicate 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 reproducibility 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 true CysC levels (R²=0.994). Assessment of intra-assay variation showed that repeatability 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**

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**Measurement of Glomerular filtration rate (GFR) is a reliable technique but is expensive and cumbersome for routine use. GFR is routinely estimated (eGFR) with serum creatinine. These equations are not widely validated in Indian population.**

**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-variable (MDRD-4), Modification of Diet in Renal Disease-6 variable (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, CCi, and DTPA GFR were 98.8 ±15.2, 98.2 ±17.9, 106.1 ±220.2, 83.3 ±38.7, 89.3 ±22.5 and 93.6 ±41.1 respectively. The mean absolute difference in GFR and percentage variation between calculated and measured GFR for CKD-EPI, MDRD-4, MDRD-6, CG, CCi were 14.7 ±16.5%, 16.2 ±17.9%, 19.8 ±22.2%, 33.2 ±36.5%, and 23.6 ±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 CCi- 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 CCi 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**

<table>
<thead>
<tr>
<th>Equation</th>
<th>20% of GFR</th>
<th>30% of GFR</th>
<th>50% of GFR</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPI</td>
<td>81.2%</td>
<td>86.31%</td>
<td>98.59%</td>
</tr>
<tr>
<td>MDRD-6</td>
<td>70.45%</td>
<td>78.77%</td>
<td>85.16%</td>
</tr>
<tr>
<td>MDRD-4</td>
<td>54.35%</td>
<td>57.73%</td>
<td>65.84%</td>
</tr>
<tr>
<td>CG</td>
<td>36.45%</td>
<td>53.06%</td>
<td>62.90%</td>
</tr>
<tr>
<td>CCi</td>
<td>45.37%</td>
<td>63.86%</td>
<td>80.99%</td>
</tr>
</tbody>
</table>

**PO2254**

**Fecal Calprotectin Correlates with Serum Albumin in Patients with CKD**

Yura Chag, Eun Sil Koh, Jongho Son, Sungjin Chung. The Catholic University of Korea, Seoul, Republic of Korea.

**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 infiltration 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. Fecal calprotectin was significantly correlated with serum albumin (r = -0.010). Patients with higher tertile of fecal calprotectin were older and likely to have lower hemoglobin. Multivariable linear regression analysis showed that fecal calprotectin was significantly correlated with serum albumin (β = -17.702, P = 0.010). Patients with higher tertile of fecal calprotectin were older and likely to have lower hemoglobin.

**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 anion exchange resin used to treat hyperphosphatemia in patients with chronic kidney disease. It does not cause hypercalcemia or vascular calcification. Common adverse effects include nausea, vomiting, diarrhea, dyspepsia and constipation. Case reports of sevelamer associated bowel perforation have been reported in the literature 2. 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 scattered yellow eosinophilic, acellular crystalline material with “fish scale” morphology within the lumen suggestive of sevelamer resin. 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 binds 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. This combination of characteristic sevelamer crystals (typically seen as bright pink linear acellular linear formations 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**

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**Introduction:** Wegner’s granulomatosis and Goodpasture’s disease are two rare causes of pulmonary-renal syndromes syndromes. Both have similar presentation and different treatment. It is crucial for any nephrologist to be aware of each condition. WG is a systemic vasculitis that 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 most often relates to anti-glomerular basement membrane antibodies against the glomerular basement membranes. It is suggested 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 poor 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 ronchi bilaterally. Labs revealed WBC of 35, Hg 5.6, hct 15.5 and platelets 594. She had a history of radiation for lung cancer. She was noted to have profound hypochromic anemia. She had a history of chronic obstructive pulmonary disease. She was started on a course of immune suppressive therapy. She was noted to have significant improvement in her anemia. She eventually was started on plasmapheresis. She was noted to have very high levels of anti-glomerular basement membrane antibodies. Subsequently a CT angiogram was obtained. During renal arteriography, the right renal artery developed dissection with minimal catheter manipulation suggestive of significant underlying abnormality. The procedure was aborted given risk for further complications including rupture of the right main renal artery. She was noted to have poor perfusion in the right kidney. She was noted to have significant improvement in her anemia. She was noted to be clinically improved and had significant improvement in her anemia. She was noted to be clinically improved and had significant improvement in her anemia.

**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 appropriate treatment 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.
beading noted, consistent with a diagnosis of FMD. The patient’s creatinine remained stable during her hospital stay, and she was initiated on losartan prior to discharge.

Discussion: Fibromuscular dysplasia can be diagnosed by histopathology or angiography. It may manifest as a systemic vascular disease involving multiple vascular beds, mimicking systemic vasculitis. Since treatment of FAN and FMD is vastly different, it is important to consider both differentials and have definitive diagnosis prior to initiation of therapy.

PO2258
Asymptomatic Sporuous Hyperuricemia Related to Waldenstrom Macroglobulinemia
Pankuj Goyal, 1 Prakash S. Gudsoorkar, 1 Charuhas V. Thakar, 1,2 University of Cincinnati Academic Health Center, Cincinnati, OH; 1Cincinnati VA Medical Center, Cincinnati, OH.

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 paraproteinemia. 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 elevated IgM level. After 30 days of treatment, his 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 (314 mg/24 hours).

He was treated with allopurinol and monitored in clinic with serial uric acid checks. He continued to remain asymptomatic despite of having a uric acid level consistently above 35 mg/dL. He was not treated with Rasburicase due to lack of symptoms and potential false elevation of uric acid in the setting of paraproteinemia.

Discussion: Paraproteins often cause factitious biochemical measurements by forming opaque precipitates with the test reagents and interfering with various automated assay methodologies. These interferences may be difficult to anticipate as they are intermittent and patient specific. Ultrafiltration of paraproteins, dilution or deproteinization of the samples can sometimes help correct these measuring errors. WM and other paraproteinemias may cause true hyperuricemia in the setting of TLS. However, the absence of other coagulopathies, anemia should raise suspicion 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 paraproteinemia.

PO2259
Is the Well-Recognized Intravascular Tamm-Horsfall Protein Polyp a Misnomer? A Case Report from a Patient with Obstructive Uropathy and Hematuria
Lives Su, Kyle Meissner, Amal Musa, Vikas D. Reddy, Jade M. Teakell, William E. Glass. University of Texas Health Science Center at Houston, Houston, TX.

Introduction: Tamm-Horsfall protein (THP), a renal epithelial glycoprotein, was originally identified from normal urine and can be the predominant constituent of urine in cases of renal proteinuria. The phenomenon of THP polyp formation in obstructive uropathy first appears in the literature about 1978. 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 (1.9 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 examination was unremarkable. Her admission labs were notable for a Cr 2.25mg/dL, potassium 3.1mmol/L, bicarbonate 15mmol/L, phosphorus 2.2mg/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 ratio 1.1. Further workup revealed urine electrolytes: Cr 39mg/dL, sodium 77mmol/L, potassium 20mmol/L and phosphorus 22.9mg/dL. Fe/Ps was 61% suggesting renal wasting. Serologic workup was negative forANA, ANCA, ncl c3, c4 and spep. Renal sonogram showed normal renal masses 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 inflammation with mononuclear cells and frequent cosinophils consistent with ATN. EM showed tubuloreticular inclusions. He was started on postop Rx which was tapered over 8 weeks. Creatinine downtrended to 1.1mg/dL.

Discussion: Vodolzumab 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 elucidated, 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.

PO2260
Vedolizumab-Induced Acute Interstitial Nephritis and Acute Tubular Necrosis
Abdulrahman Muzib, Rushang Parikh, Vanesa Bijol, Nupur N. Uppal, Mala Sachdeva. Donald and Barbara Zucker School of Medicine at Hofstra/ Northwell, Great Neck, NY.

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 hyperparathyroidism and calcium oxalate nephrothiasis 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 0.9mg/dL. Approximately one week prior to admission she was found to have a Cr of 2.0mg/dL. She continued to receive her IV and oral infusion. Her physical exam was unremarkable. Her admission labs were notable for a Cr 2.25mg/dL, potassium 3.1mmol/L, bicarbonate 15mmol/L, phosphorus 2.2mg/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 ratio 1.1. Further workup revealed urine electrolytes: Cr 39mg/dL, sodium 77mmol/L, potassium 20mmol/L and phosphorus 22.9mg/dL. Fe/Ps was 61% suggesting renal wasting. Serologic workup was negative forANA, ANCA, ncl c3, c4 and spep. Renal sonogram showed normal renal masses 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 inflammation with mononuclear cells and frequent cosinophils consistent with ATN. EM showed tubuloreticular inclusions. She was started on postop Rx which was tapered over 8 weeks. Creatinine downtrended to 1.1mg/dL.

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 elucidated, 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.

PO2261
An Unusual Case of Granulomatous Interstitial Nephritis (GIN)
Charis E. Whitney, Ronald L. Mars, University of Florida Health Science Center-Jacksonville, Jacksonville, FL.

Introduction: A 28 Y/O man was admitted with stage 5 CKD. He was entirely asymptomatic with a negative PMH except for recent HTN & proteinuria. Entire proteinuria w/u was negative. PE was unremarkable. Kidney biopsy showed advanced glomerulosclerosis with chronic non-casing GIN. Etiology was uncertain except for history of BCG vaccination. BCG induced GIN was proposed. He was given a trial of ACE-I's, but ultimately required long term hemodialysis (HD).

Case Description: A 28 Y/O Hispanic male with 1 yr PMH of untreated HTN & proteinuria presented with BUN 88, Cr 7.85. 1 day after foot surgery Cr increased to 8.14 A/H NPO. He was discharged a day later on diazoxide. 1 year ago he was diagnosed with HTN & proteinuria. He had never received f/u or treatment. PMH was negative. FIH was significant for a cousin with ESRD s/p kidney transplant & an uncle with diabetes. Full proteinuria w/u was (-). Renal US revealed normal size kidneys & increased cortical echogenicity c/w medical renal disease. ACE-I's were added. We continued to improve, with BUN & Cr improving but no renal function & was then started on HD. Kidney biopsy revealed acute tubular injury with regeneration changes, acute & chronic interstitial nephritis with a few granulomas, 75% global glomerulosclerosis, mild tubular atrophy & interstitial fibrosis. GMS & AFB stains were negative for fungus & mycobacteria. No electron dense deposits (EDD's) were seen on electron microscopy. Further discussion with patient revealed he received BCG vaccine when 2 weeks old.

Discussion: Bacillus Calmette-Guérin (BCG) vaccine is a live but attenuated strain of Mycobacterium bovis used to protect against TB in many countries with a high prevalence of TB. BCG has been implicated in the development of granulomatous disease in multiple organs, but rarely in the kidneys. Our patient received an intra-dermal BCG injection 2 wks after birth & had no sequelae or side effects. The historical (-) PMH, absence of infections or infectious process, (-) serologic w/u, (+) history of environmental exposures made the incidental discovery of asymptomatic stage 5 CKD with proteinuria all the more surprising. The unexpected finding of GIN raised the consideration for stimulated immunity & granuloma formation from latent BCG vaccine. While literature documents granuloma formation in other organs, its occurrence in kidneys & potential contribution to progressive CKD seems less common, but should not to be overlooked.

PO2262
An Unusual Case of AKI
Malar Khadrain, Cynthia Miracle, Haiyan Zhang. University of California San Diego, La Jolla, CA.

Introduction: New-onset nephritic syndrome often requires kidney biopsy for diagnosis. Pathology is at times insufficient.

Case Description: An 81-year-old Hispanic female with HTN, CKD stage III presented with rash, fever, peripheral eosinophilia, AKI and diagnosed with DRESS
ALECT2 amyloidosis after steroids for allergic symptoms. This potential interplay between have triggered amyloidogenesis. A prior case report describes a patient who developed suspicion for preceding immune dysregulation, in the form of DRESS/steroids, that may patients who often have mixed clinical pictures. Circumstances leading to this case raise the recognition of disproportionate proteinuria was essential to question the diagnosis AIN and ALECT2 amyloidosis superimposed on a background of hypertensive changes; by ALECT2 amyloidosis and be associated with clinical sequelae. Cardiac involvement in ALECT2 amyloid prevalence populations. Complications related to systemic disease transplantation and should be considered in older patients, especially from higher spectrometry revealed ALECT2 as the amyloidogenic protein. Autopsy revealed massive amyloid deposition in the native kidneys, adrenals, spleen, marrow biopsy did not show a plasma cell dyscrasia. Kidney biopsy noted amyloidosis (Congo red positive deposits in glomeruli, vessels, interstitium) with 56% global glomerulosclerosis and >60% severe IFTA. Mild interstitial inflammation with occasional eosinophils suggested resolving AIN. Severe findings of hypertensive sequelae noted. Immunofluorescence was 2+ for IgG and kappa. Electron microscopy showed 10nm fibrils and severe podocyte foot process effacement. Mass spectrometry diagnosed ALECT2 amyloidosis.

Discussion: Our case is unusual in having three simultaneous pathologies, namely AIN and ALECT2 amyloidosis superimposed on a background of hypertensive changes; the recognition of disproportionate proteinuria was essential to question the diagnosis and avoid early closure on AIN. Concurrent renal pathologies are a common finding in patients with ALECT2 amyloidosis, underscoring the utility of kidney biopsy in these patients who often have mixed clinical pictures. Circumstances leading to this case raise suspicion for preceding immune dysregulation, in the form of DRESS/steroids, that may have triggered amyloidogenesis. A prior case report describes a patient who developed ALECT2 amyloid after steroids for allergic symptoms. This potential interplay between genetic and environmental factors requires further investigation.

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 hypertensive bradycardic arrests lead 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 venales 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 C5b9-ELISA to Identify Patients with Atypical Hemolytic Uremic Syndrome

Martin Reinhardt, Hermann G. Haller, Yulia Kiyana. Medizinische Hochschule Hannover Zentrum Innere Medizin, Hannover, Germany.

Background: Discrimination between different diseases in patients suffering from thrombotic microangiopathies is often challenging. Measuring C5b9 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 C5b9-ELISA to measure C5b9-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 C5b9-depositions 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 C5b9-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 Tukeys-multiple comparisons test.

Conclusions: We described a novel, fast and reproducible ELISA to identify aHUS-patients by measuring C5b9-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.

ELISA-results with 95 % CI. A: C5b9-deposits in different patients. B: C5b9-deposits before and after two doses of eculizumab in patient 2 compared to healthy control 1.

PO2265

Chronic Neurological Impairment in Patients with Thrombotic Thrombocytopenic Purpura: Preliminary Findings in a Comprehensive MRI Protocol

Jeff Hamilton, Michael T. Jurkiewicz, Jonathan D. Thiessen, Shih-Han S. Huang. Western University, London, ON, Canada.

Background: Thrombotic thrombocytopenic purpura (TTP) is a life-threatening blood disorder characterized by insufficient activity in ADAMTS13 (a disintegrin and metalloproteinase with thrombospondin type 1 motif, member 13). This protein prevents blood clotting, so in TTP there is spontaneous clotting throughout the microvasculature. Treatment includes plasma exchange therapy and immunosuppressants to improve fever, thrombocytopenia, and kidney failure. However, neurological changes, such as seizures and confusion, persist. There is limited research on TTP on the brain but it is known that TTP presents similar pathology to stroke. This study aims to better understand the long-term impact of TTP on the brain using a comprehensive magnetic resonance imaging (MRI) protocol and cognitive testing.

Methods: 13 patients (5 male, mean age 44.5) in hematological remission were recruited. Participants had a 65-minute MRI scan (Siemens mMR Biograph 3T) based on best-practice guidelines for imaging stroke. The protocol included five qualitative acquisitions and three quantitative acquisitions. Participants also completed a 40-minute cognitive test (Cambridge Brain Sciences) to assess cognitive impairment.

Results: Table 1 summarizes the findings across qualitative acquisitions. The most salient findings were the white matter hyperintensities seen in the T2 FLAIR in Image 1. 12 participants completed the cognitive testing and there is evidence of cognitive impairment.
PO226 Persistent Coagulation Abnormalities in ESRD After 1 Year of Follow-Up
Emily Rontekoe, Vinod K. Bansal, Fakihma Siddiqui, Debra Hoppensteadt, Jawed Fareed. Loyola University Medical Center, Maywood, IL

Background: Common to end-stage renal disease (ESRD), coagulation abnormalities can lead to severe bleeding events or excessive thrombosis 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 collected 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
Rossan Boweed,1 Geoffrey I. Johnston,1 Linghong Huang, James Z. Song,2 Tim S. Schmidt,2 Allison L. Bigley,1 Graham Oggi,4 Eric Wong,1 Elizabeth S. Thomson,1 Jane Y. Chan,3 Anastasia Raivskas,1 Timothy S. Johnson,1 UCB Pharma, Slough, United Kingdom; 2Prisys Biotechnology, Shanghai, China; 3OracleBio, Chapelhill, United Kingdom; 4University of Oxford, Oxford, United Kingdom; 5Veramed, London, United Kingdom.

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 at the first month of 2020 was done. Adequacy was defined by the number of glomeruli for native renal biopsy (Bx) samples in our laboratory over time.

Results: From 2004 to 2018, there was a significant change in adequate biopsies. Deep nephrologists decreased from 29.7% to 28.5% to 14.2% to 12.7% in 2018. The needle gauge significantly changed from 27G to 22G to 18G to 16G in 2018. The needle gauge significantly changed from 27G to 22G to 18G to 16G in 2018.

Conclusions: Inadequate Tissue for Renal Biopsy Analysis Has Significantly Increased Since the Switch to Interventional Radiology (IR)
Patrick D. Walken,1 Vanessa Moreno,2 Caleb Nissen,3 'Arkana Laboratories, Little Rock, AR; 1University of Arkansas for Medical Sciences, Little Rock, AR

Background: The aim of this study was to determine the incidence of inadequate native renal biopsy (Bx) samples in our laboratory over time.

Methods: A retrospective study of native kidney biopsy adequacy from 2004 through the first month of 2020 was done. Adequacy was defined by the number of glomeruli for light microscopy (LM) as follows: 1. Ideal ≥20; 2 Adequate 10-19; Limited 4-9; Miss 0-3. An in-depth study of kidney biopsies received in 2004 and April-August of 2018 was conducted. Comparisons were made with 29.3 mL/min/1.73m². At the end of follow-up, eGFR was 39.6 ± 20.9 mL/min/1.73m². The mean miss rate changed from 2% in 2004 to 7% in 2009 through 2018. The needle gauge significantly changed from 27G to 22G to 18G to 16G in 2018.

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Background: The aim of this study was to determine the incidence of inadequate native renal biopsy (Bx) samples in our laboratory over time.
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 menophaeric kidney from 10 weeks to 21 weeks of gestation were identified from our surgical pathology and autopsy cases for comparison with menophaeric 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, menophaeric and metanphreric 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 mesophaeric glomerular and tubular structures at 4 weeks but this expression disappeared in the menophaeric 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 mesophaeric kidneys revealed brush borders on PAS stained sections from 7 to 10 weeks suggestive of reabsorption capacity. The PT of mesophaeric at 7 weeks stained positively for KIM-1, suggestive of acute tubular injury during apoptosis processes. The menophaeric showed expression of markers in respective renal compartments, similar to those in mesophaeric.

**Conclusions:** Human mesophaeric can have GATA3+ mesangial cells in the glomeruli. Although structures are simplified (no loop of Henle and collecting ducts), the human mesophaeric nephrons include primitive glomeruli, PT showing brush borders and distal tubules, having morphological features similar to those of advanced metanphric 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.

**PO2272**

### Monogenic Causes of Nephrolithiasis or Nephrocalcinosis in Korean Children

Jeong yeon Kim,1 Beomhee Lee,2 Heeyeon Cho,1 Department of Pediatrics, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; 2Department of Pediatrics, Asan Medical Center Children’s Hospital, University of Ulsan College of Medicine, Seoul, Republic of Korea.

**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 NL/NC and underwent genetic test under suspicion of hereditary nephropathy from March of 2013 to January of 2020 in Samsung Medical Center, 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/NC (15%). Total 13 pathogenic gene mutations were detected in 16 patients (80%): 5 genes (SCL3A1, GRIK1, CLCN5, OCLR1, CLCNKB) were known to cause monogenic forms of NL/NC and 8 genes (PA2X, PKD1, HNF1B, SLC36A2, SLC34A1, SLC34A2, SLC34A3, SLC33A1) were newly detected in this study. Three pathogenic autosomal recessive mutations were detected in 3 individuals; BUB1B (n=1), GRIK1 (n=1), VPS33B (n=1). We also detected pathogenic mutations in 6 autosomal dominant genes in 7 individuals; CLCNKB (n=1), SLC3A1 (n=1), PA2X (n=1), HNF1B (n=2), SLC11A (n=1), PKD1 (n=1), SLC36A2 (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.

**PO2273**

### Trans IL-6 Signaling Does Not Distinguish Between Pediatric Patients with and Without Scarring After Febrile Urinary Tract Infection

Sudipti Gupta, Sara E. Lautenbiser, John D. Spencer, Brian Becknell, Christina B. Ching, Nationwide Children’s Hospital, Columbus, OH.

**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 putative role in mediating renal fibrosis 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 (≥38°C) UTI (urine culture ≥50K uropathogen) with documented presence or absence of renal scarring on imaging. Patients were not actively infected at 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
Bacterial suspension was inoculated with a catheter transurethrally. To assess the colony-clearing UPEC UTIs resistant to experimental UTI.

David Human Neutrophil Peptide 1-3 Protects the Urinary Tract from PO2275 Febrile and Afebrile Urinary Tract Infection

Results: 50 urines from patients with a history of febrile UTI were collected: 23 with and 27 without scarring. The groups were not significantly different in age or gender. Urine IL-6 levels (pg/mL) in patients with and without scarring were not significantly different between those with and without scarring. While IL-6 values significantly correlated with sgp130 values (p=0.0004) in those without scarring, the values did not correlate in those with scarring (p<0.05). Ratios of IL-6/sgp130 and sIL-6R/sgp130 were not different between groups.

Conclusions: This study found that expression of trans IL-6 signaling in those with renal scarring compared to those without due to a lack of correlation of sgp130 with IL-6 in those with scarring. The absolute values and ratios of these markers of trans IL-6-signaling, however, are not significantly different between individuals with a history of febrile UTI with and without renal scarring in the non-acute setting.

Funding: NIDDK Support

PO2274

Markers of Trans IL-6 Signaling Are Not Differentially Induced During Febrile and Afebrile Urinary Tract Infection

Sudipti Gupta, Sara E. Lautzenhiser, John D. Spencer, Brian Becknell, Christina B. Ching. Nationwide Children’s Hospital, Columbus, OH.

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 in this study. 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 (axillary temperature ≥38°C) compared to those without (<38°C). Patients were included in the analysis if they had a positive urine culture (>50K CFU of a uropathogen) and for those without a fever if they had symptoms of dysuria, urgency, frequency, or new or worsening urinary incontinence. Those with fever were termed afebrile UTI and those without a fever were termed febrile UTI.

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.

Funding: NIDDK Support

PO2275

Human Neutrophil Peptide 1-3 Protects the Urinary Tract from Uropathogenic Escherichia coli Infection in Humanized Mouse Model

Jorge J. Canas, Jenaya Hooks, Sam W. Arregui, Andrew L. Schawderer, David S. Hains. Division of Pediatric Nephrology, Department of Pediatrics, Indiana University School of Medicine, Indianapolis, IN.

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-defensin DEF A1A3. species as a causative organism (OR 6.222; 95% CI 2.396-15.46; P<0.001), previous antibiotic exposure to patients (OR 2.418; 95% CI 1.071-5.461, P=0.04), and stayed longer in hospital than the ESBL-negative study group (7.0 days vs. 4.5 days, <0.001).

Methods: We generated female mice with a Rnase6<sup>EGFP<sup> knock-in allele, human RNASE6 transgenic, or controls on a C57BL/6J genetic background. We identified cellular sources of RNase 6 along with the consequences of its gain and loss of function during experimental urinary tract infection (UTI).

Results: Rnase6<sup>EGFP<sup> mice 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.

Funding: NIDDK Support

PO2277

Risk Factors for Urinary Tract Infection Caused by Extended-Spectrum Beta-Lactamase Gram-Negative Bacteria in Infants

Yi Hong Ahn, Hyun Kim, Jyunyeong Lee, Seonhee Lim, Hee Gyang Kang, Yu-Jeong Han, Ji Hyeon Kim, Jyunyeong Lee, Seonhee Lim, Hee Gyang Kang. 1Seoul National University Children's Hospital, Seoul, Republic of Korea; 2Seoul National University Bundang Hospital, Seongnam, Republic of Korea; 3Inha University Hospital, Incheon, Republic of Korea.

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 1.2-5.4) months of age. Two (0.4%) 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 1.071-5.461, P=0.04), and Klebsiella species as a causative organism (OR 6.222; 95% CI 2.396-16.158, P=0.001) were associated with ESBL positivity. 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 infants with UTI. Antibiotics exposure on both parents and infants 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
Vimal Master sankar rai, University of Illinois College of Medicine at Peoria, Peoria, IL.

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. Urine 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 hypercalciuria 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 excretions 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 uric acid (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
Ashley R. Jackson, Birong Li, Brian Becknell. Center for Clinical and Translational Research, Abigail Wexner Research Institute at Nationwide Children’s Hospital, Columbus, OH; Division of Pediatric Nephrology, Nationwide Children’s Hospital, Columbus, OH.

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 models. The objective of this study was to determine temporal progenitor-progeny relationships responsible for bladder urothelium generation and regeneration.

Methods: Using Ker5+;CreERT2;Rosa26 mice, K5-UCs were inducibly and permanently labeled with tdTomato (tdT). Tamoxifen (TMX) was administered at postnatal day (P) 1, 7, 14, 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 quantify tdT, K5, (uroplakin), Upk and K20 expression.

Results: Fate mapping analysis found that 22% (TMX0;SAC0) and 23.5% (TMX0; SAC0) of neonatal tdT+ UCs differentiated into adult Upk+ UCs (tdT-;Upk+ mostly intermediate cells) by P42 compared to 9% (TMX0;SAC0) or 2.25% (TMX0;SAC0) of juvenile tdT+ UCs, and 0% adult (TMX0;SAC0) (P<0.01, ANOVA). Following urothelial injury, 63% (TMX0;Cyc-); 54.33% (TMX0;Cyc-); and 69% (TMX0;Cyc-;Cyc0) of umbrella cells expressed tdT2 (tdT2;K5+;Upk20). Adult (TMX0;Cyc+;Cyc0) 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 tdT+ UCs regenerate umbrella cells, while adult tdT+ 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 acute 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, Stefano Ghirardello, Valentina Capone, Gianluigi Ardissino. 1NICU, 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 dehydrations, 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 grandfathers, 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/L vs 1.4 ± 0.3 mg/L, p = 0.01). 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/L, IC 95% 0.1-0.3 in, p = 0.01).

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, Hailey W. Gavigan, James A. Rowe, Brenda Poindexter, Kelli A. Kralilman, Alexandra Schmerger, Chunyan Liu, Shelley Ehrlich, Meera Kotagal, Stuart Goldstein. 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 alone, 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).

Conclusions: 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

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**Results:** A total of 141 neonates underwent 192 surgical procedures. AKI occurred in 90% of infants. AKI was 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-operational AKI (p ≤ 0.001 to 0.0536). 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 clinicians a guideline to avoid further FO. 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 Type</th>
<th>Preoperative uNGAL (ng/ml)</th>
<th>12 hour post-op</th>
<th>24 hour post-op</th>
<th>36 hour post-op</th>
<th>48 hour post-op</th>
<th>72 hour post-op</th>
<th>96 hour post-op</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emergent</td>
<td>240 (164,411)</td>
<td>260 (171,464)</td>
<td>234 (146,393)</td>
<td>204 (134,339)</td>
<td>204 (134,339)</td>
<td>221 (139,339)</td>
<td>190 (116,305)</td>
</tr>
<tr>
<td>Routine</td>
<td>72 (22-95)</td>
<td>82 (46-123)</td>
<td>67 (32-117)</td>
<td>57 (29-103)</td>
<td>40 (30-53)</td>
<td>40 (30-53)</td>
<td>57 (30-103)</td>
</tr>
</tbody>
</table>

Abbreviations: Renal Angina Index (RAI)

**Results:** The optimal cutoff for creatinine-based DayAKI was found to be stage 3; the optimal cutoff for RAI was stage 3; and the optimal cutoff for uNGAL was 0.79 (95% CI: 0.70, 0.87) and 0.79 (95% CI: 0.69, 0.82) respectively, although each scoring measure differed in sensitivity and specificity. The modified RAI had an optimal cutoff of ≥ 10 and the highest AUC (0.79; 95% CI 0.72, 0.85) with a high sensitivity and moderate specificity for prediction of CRRT requirements (table 1).

**Conclusions:** As a more accurate tool for discriminating patients in need of CRRT, a modified RAI has numerous potential implications. Identifying patients who ultimately require CRRT at an earlier timepoint may influence timing of CRRT initiation in an attempt to improve nephrotoxic exposure further. Furthermore, the diagnostic capabilities of the modified RAI may be further refined by the addition of urinary biomarkers. These findings should be validated in a larger cohort.

**Table 1**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Stage</th>
<th>Sensitive (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>PPV (95% CI)</th>
<th>NPV (95% CI)</th>
<th>TPR (95% CI)</th>
<th>TNR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRRT</td>
<td>1.2</td>
<td>0.61 (0.59, 0.63)</td>
<td>0.85 (0.83, 0.87)</td>
<td>0.83 (0.81, 0.84)</td>
<td>0.61 (0.59, 0.63)</td>
<td>0.85 (0.83, 0.87)</td>
<td>0.61 (0.59, 0.63)</td>
</tr>
<tr>
<td>uNGAL</td>
<td>0.5</td>
<td>0.87 (0.85, 0.88)</td>
<td>0.88 (0.86, 0.90)</td>
<td>0.87 (0.85, 0.88)</td>
<td>0.88 (0.86, 0.90)</td>
<td>0.88 (0.86, 0.90)</td>
<td>0.87 (0.85, 0.88)</td>
</tr>
</tbody>
</table>
| Modification of the Renal Angina Index for Identifying Need for Renal Replacement Therapy in Pediatric Shiga Toxin-Producing Escherichia coli-Associated Hemolytic-Uremic Syndrome (STECK-HUS): A Single Center’s 12-Year Experience

Neha D. Pottanatt, Sarah P. Andreoli, Chiuee Miller, Myda Khalid. Indiana University Riley Hospital for Children, Indianapolis, IN.

**Background:** Half to 2/3 of children with STEC-HUS require renal replacement therapy. The modality is chosen based on a center’s individual experience and its association with complications.

**Methods:** We performed a retrospective cohort analysis using electronic medical records and chart review of 80 patients with STEC-HUS identified through billing data from July 1, 2008 to May 30, 2020. Cases of Streptococcal pneumoniae associated HUS and atypical HUS were excluded.

**Results:** Dialysis was required in 47 patients (59%). Except for one patient, acute PD was chosen as the initial modality. 43 patients (91%) received PD successfully immediately after the catheter was placed. Four patients required a modality change to either hemodialysis (HD) or continuous renal replacement therapy (CRRT). Leaking of dialysate around the catheter exit site was noted in only 5 patients, out of which only one underwent a catheter revision and resumed PD successfully, two were switched to HD, and two patients had renal recovery allowing for cessation of dialysis. Peritonitis occurred in a single patient but did not lead to a change in modality. In two patients, PD was unsuccessful due to severe intestinal ischemia/collitis, and these patients were switched to CRRT. A central venous catheter (CVC) was often placed at the time of the PD catheter (40 patients). 46 patients had thrombocytopenia (<100,000/mm3) prior to PD catheter and/or CVC placement. Despite having a mean preoperative platelet count of 42,100/mm3, only 6 patients received a platelet transfusion. Furthermore, 15 patients with preoperative platelets between 15,000 – 35,000/mm3 did not have a bleeding event and did not receive a transfusion.

**Conclusions:** During a time when HD and CRRT have become the more preferred modalities for acute dialysis in children in the US, acute PD is safe and successful in STEC-HUS. We describe a low complication rate, despite immediate use of the PD catheter, indicating that acute PD can be performed before the exit site heals. Platelet transfusions in STEC-HUS patients confer greater odds of AKI and those with AKI had worse long-term outcomes. Attention to kidney function should be paid to neonates with PD catheter and CVC placement.

**PO2285**

**Post-Operative Fluid Overload Is Associated with AKI and Elevated Urinary Neutrophil Gelatinase-Associated Lipocalin Values**

Cara L. Slagle, Hailey W. Givigan, James A. Rowe, Brenda Poidexter, Kelli A. Krrallman, Alexandra Schmeger, Meera Kotagal, Shelby Ehrlich, Chunyan Liu, Stuart Goldstein. Cincinnati Children’s Hospital Medical Center, Cincinnati, OH.

**Background:** Positive fluid accumulation (FO) in neonates is associated with increased morbidity and mortality and may represent underlying acute kidney injury (AKI). AKI is defined by changes in serum creatinine (sCr) and urine output (UOP). FO can be unreliable in the setting of FO. Urinary neutrophil gelatinase-associated lipocalin (uNGAL) offers promise as an alternative biomarker in assessing AKI in patients with FO.

**Methods:** Infants undergoing a general surgical procedure, excluding gastric tube placement alone, were prospectively enrolled. uNGAL values were obtained pre-op and on post-op days (0-3) at six time points. FO was defined as 10% weight increase from pre-op weight during PODs 0-5. Percent FO was calculated using post-op net fluid balance=[pre-op weight] + [weight gain during PODs 0-5] - [pre-op weight]. The AUC was calculated by Bland-Altman analysis using median and IQR data. The uNGAL threshold for FO was determined as the 90th percentile of uNGAL values and did not receive a transfusion.

**Conclusions:** Positive fluid accumulation in neonates is associated with increased morbidity and mortality and may represent underlying acute kidney injury (AKI). AKI is defined by changes in serum creatinine (sCr) and urine output (UOP). FO can be unreliable in the setting of FO. Urinary neutrophil gelatinase-associated lipocalin (uNGAL) offers promise as an alternative biomarker in assessing AKI in patients with FO.

**Methods:** Infants undergoing a general surgical procedure, excluding gastric tube placement alone, were prospectively enrolled. uNGAL values were obtained pre-op and on post-op days (0-3) at six time points. FO was defined as 10% weight increase from pre-op weight during PODs 0-5. Percent FO was calculated using post-op net fluid balance=[pre-op weight] + [weight gain during PODs 0-5] - [pre-op weight]. The AUC was calculated by Bland-Altman analysis using median and IQR data. The uNGAL threshold for FO was determined as the 90th percentile of uNGAL values and did not receive a transfusion.

**Conclusions:** Positive fluid accumulation (FO) in neonates is associated with increased morbidity and mortality and may represent underlying acute kidney injury (AKI). AKI is defined by changes in serum creatinine (sCr) and urine output (UOP). FO can be unreliable in the setting of FO. Urinary neutrophil gelatinase-associated lipocalin (uNGAL) offers promise as an alternative biomarker in assessing AKI in patients with FO.

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**PO2286**

**Use of B-Type Natriuretic Peptide as a Quantitative Marker of Fluid Overload in Neonatal Renal Replacement Therapy**

Nourreddin D. Nourbakhsh,1,2 Nadine M. Benador,1,2 Comprehensive Kidney Care Center, Rady Children’s Hospital, San Diego 1Rady Children’s Hospital, San Diego, San Diego, CA; 2University of California San Diego, La Jolla, CA.

**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 converted to HDVHD, 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 in this patient with RRT.

**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.

**PO2287**

**Comparison of Nafamostat Mesylate and Regional Citrate Anticoagulation for Anticoagulation in Pediatric CRRT**

Mai J. Miyaji,1,2 Kelli A. Kraliman,1 Kentaro Ide,1 Stuart Golstein,1 1Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; 2National Center for Child Health and Development, Kokuritsu Kenkyu Kaisatsu Hojin Kokuritsu Seiiku Iryo Kenkyu Center, Setagaya-ku, Japan.

**Background:** Regional Citrate Anticoagulation (RCA) is the preferred anticoagulant for CRRT in the US and 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 in, 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.

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**Fig. 1** Kaplan-Meier curves of time to spontaneous filter failure (p=0.085)

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**PO2288**

**Renal Replacement Therapy and Mortality Rates for Children with Posterior Urethral Valves and Prune Belly Syndrome**

Emily J. Stonestock,1 Yuri V. Sebastião,1 Brian Becknell,1,2 Christina B. Ching,1,2 Daryl J. McLeod,1,3 Nationwide Children’s Hospital, Columbus, OH; 1Center For Clinical and Translational Research, The Research Institute at Nationwide Children’s Hospital, Columbus, OH; 3Center for Surgical Outcomes Research, The Research Institute at Nationwide Children’s Hospital, Columbus, OH.

**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 one of four cbo’s PHS hospitals 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:

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

**Underline represents presenting author.**
Preterm Birth in Mice Results in Differential Gene Expression and Premature Cessation of Nephrogenesis

Aleksandra Cwiek, Kimberly Deronde, Masako Suzuki, Kimberly J. Reidy, Jennifer R. Charlton, Albert Einstein College of Medicine, Department of Genetics, New York, NY; Children’s Hospital at Montefiore, Department of Pediatrics, Division of Nephrology, New York, NY; University 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 (25 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.

Gestational Age (GA) Affects Urine Biomarkers by Postnatal Age but Most Converge by 34 Weeks Post-Menstrual Age (PMA)

David J. Askenazi, Brian A. Halloran, Robert Schmicker, Patrick J. Heagerty, Sandra Jial, Stuart Goldstein, Sangeeta R. Hingorani, PENUT Investigators, The University of Alabama at Birmingham School of Medicine, Birmingham, AL; University of Washington, Seattle, WA; Cincinnati 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), were evaluated by electrochemiluminescence; creatinine by mass spectrometer. 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 day) 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, UROMOD, 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 (%)</th>
<th>AKI (%)</th>
<th>p-value</th>
</tr>
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<tr>
<td>Age (months) digestive tract region</td>
<td>1.9 ± 2.1</td>
<td>3.9 ± 3.1</td>
<td>0.04</td>
</tr>
<tr>
<td>Gender (male/female) mean</td>
<td>53.6/16.8</td>
<td>10/7.3</td>
<td>0.76</td>
</tr>
<tr>
<td>MBls, N (%)</td>
<td>5/69%</td>
<td>1/14.5%</td>
<td>0.64</td>
</tr>
<tr>
<td>Length of stay (days) mean</td>
<td>170.195</td>
<td>168 ± 95</td>
<td>0.99</td>
</tr>
<tr>
<td>Transient with NINJA (%)</td>
<td>7 (39%)</td>
<td>1/11 (9.1%)</td>
<td>0.47</td>
</tr>
<tr>
<td>Morbidity, N (%)</td>
<td>6</td>
<td>1/11 (9.1%)</td>
<td>0.29</td>
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PO2292
Baby NINJA (Nephrotoxic Injury Negated by Just-in-Time Action) Transfusion Rates
Hailey W. Gavigan, Cara L. Slagle, Kelli A. Krallman, Brenda Poindexter, David K. Hooper, Stuart Goldstein. Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

Background: Acute kidney injury (AKI) is associated with poor outcomes in neonates. Nephrotoxic medication (NTM) exposure is a common cause of AKI. Nephrotoxic 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 SCr 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 eras, 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>Cr value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cr compliance (%)</td>
<td>45.1</td>
<td>80.1</td>
<td>82.6</td>
<td>0.06</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>All HbCrC transfusion rate per 1000 NICU patient days</td>
<td>0.56</td>
<td>0.89</td>
<td>0.58</td>
<td>0.89</td>
<td></td>
</tr>
<tr>
<td>NINJA HbCrC transfusion rate per 1000 NICU patient days</td>
<td>0.41</td>
<td>0.84</td>
<td>0.42</td>
<td>0.84</td>
<td></td>
</tr>
<tr>
<td>All CR - (SCr - NTM baseline) (case &lt;1000 NUCU patient days)</td>
<td>23.5</td>
<td>25.4</td>
<td>21.3</td>
<td>0.01</td>
<td>0.04</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 Iragorri, Randall Jenkins. 1Oregon Health and Science University; Portland, OR, 2Boise State University, Boise, ID.

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.
Children with a History of Low Birth Weight (LBW) Show Greater Reduction in Kidney Function Than Previously Described Using the Updated Schwartz Equation

Kaye E. Brathwaite,1 Rebecca Levy,1 Harini Sarathy,2 Ilir Agalli1,2 Tanya S. Johns,1 Kimberly J. Reidy,1,2 Frederick J. Kaskel,1,2 Michiel L. Melamed,1,2 Children’s Hospital of Philadelphia, Philadelphia, PA; 1University Albert Einstein College of Medicine, Bronx, NY; 2Montefiore Medical Center, Bronx, NY; 1University of California San Francisco, San Francisco, CA.

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 based on histology are available; genetic analyses are not yet included. Efforts to improve the equation for CB equation is limited. A study using the Counahan-Barrat (CB) eGFR estimation showed a greater association of LBW and reduced kidney function 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 1.1-1.97) 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

FCGG Renal Biopsy Network: First Epidemiological Report on Pediatric Renal Disease

Noel Knops,1 Johen M. De Meester,1 Amélie Dendooven,2 Wim Laurens,1 Ben Sprangers,1 Elena N. Levchenko,1 AZ Nikolaas, Sint-Niklaas, Belgium; 1Katholieke Universiteit Leuven Universitaire Ziekenhuizen Leuven Campus Gasthuisberg, Leuven, Belgium; 1Universitair Ziekenhuis Gent, Gent, Belgium.

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 study aim was to define options for pediatric eGFR reporting that optimize accuracy and minimize the impact of missing concurrent height in routine lab work.

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/1.73m. 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 mean age was 13.6 years, 49% were males, 49% were white, 25% were black, 19% were Mexican-American, and 7% were other race. All higher percentage of children with LBW was seen in worse poverty groups. Mean eGFRs in those born LBW were 103 and 107mL/min/1.73m 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, 30% vs 21.4%. The Schwartz equation showed a greater association of LBW and reduced kidney function 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 1.1-1.97) 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.

PO2296

Facts Related to Significant Albuminuria or Low Glomerular Filtration Rate in Adolescents from a Population with a High Prevalence of CKD of Unknown Origin

Jose M. Arceola Guerra,1 Cesar M. Gutierrez, Izel Ovalle, Mariana J. Macias,2 Andrina L. Garcia Diaz.1,2 Centro Hospitalario do Estado de Mexico, Mexico.

Background: Chronic kidney disease (CKD) of unknown origin has been recognized as the leading cause of kidney disease in young adults in some underdeveloped countries. In Aguascalientes Mexico we report a high prevalence of treated CKD (1997 ppm), with more than half (54%) of unknown cause. The peak of prevalence is between 20 - 30 years (45%), being in that group 73% CKD of unknown origin. For this reason, a CKD screening study was designed in high school students in the state. The aim of this report is to describe the findings of a pilot study obtained in the first three schools.

Methods: Cross-sectional study of high school students. Determination of albumin/creatinine ratio was performed in isolated urine sample and standardized serum creatinine to calculate eGFR with Schwartz formula, an abnormal albumin/creatinine ratio>30 mg/ gr and GFR<75 ml/min were defined as CKD. Students and parents were questioned about potentially risk factors. For the multivariate analysis, only students with complete questionnaires were included.

Results: During March 2020, three high schools in the municipality of Calvillo (Aguascalientes) were visited, accepting entry to the study 187 students out of 260 (72%). The average age was 13.3 years (IQR 12-14) with a predominance of males (n = 109, 58.2%). 33 students with ph CKD were detected (17.6%), 32 of which were due to the presence of abnormal albumin/creatinine ratio. Only two patients had low GFR, one with 43 ml/min and the other with 75 ml /min. Four patients presented macroalbuminuria, the rest microalbuminuria. In the multivariate analysis, next variables remained significant: economic income less than 4,000 Mx$, (OR 4.4, 95% CI, 1.3 - 14.7), frequent NSAID intake (OR 3.5, 95% CI 1.16 - 13, P=0.02), a son or brother affected by diabetes (OR 4.3, 95% CI 1.2 - 14.5, P < 0.01), use of clay dishes by parents and grandparents (OR 4.3 95% CI 1.4 - 12.9, P < 0.01), and BMI <17 kg / m2 (OR 5.8, 95% CI, 1.8 - 18.7, <0.01).

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

Underline represents presenting author.

698
PO2298
Measurement of GFR and Vasoactive Substances in Children with Sickle Cell Anemia
Oluwadamilola Ejike,1 George J. Schwartz,2 Susan Legan,3 Amy M. Becker,4 Raymond P. Quigley,5 Baylor Medical Center, San Antonio, TX; 2University of Rochester Medical Center, Rochester, NY; 3University of Texas Southwestern Medical Center at Dallas, Dallas, TX; 4Driscoll Children’s Hospital, Corpus Christi, TX.

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: Subjects: SCA:32 and Control:13 The GFR of the sickle cell group was 148 ± 36 ml/min/1.73 m2 (Mean and SD) and the control group was 130 ± 17 ml/min/1.73 m2. The p-value (unpaired t-test) is 0.03 and thus is statistically significant. However, the SCA group had 21/32 with a GFR >130 while the control group had only 3/13 (p=0.019). Thus, there were more patients in the SCA group with hyperfiltration. There was no difference in urinary cGMP or PGE2. However, PGF2α was higher in the control group. Surprisingly, the urinary angiotensinogen (factored for urinary creatinine) was lower in the SCA group than in the controls (see table).

Cell Angiotensinogen / urine creatinine
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?
Melvin Chan, Amy C. Wilson, Neha D. Pottanat, Michelle C. Starr. Indiana University School of Medicine, Indianapolis, IN.

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: A total of 14 families were enrolled. 12 of 14 (86%) of children with ESKD were FI, and all 12 (100%) reported that COVID had worsened their FI status. The intraincreal remi-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).

PO2300
Incidence of Hypercalcemia with Calcitriol Compared with Paricalcitol in Pediatric Patients Receiving Hemodialysis
Rohan Dwivedi, Jennifer L. Morris, Jessica Geer, Poyyappakam Srivaths, Sarah J. Swiftz. Texas Children’s Hospital, Houston, TX.

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 received in-center doses of both paricalcitol and calcitriol or if they had incomplete data. Pts were not excluded from either group if they had an active prescription for oral calcitriol for home. Data were collected for 6-months from the date of the first in-center calcitriol or paricalcitol dose. The primary objective was to evaluate the incidence of hypercalcemia in those receiving calcitriol compared to paricalcitol. Secondary objectives included the incidence of hyperphosphatemia, high calcium-phosphorus product, and hyperparathyroidism (PTH). Data were evaluated using descriptive statistics, Mann-Whitney-U and Fisher’s Exact test.

Results: 34 pts met the criteria for the study (calcitriol group=15; paricalcitol group=19). The groups had no statistically significant differences at baseline. Patients in the paricalcitol group received an average weekly dose of 14 ± 7 mcg, equivalent to 4.67 ± 2.33 mcg of calcitriol compared to 2.36 ± 1.51 mcg in the calcitriol group (p=0.002). There were no differences between the time averaged serum calcium, phosphorus, calcium-phosphorus product, and iPTH between the two groups. Between the paricalcitol and calcitriol groups the incidence of hypercalcemia events per patient (EPP), based on age-related normal calcium was 1.11 and 0.53 (p=0.23), hyperphosphatemia EPP was 3.4 and 2.67 (p=0.20) and high iPTH EPP was 2.63 and 2.2 (p=0.38).

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 ped's population.
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 alpha-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 fall in eGFR of >50% and need for dialysis or transplantation.

Results: Of the 375 children included, median age was 12 years [IQR, 8-15], 227 (61%) 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 [KIM1 aHR; 2.6 (95% CI: 1.6-4.1), MCP1 aHR; 2.8 (95% CI: 1.7-4.7)] compared to those 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 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 quarter [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 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.

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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/day and 17 received the control dose of 400 IU/day. 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.

B=baseline
W=4 week

PO2304

Improving Metabolic Acidosis in Patients with CKD


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 progression1-2. Current guidelines

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
recommend bicarbonate supplementation for CKD patients with serum bicarbonate < 22mmol/L. Review of our nephrology division’s clinical practice in the past year found that 36% of patients with CKD stage 3-5 were acidotic, although only 25% of these received an intervention to address the acidosis. Our aim is to increase the percentage of interventions for acidosis in this population from 25% to 50% by June 30, 2020.

Methods: Monthly reports were generated for patients with CKD stage 3-5 and acidosis in the nephrology clinic. Our outcome measure is the percentage of acidic patients. Process measures include the percentage of acidosis recognition, appropriate intervention, and patients on bicarbonate treatment. The balancing measure is patients with alkalosis (bicarbonate > 28mmol/L) while on supplementation. A multidisciplinary team identified multiple root causes and baseline data identified that lack of provider recognition of mild acidosis (bicarbonate 20-22) was the primary driver why treatment was not initiated. Countermeasures were developed to address this gap.

Results: Using PDSA cycles, we have implemented 2 countermeasures. Initially, we utilized provider directed feedback to notify those who had patients with untreated acidosis in the past month. Then, an education session was completed in March 2020. Our goal of increasing interventions for acidosis to 50% was exceeded by March 2020 (75%). There was also a decrease in the number of acidic patients, increase in provider recognition and bicarbonate treatment, with no increase in patients with alkalosis (Figure 1).

Conclusions: Utilizing provider directed feedback along with educational sessions have effectively increased the percentage of CKD stage 3-5 patients who are appropriately treated for acidosis. Further interventions are ongoing.

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), Streptococcal 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.

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 (25OHD) 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 25OHD <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 maximin 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 a30 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 >30mg/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 therapy (p=0.24) or maintenance phase therapy (p=0.05). There was no hypercalcemia 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.

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,
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 hypercalcemia (IIH) 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 IIH 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 variants could cause this patient to develop PH1. The combined effects of IIH 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 Syndrome: Due to Anti-Tubular Basement Membrane Antibody Disease
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Introduction: Immunodysregulation, polyendocrinopathy, enteropathy, X-linked (IPEX) syndrome is caused by a de novo heterozygous c.1376A>T (p.K459M) mutation in the Cullin 3 gene (FOXL3). The transcription factor affecting the function of circulating regulatory T cells. Previously described renal manifestations were immune complex deposition in a membranous- pattern and interstitial nephritis. Here we report novel renal manifestations of IPEX syndrome.

Case Description: 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.Ala145Val mutations in the FOXL3 gene. He underwent stem cell transplant at 6 months of age from a fully matched unrelated donor. Post stem cell transplant he had improved chimerism with low but relatively stable donor T cells. He 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, calcium, 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 nephrotic-range tubular proteinuria, proximal RTA, phosphaturia, calciuria, 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: Pseudohypokalemicosthenia (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, renal acidosis, and growth retardation. 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 female presented with unexplained hyperkalemia due to Cullin-3 Mutation. Treatment with thiazide diuretics resulted in rapid correction of her hyperkalemia.

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.

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 perhaps 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, hyperacide gastric 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 bacteremia 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, diagnosed with skin biopsy. He also had persistent high serum creatinine with normal urine analysis. 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 10yo female, previously diagnosis 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 182/12, BUN 99 mg/dl, Cr 7.86 mg/dl, haptoglobin < 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-β2 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
a rescue therapy for TMA associated with CAPS. After 2 weeks 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 pelvocaliectasis 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 ~0.2mg/mg but this rises to abnormal (~0.2mg/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.
Cyanotic Nephropathy (CN) in Pre-Fontan Congenital Cyanotic Heart Disease (CCHD) with Solitary Kidney

**PO2318**

**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 10 yo 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). C5, C4, ANA, dsDNA, ANCA were normal. Ultrasound showed solitary left kidney with nephromegaly (12.5cm, 1000g/renal). Randomized diastolic flow. MRI abdomen showed dilatation of the left renal vein and IVC. Renal biopsy showed marked glomerular enlargement, segmental mesangiolysis with erythrocytolyis, and irregular thickening of glomerular capillaries. EM showed widespread subendothelial widening and remodeling of basement membranes without immune deposits, consistent with CN (Figure 1).

**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/isosorbide dinitrate.

Therapeutic plebotomy 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

**PO2319**

**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.

Managing Pediatric Renal Cell Carcinoma in Jehovah’s Witness Patient

**PO2321**

**Introduction:** Pediatric Renal Cell Carcinoma (pRCC) is rare in children and adolescents and only account for about 5% of pediatric renal neoplasms. The driver mutation of the majority of these tumors is due to cytogenetic translocations involving the MiT family of transcription factors. Surgical resection of the mass is the main treatment and depending on the advancement of the cancer, can result in a complete nephrectomy. Due to complexity of surgery and the risk of blood loss, treatment can be complicated by a patient’s religion that decline blood product transfusions, such as Jehovah’s Witness. This case describes an already rare cancer requiring a unique medical management due to a family’s religious belief.

**Case Description:** A previously healthy 14-year-old male presented complaining of left flank pain. Patient was hemodynamically stable to the 120s, and initial vital signs were 133/81 that self resolved. Due to persistent pain with unknown etiology imaging was obtained and MRI revealed 8 cm solid mass in the left kidney with a dilated and thrombosed left renal vein. The mass could not be differentiated between Wilms Tumor or pRCC, and a complete nephrectomy was decided to be the best course of treatment. Due to family’s religious background of Jehovah’s Witness a multi-disciplinary approach was considered to reduce the need for blood transfusions. Patient received daily erythropoietin injections and iron supplementation about three weeks prior to nephrectomy to stimulate red blood cell production post-operatively. Additionally, on the day of his procedure, interventional radiology (IR) first emobilized the left renal artery leading to tumor followed immediately by a left radical nephrectomy. Patient tolerated the procedure well with minimal blood loss and only had mild anemia. He required no post-operative blood transfusion. There was mild increase in creatinine level 6 weeks after kidney status-post nephrectomy that has since improved. Pathology report came back and confirmed clear cell renal cell carcinoma. Cytogenetic screen showed a translocation of...
the transcription factor E3 (TFE3) gene. Patient did well post-operatively with no signs of cancer on recent imaging and did not require any chemotherapy.

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

Eduardo La Porta,1,2 Isabella Pisani,1 Maura Faraci,1 Francesco P. Pilato,3 Luca Lanino,4 Daniela Verzola,4 Giacomo Garibotto,4 Angela R. Sementa,4 Letizia Gnetti,4 Enrico E. Verrina,4 Istituto Giannina Gaslini, Genova, Italy; Istituto Clinico Ligure di Alta Specialita, Rapallo, Italy; Ospedale Universitario, Parma, Italy; Ospedale Policlinico San Martino, Genova, Italy.

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, microhematuria, proteinuria, and granular casts). A renal biopsy was performed. Light microscopy showed tubulointerstitial inflammatory infiltrate, thickening of the glomerular basement membranes, and subepithelial deposits. 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 RD, a therapy with steroids was started, without clinical response.

Discussion: IgG4 RDK in adults with simultaneous TIN and MGP has been reported in a few cases. This is the first documented case of IgG4 RDK 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.

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

Table: AUC, sensitivities, and specificities of different ambulatory SBP measures in predicting LVH

PO2323

Is a Single Static Cut Point Useful to Define Ambulatory Hypertension in Youth? The SHIP AHYO Study

Ghilam Hamdani,1 Michael A. Ferguson,4 Marc Lande,4 Kevin E. Meyers,3 Mark Mitschefske,1 Joshua A. Samuels,1 Joseph T. Flynn,5 Elaine M. Urbina,1 The SHIP AHYO Investigators; 1Schneider Children's Medical Center of Israel, Petah Tikva, Israel; 2University of Rochester Medical Center, Rochester, NY; 3Cincinnati Children's Hospital Medical Center, Cincinnati, OH; 4Seattle Children's Hospital, Seattle, WA; 5The Children's Hospital of Philadelphia, Philadelphia, PA; 6Boston Children's Hospital, Boston, MA; 7University 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 utilize for the diagnosis of 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 Ontrak device (Spacelabs Inc., Snoqualmie, WA). ABP index was defined as mean ABP above and below height-specific 95% 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

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

706
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 0.983, 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

<table>
<thead>
<tr>
<th>Model</th>
<th>Odds Ratio (95% CI)</th>
<th>p-value</th>
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<tr>
<td>Model 1 (Unadjusted)</td>
<td>1.27 (1.07, 1.51)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Model 2 (Adjusted for age, sex, and race)</td>
<td>1.32 (1.02, 1.72)</td>
<td>0.031</td>
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<tr>
<td>Model 3 (Adjusted for age, sex, race, BMI category, premature birth, and gestational age)</td>
<td>1.40 (1.04, 1.88)</td>
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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.3 TRIBE-AKI Consortium, Yale University, New Haven, CT; 3Hospital for Sick Children, Toronto, ON, Canada; 1Johns 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 (CHD) 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 procedure, and had a combined procedure, and 7 were not defined. Hypertension, microalbuminuria, and eGFR<90, and eGFR<60 was 15%, 8%, 9%, and 1%, respectively, at the 5-year visit.

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 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
Shruti Shah, Andrew M. South. Wake Forest University School of Medicine, Winston-Salem, NC.

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 undescibed. 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=0.13) were modestly associated with PRES. eGFR (aOR 1.0 per 1 ml/min increase, 0.98-1.02, p=0.02) and albumin (aOR 1.7 per 1 g/dl increase, 0.73-3.93, p=0.50) and hemoglobin (aOR 1.12 per 1 g/dl increase, 0.81-1.56, p=0.48) were 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.

Funding: Other NIH Support - Spectrum Stanford Center for Clinical and Translational Research and Education (NHICATs T1L TR001084), the Wake Forest Clinical and Translational Science Award (NHICATs UL1 TR001420)

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 SLEDAl-AKR. 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 (LHV) was defined by sex, age specific left ventricular mass index (LVMi) ≥ 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 hypertensive LN was detected in 84.4% (n=28) and 37.5% of them was 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 was 20 mg, 10.5 mg, 2.3 mg, and 0.6 mg in stage 1, 2, 3, and 4, respectively. The prevalence of HTN, including 2 transient HTN, was 34.4% (n=28) and 37.5% of them was 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 was 20 mg, 10.5 mg, 2.3 mg, and 0.6 mg in stage 1, 2, 3, and 4, respectively. The prevalence of HTN, including 2 transient HTN, was 34.4% (n=28) and 37.5% of them was class IV (n=12). The prevalence of HTN, including 2 transient HTN, was 34.4% (n=28) and 37.5% of them was class IV (n=12). The prevalence of HTN, including 2 transient HTN, was 34.4% (n=28) and 37.5% of them was class IV (n=12). The prevalence of HTN, including 2 transient HTN, was 34.4% (n=28) and 37.5% of them was class IV (n=12). The prevalence of HTN, including 2 transient HTN, was 34.4% (n=28) and 37.5% of them was class IV (n=12).

Conclusions: In conclusion, HTN in cSLE is associated with BMI and renal activity at SLE diagnosis. Also, HTN affect long term damage accumulation in cSLE.
PO2329
Hemodialfiltration Maintains a Sustained Improvement in BP Compared with Conventional Hemodialysis in Children: The HDF, Heart and Height (3H) Study
Francesca De Zan,1 Colette J. Smith,1 Aysun Bayazit,2 Karolis Azukaitis,3 Sevcan A. Bakkaloglu,1 Fabio Pagliolonga,3 Mohan Shenoy,1 Manish Sinha,1 Branka B. Spasojevic,5 Claus Peter Schmieder,10 Franz S. Schaefer,10 Enrico Vidal,11 Rukshana Shroff,12 University Hospital of Padova, Padova, Italy; 1UCL Institute of Global Health, London, United Kingdom; 2Cukurova Hospital, London, United Kingdom; 9University Children’s Hospital, Belgrade, Serbia; 7Royal Manchester Children’s Hospital, London, United Kingdom; 4Clinic of Pediatrics, Vilnius University, Vilnius, Lithuania; 3Gazi University Hospital, Ankara, Turkey; 10Division of Pediatrics, Department of Medicine, University of Barcelona, Barcelona, Spain; 11Division of Pediatrics, Department of Medicine, University of Udine, Udine, Italy; 12Great Ormond Street Hospital for Children NHS Foundation Trust, and University College London Institute of Child Health, London, United Kingdom.

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 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-SDS >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 (β=0.83 [95%CI 0.51 to 1.15] SDS for HD vs HDF, p<0.0001) and higher IDWG (β=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 IDWG0, but not anti-hypertensive medications, was associated with a higher MAP-SDS in both groups of the mechanisms of 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 Nephrin and HLA-DR to HEK293T cells and assessed the expression patterns by flow cytometry and immunoprecipitation.

Results: Nephrin 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-DRBI*08:02-DRB1*13:02). While Nephrin was not detected in the absence of HLA-DR. [Discussion] Podocytes are sometimes considered as hematopoietic 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 Nephrin 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-DR could be associated with SSNS, the binding of specific molecules, such as nephrin or Nephmis, 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.

Funding: Government Support - Non-U.S.

PO2331
Efficacy and Safety of Ravulizumab in Pediatric Patients with Atypical Hemolytic Uremic Syndrome Previously Treated with Eculizumab: 26-Week and 1-Year Data
Larry A. Greenbaum,1 Noaya Fujita,2 Brigitte V. Adams,3 Alvaro Madrid Arias,3 Masayo Ogawa,2 Stephan Ortitz,3 Marc Vallec2,1 Kazuki Tanaka,2 1Emory University School of Medicine and Children’s Healthcare of Atlanta, Atlanta, GA; 2Aichi Shoni Hoken Iryo Sogo Center, Obu, Japan; 3Alexion Pharmaceuticals Inc, Boston, MA; 4Queen Fabiola Children’s University Hospital, Brussels, Belgium; 5Children’s Nephrology and Renal Transplantation Service, Children’s Maternity Hospital Sant Joan de Déu, University of Barcelona, Barcelona, Spain.

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-naïve 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) x10^9/L; LDH, -1.0 (17.9) 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.

Funding: Commercial Support - Alexion Pharmaceuticals, Inc., Government Support - Non-U.S.

PO2332
Typical Hemolytic Uremic Syndrome in Children: A Single-Center Experience
Siddharth A. Shah, University of Louisville, Prospect, KY.

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 anemia (Hemolytic anemia (iv) fluids in the initial timeline of disease presentation 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=0.045), 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 (includes 3 with CKD and 1 with ESRD who required kidney transplant) after one year. The count >20000 cells/mm3 (at p=0.001) 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 discharge and 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.

PO2333
Targeting Bloody Diarrhea to Fight Shiga Toxin-Producing Escherichia coli-Hemolytic Uremic Syndrome in Children: The Experience of the ItaKid HUS Network
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Background: Bloody diarrhea (BD) is often the first distinctive sign of hemolytic uremic syndrome (eHUS), the leading cause of acute kidney injury in infants, caused by shiga toxin (Stx)-producing Escherichia coli (STEC) infection. The few days prior the development of the renal complication, when bloody diarrhea is the only symptom, represent a window for better understanding, preventing or mitigating HUS. The present study aims at identifying patients at risk for HUS early and at evaluating the rate of BDs associated with STEC infection.

Methods: This multicenter case series study was performed between 2010 and 2019 in Pediatric emergency departments and clinics belonging to a network of 63 pediatric hospitals in Northern Italy (referral population: 12 million general population; 2.3 million children). 4767 screened samples, 214 (4.5%) turned out to be positive for Stx genes (1 and 2) using a Reverse Dot blot assays (Genotype EHEC - Arnika) until 2018 and Real Time PCR (RIDA Gene-Relab) thereafter. Stx-positive cases were further investigated for E.coli serogroups. Children positive for Stx genes were monitored for hemoglobinuria, blood tests to rule in or out the diagnosis of STEC-HUS were done if urine dipstick turned positive for hemoglobinuria.

Results: Out of the 4767 screened samples, 214 (4.5%) turned out to be positive for either Stx1 (n: 62; 29.0%) or Stx2 (n: 97; 45.3%) or both (n: 55; 25.7%). 34 patients out of the 214 (15.9%) developed eHUS (0.71% of BDs). Patients infected with STEC producing Stx2 alone were at higher risk for eHUS compared with Stx1+2 (23.7% vs. 12.7%) while Stx1 alone was only exceptionally associated with eHUS (1.1%). The most frequent serogroup found in patients with Stx+BD was the O157 while in patients with eHUS the O26 was the most (36.5% of cases), followed by O157 (20%).

Conclusions: STEC is all but a rare cause of BD in children thus the screening for Stx positive BD is recommended. We also suggest to monitor patients carrying Stx2 closely with urine dipstick for hemoglobinuria every 12 hours for the early detection of eHUS together with providing them with generous fluid infusion.

PO2334
Hemoglobinuria for the Early Identification of STEC-HUS in High-Risk Children
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Background: Shigatoxin-producing Escherichia coli – associated hemolytic uremic syndrome (STEC-HUS) represents one of the main causes of acute kidney injury in children and can be associated with several extrarenal complications. Its management is entirely based on supportive care, which includes generous fluid infusions, since delayed treatment has been described to have a worse outcome, compared to early recognition and overhydrated patients. The present study aims at validating urine dipstick/urinalysis for hemoglobinuria as a early test to screen patients at high risk for the development of STEC-HUS (children with bloody diarrhea secondary to Shigatoxin – Stx – 2 or 1+2) for the early diagnosis of the disease.

Methods: Since 2010, a network 63 pediatric units (the ItaKid-HUS Network) has been developed in Northern Italy, with the aim of the early identification and management of STEC infections and STEC-HUS. Once a patient with bloody diarrhea (BD) is identified as Stx positive, he/she is rehydrated as appropriate and followed up with urine dipstick/urinalysis for hemoglobinuria until HUS develops or diarrhea resolves. We here reviewed all the urine dipstick/urinalysis results from pediatric patients with Stx positivity either with BD only (Group 1) or with ongoing HUS (Group 2) from 2010 to 2019. Results: A total of 100 children were eligible for the study. In Group 1, 22/63 patients had or developed hemoglobinuria while the remaining 41/63 were and remained negative. In 15/22 positive cases, blood tests ruled in a ongoing HUS, while in the remaining 7 the diagnosis was excluded. Among the 41 negative patients no one developed HUS. As expected 37 children in Group 2 (already ongoing HUS) all had hemoglobinuria at admission.

Conclusions: Hemoglobinuria shows a sensitivity of 100% (95% CI 93-100%) and a specificity of 85% (95% CI 74-93%), with positive predictive value of 68% and negative predictive value of 100% in diagnosing ongoing HUS. Thus, urine dipstick or urinalysis for the detection of hemoglobinuria can be proposed as an easy, fast, inexpensive and repeatable test to screen patients at high risk for the development of STEC-HUS and to start supportive treatment as soon as possible.

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 glomerulus, 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 ≥1+. Patients reporting positive urine dipstick were addressed to laboratory investigations to rule in or out, the diagnosis of aHUS relapse.

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 acceptably 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 glomerulus. 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-targeted 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 19 patients (74% of the 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 C3GN patients had higher C5b-9 and lowered 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 C3GN) had a GFR below 60 ml/min/1.73m².

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 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 years vs 12.7 years, p<0.001), episode of gross hematuria (8.0 vs 24.3%, p<0.0007), duration from 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 (94.0 vs 59.2%, p<0.0001), S1 (21.0 vs 37.2%, p<0.0004), T present (28.0 vs 46.1%, p=0.004), C present (72.0 vs 58.1%, p=0.02) and G present (8.0 vs 19.1%, p=0.01), but no difference in that of E1 (52.8 vs 42.2%, p=0.0004), T present (28.0 vs 46.1%, p=0.004). Electron microscopic findings showed significant difference in the frequency of glomerular basement membrane (0.7 vs 0.05%, p<0.0001). Degree of proteinuria is positively correlated with the frequency of M1 and equal or greater severity of S1 (r=0.38, p<0.01). Electron microscopic features of IgAN are similar to those of IgAVN.

Conclusions: IgAVN has higher frequency of M1 lesion regardless of degree of proteinuria, a frequent proteinuria of chronic lesions such as T, S, and G, and a 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.

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

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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 to creatinine ratio mg/mg: UPCR ≥ 0.2), 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. 18/2962 (6%) 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

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 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.

Funding: NIDDK Support, Private Foundation Support

PO2345
Vaccination Status in Pediatric Kidney Transplants: An Integrated Pediatric Transplant Research Database Study
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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 years. 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% (MCV); 72% (MMR).

Post-transplant vaccination series was ≥95% complete for all vaccines except PCV23 (43%); HPV4/9 (37%); MCV (30%).

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 Pediatric Quality of Life (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.
PO2346
Decreased CD28 Expression in Memory CD4+ T Cells in Children Awaiting Kidney Transplant Is Associated with Increased Expression of Senescence Markers

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Background: Despite improved patient and graft outcomes with CD28-CD80/86 costimulation blockade, increased early acute rejection has hindered the widespread use of this strategy (Cytocare) for kidney transplant. Our group has previously reported lower pre-transplant frequencies of CD28+ effector helper T cells (CD4+CD28+CCR7-) with decreased functional capacity in adults that were subsequently free from early rejection on belatacept. 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 (CD38) and cytotoxicity (Perforin, Granzyme B) on memory CD4+ T cells.

Results: None of the children had CD28-CD4+ T cells 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-CD4+ T cells 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+ Fig1C) 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+ T EM cells that have lost CD28 expression and bear markers suggestive of impaired function, a phenotype reminiscent of adults with decreased risk for early rejection on belatacept. The functional capacity of these cell populations in children needs further study.

Funding: NIDDK Support, Clinical Revenue Support

PO2347
Predicting Allograft Survival in Young Pediatric Kidney Transplant Recipients
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Background: Kidney transplantation (kTx) presents specific challenges in young pediatric 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
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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 (ATG) ≤ 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 proved 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. Subcortical/borderline findings were included with or without treatment. Additional DSA testing and/or biopsies were done if there was a clinical concern.

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

PO2349
Pediatric-Specific Models Improve Prediction of Kidney Transplant Survival for Children Under 5 Years Old
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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-B mismatches, were significant predictors for deceased donors (SP-KDPI model) while race, age, HLA-B mismatch and donor/reipient 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.
**PO2352**

**Variability in Surveillance Monitoring and Management of Donor-Specific Antibodies Among Pediatric Transplant Programs Participating in the Improving Renal Outcomes Collaborative (IROC)**

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**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 MFI trend in interpreting DSA results and 10 (34%) centers use C1q complement fixing 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 (58%) to intensification of baseline immunosuppression (65% to 69%). 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 18/29 (61%) use 2 doses with variable frequency. Of centers using CNI+IVIG as monotherapy for treatment of DSA+ AMR, 12/20 (60%) use 1 g/kg/dose and 6/20 (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.

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**PO2353**

**Assessment of Pediatric Nephrology Programs’ Readiness to Participate in Prospective Clinical Trials**

Shyamne Hetley,1 Noel Howard,1 H. William Schnaper,2 William E. Smoyer,3 Katherine M. Dell,4 Coleman Gross,5 Katherine Twombly,6 Tetyana L. Vasylyeva,1 Scott E. Wenderfer,1 7 Texas Tech University Health Sciences Center School of Medicine, Amarillo, TX; 2Northwestern University Feinberg School of Medicine, Chicago, IL; 2Nationwide Children’s Hospital, Columbus, OH; 7Cleveland Clinic, Cleveland, OH, 51Relypsa Inc, Redwood City, CA; 5Medical University of South Carolina, Charleston, SC; 7Baylor College of Medicine, Houston, TX.

**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. As such, it would give consideration to the sites for prospective trials and educate the programs about steps needed in clinical research.

**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 conduction of clinical research. Availability of 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 regards to patients’ and parents’ 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 additive 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

Ovindamola C. Adebayo,1,2 Dieumerci Betukumusu Kabasele,3 Agathe B. Nkoy,1 Pepe M. Ekulu,1 Veerle Labarque,2 Lambertus P. Van den heuvel,1,4 Elena N. Levchenko.1 Laboratory of Pediatric Nephrology, Department of Development and Regeneration, Katholieke Universiteit Leuven, Leuven, Belgium;1 Centre for Molecular and Vascular Biology, Department of Cardiovascular Sciences, Katholieke Universiteit Leuven, Leuven, Belgium;1 Division of Nephrology, Department of Pediatrics, University Hospital of Kinshasa, Faculty of Medicine, University of Kinshasa, Kinshasa, Congo (the Democratic Republic of the);3 Department of Pediatric Nephrology, Radboud University Medical Centre, Nijmegen, Netherlands.

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 hyperfiltration 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.

PO2356

Disparities in Kidney Failure Care for Children: A Global Survey

Rovenwa Lalji,1,2 Anna Francis,1,3 Germaine Wong,1,4 David W. Johnson.1,5 on behalf of the Pediatric GKHIA working group 1The University of Queensland Faculty of Medicine, Herston, QLD, Australia;2 Princess Alexander Hospital, Wooloongabba, QLD, Australia; 3The University of Sydney, Sydney, NSW, Australia; 4Westmead Institute for Medical Research, Westmead, NSW, Australia; 5Queensland Children’s Hospital, South Brisbane, QLD, Australia.

Background: Globally, the capacity to access and deliver kidney replacement therapies (KRT - dialysis and transplantation) to children has never previously been described. The present study reports current disparities in access to kidney care between children and adults worldwide based on the results of the 2018 International Society of Nephrology Global Kidney Health Atlas (GKHA) survey.

Methods: A mixed methods analysis of pediatric-specific data from the 2018 GKHA survey were used. Respondents were from countries categorized as low (LIC), lower-middle (LMIC), upper-middle (UMIC) or high income (HIC) according to 2018 World Bank income classification. Descriptive statistics were used for the population-based analysis of health expenditure across different world bank countries. Open text responses were thematically analyzed using HyperRESEARCH.

Results: Responses were received from 160 (88%) of 182 countries, including LIC (n=26, 16%), LMIC (n=36, 23%), UMIC (n=39, 24%) and HIC (n=59, 37%). Child access to end stage kidney disease care (ESKD) and KRT differed from adults in 29% and 23% of countries, respectively. Lower income countries were associated with graded increases in disparate access to ESKD (LIC 62%, LMIC 38%, UMIC 18%, HIC 19%) and KRT care (LIC 58%, UMIC 33%, UMIC 13%, HIC 9%). Five themes explained access disparities for children: inadequate resources for KRT; kidney failure care is expensive and incurs lifelong costs; priority and access based on a country’s economic status; a lack of child-specific resources; and longer travel distances for children.

Conclusions: There are significant disparities worldwide in care for children with kidney failure when compared with adults, particularly in low resource settings. Future policy and advocacy efforts are needed to promote universal, equitable kidney care for children globally.

Funding: Government Support - Non-U.S.

PO2364


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 regards to patients’ and parents’ 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 additive 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.

Funding: Government Support - Non-U.S.
PO2357
Clinical and Biopsy Characteristics in a Pediatric Cohort of C3 Glomerulonephritis (C3G) and Immune Complex Membranoproliferative Glomerulonephritis (IC-MPGN)
Bradley P. Dixon,2 Amy Goodwin Davies,3 Hanieh Razzaghi,1 Sherin Meloni,1 Melissa E. Thomas,3 Joseph T. Flynn,4 Donna J. Claes,5 Mark Mitsnefes,5 Brian R. Storrier,5 Vikas R. Dhamidharka,1 Caroline A. Gluck,1 Joshua Zaritsky,1 Michael J. Somers,5 Mahmoud Kallash,5 William E. Smoyer,5 Susan L. Furth,5 Christopher B. Forrest,1 Benjamin L. Laskin,5 Michelle Denburg,3 ‘Renal Section, Department of Pediatrics, University of Colorado School of Medicine, Aurora, CO; ‘Children’s Hospital Colorado, Aurora, CO; ‘The Children’s Hospital of Philadelphia, Philadelphia, PA; ‘Seattle Children’s Hospital, Seattle, WA; ‘Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; ‘Washington University in Saint Louis School of Medicine, Saint Louis, MO; ‘Nemours/Alfred I. DuPont Hospital for Children, Wilmington, DE; ‘Boston Children’s Hospital, Boston, MA; ‘ Nationwide 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 prognosticate 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.
Results: Of 285 identified patients, 173 were true cases of C3G or IC-MPGN (p = 0.005). 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 compared to IC-MPGN (p = 0.006) (Table 3).
Conclusions: Patients with C3G and IC-MPGN can be identified and characterized by the use of a computable phenotype, allowing the creation of robust databases to define clinical predictors of treatment response. This may prove to be a vital asset for recruitment into clinical trials of complement-targeted agents likely beneficial to this patient population.
Funding: NIDDK Support, Commercial Support - Mallinckrodt Pharmaceuticals

PO2358
Efficacy and Safety of Ravulizumab in Pediatric Patients with Atypical Hemolytic Uremic Syndrome Sickle to Complement Inhibitor Treatment: 26-Week and 1-Year Data
Gema Arieta,1 Bradley P. Dixon,2 Seong Heon Kim,3 Gaurav Kapur,3 Teri Jo Mauch,1,4 Stephanie Ortiz,1 Marc Vallee,1 Andrew E. Denker,5 Hee Gyung Kang2 Larry A. Greenbaum,3 ‘Hospital Vall d’Hebron, Barcelona, Spain; ‘University of Colorado School of Medicine, Aurora, CO; ‘Pusan National University Children’s Hospital, Seoul, Republic of Korea; ‘Children’s Hospital of Michigan, Detroit, MI; ‘University of Nebraska Medical Center, Omaha, NE; ‘Alexion Pharmaceuticals Inc, Boston, MA; ‘Emory University School of Medicine and Children’s Healthcare of Atlanta, Atlanta, GA; ‘Seoul National University College of Medicine, Seoul, Republic of Korea.
Background: Ravulizumab is a complement C5 inhibitor derived from eculizumab, with an increased half-life extending the maintenance dosing schedule from every 2–3 to every 4–8 weeks. We evaluated the efficacy and safety of ravulizumab to resolve active thrombotic microangiopathy (TMA) in children with atypical hemolytic uremic syndrome (aHUS) naïve to complement inhibitors.
Methods: ALXN1210-aHUS-312 (NCT03131219) is a phase 3, single-arm trial in children with TMA due to aHUS. Patients received ravulizumab every 4–8 weeks, depending on bodyweight. 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 and 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 long-term treatment (Table). Mean (SD) increase in eGFR from baseline was 19.2 (30.1) mL/min per 1.73 m2 at 26 weeks, and 25.4 (41.7) mL/min per 1.73 m2 at 50 weeks. Of 6 patients on dialysis at baseline, 5 (83.3%) discontinued dialysis by week 26, and the last patient by week 50. Complete free C5 inhibition was sustained throughout the trial. No unexpected adverse events, deaths, or meningococcal infections occurred.

Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>N</th>
<th>26</th>
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</thead>
<tbody>
<tr>
<td>C3G</td>
<td>71</td>
<td>173</td>
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<tr>
<td>IC-MPGN</td>
<td>52</td>
<td>92</td>
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</table>

Table 2. Age at diagnosis (years)

<table>
<thead>
<tr>
<th>C3G</th>
<th>IC-MPGN</th>
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<tbody>
<tr>
<td>0-6</td>
<td>40 (28%)</td>
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<tr>
<td>7-10</td>
<td>66 (26%)</td>
</tr>
<tr>
<td>11-14</td>
<td>48 (22%)</td>
</tr>
<tr>
<td>15-20</td>
<td>12 (20%)</td>
</tr>
<tr>
<td>21+</td>
<td>2 (12%)</td>
</tr>
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</table>

Table 3. Biopsy Characteristics

<table>
<thead>
<tr>
<th>C3G</th>
<th>IC-MPGN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complement C3 (g/ml)</td>
<td>42.1 (9.8)</td>
</tr>
<tr>
<td>Kidney transplant</td>
<td>12 (6.9)</td>
</tr>
<tr>
<td>Serum albumin (g/dL)</td>
<td>2.4 (2.0)</td>
</tr>
</tbody>
</table>

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
Conclusions: Ravalizumab 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>Complete TMA response</th>
<th>Partial TMA response</th>
<th>Nonresponse</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMA response</td>
<td>14 (77.8)</td>
<td>7 (38.9)</td>
<td>8 (44.4)</td>
<td>29 (100)</td>
</tr>
<tr>
<td>Partial TMA response</td>
<td>13 (71.4)</td>
<td>7 (38.9)</td>
<td>8 (44.4)</td>
<td>28 (100)</td>
</tr>
<tr>
<td>Nonresponse</td>
<td>2 (10.5)</td>
<td>3 (16.7)</td>
<td>2 (11.1)</td>
<td>7 (100)</td>
</tr>
<tr>
<td>Total</td>
<td>29 (100)</td>
<td>17 (100)</td>
<td>18 (100)</td>
<td>64 (100)</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

Richard A. Zager,1,2 Ali C. Johnson,1 Alvayo F. Guillem,3 Donald J. Keyser,3 Bhupinder Singh,1,4 Fred Hutchinson Cancer Research Center, Seattle, WA; 1University of Washington Department of Medicine, Seattle, WA, US, Department of Medicine, Irvine, CA; 2Renibus Therapeutics, Southlake, TX; 3University of California Irvine, University of California Irvine, Irvine, CA, US, Department of Medicine, Irvine, CA.

Background: Oxidative stress is a hallmark and mediator of CKD. Diminished antioxidant defenses are thought to be partly responsible. However, there is currently no way to prospectively screen for antioxidant enzymes in humans. RBT-6 (n=18) or protoporphyrin IX; SPP) induces mild, transient oxidative stress in animal models, triggering increased expression of select antioxidant proteins (eg, heme oxygenase 1 [HO-1], NADPH [H] dehydrogenase [quinoxine] 1, 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 general responsiveness 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 1.73m²) or stage 4 CKD (n=12; eGFR 15–29 ml/min per 1.73m²) 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 AKI 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 responsiveness/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

Yan Chen,1,2 Leila R. Zelnick,3,4 Andrew N. Hoofnagle,2,4 Catherine K. Yeung,2,5 Laura M. Shireman,1 Calder C. Brauchla,1 Ian H. de Boer,1,5 Jonathan Himmelfarb,1 Bryan R. Kestenbaum,2,3 1University of Washington Department of Epidemiology, Seattle, WA; 2Kidney Research Institute, Seattle, WA; 3University of Washington Department of Medicine, Seattle, WA; 4University of Washington Department of Laboratory Medicine, Seattle, WA; 5University of Washington Department of Pharmacy, Seattle, WA.

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 secretory solutes in sequential timed plasma samples and timed urine collections. We compared iohexol GFR (iGFR) with the kidney clearances of secretory solutes in sequential timed plasma samples and timed urine collections.

Results: Kidney 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. 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.

Conclusions: Mice on adenoine 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 Kim-1, an early tubular injury marker, 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 adenoine 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 secretion. This suggests a component of oat1 inhibition and/or involvement of other transporters.

Funding: Commercial Support - AstraZeneca

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
The Influence of Vitamin D Status and CKD on the CYP3A Metabolism Substrate Midazolam

Stacey M. Tuyet,1 Linda Prebheela,2 Michael F. Wenpe,1 Michel Choncol,2 Nirav A. Shah,3 Thomas D. Nolin,3,4 Melanie S. Joy,1,2 University of Colorado, Skaggs School of Pharmacy and Pharmaceutical Sciences, Aurora, CO; 2University of Colorado, Division of Renal Diseases and Hypertension, Aurora, CO; 3University of Pittsburgh, Department of Pharmacy & Therapeutics, Pittsburgh, PA; 4University of Pittsburgh, Department of Medicine Renal Electrolyte Division, Pittsburgh, PA.

Background: Patients with chronic kidney disease (CKD) have a high prevalence of vitamin D (ViD) 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 ViD in CKD. This study sought to investigate the role of ViD status (deficient vs. replete state) 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 ViD deficiency (25(OH)D < 30ng/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 D3, 5000 IU daily for up to 14 weeks to repletion (25(OH)D > 30ng/mL) and were again given one dose of oral D3, 5000 IU and MDZ 2 mg. Blood was serially collected for up to 48 hours 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 parameter estimates (N=25) were: central volume of distribution (Vc/F) 95 L (26.8%), clearance (CL/F) 31.1 L/h (25.0%), peripheral volume of distribution (Vp/F) 213 L (39.5%), inter-compartmental clearance (Q/F) 36.5 L/h (24.3%), and absorption rate constant (k) 16.4 h^-1 (42%). Individual subject PK parameter estimates were determined from the 2-compartment PK model (Table).

Conclusions: ViD 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 to induce. Regardless of phase, which may be due to decreased renal elimination or reduced ability to induce CYP3A secondary to renal impairment. Future analyses will explore the ability to induce P450 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.

Funding: Other NIH Support - NIGMS

PO2363

Effect of Kidney Disease and Vitamin D Repletion on Drug Transporter Activity

Morgan A. Casal,1 Linda Prebheela, Raymond E. West,1 Nirav A. Shah,2 Michel Choncol,3 Melanie S. Joy,1,2 Thomas D. Nolin,1,2 University of Pittsburgh School of Pharmacy, Pittsburgh, PA; 2University of Colorado School of Medicine, Aurora, CO; 3University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences, Aurora, CO.

Background: CKD patients exhibit altered nonrenal drug clearance, which is reflected in numerous drug metabolism and transport pathways. Vitamin D (ViD) deficiency is common in CKD, and ViD-mediated regulation has been implicated in decreased renal and nonrenal transporters. This study aimed to elucidate the impact of ViD status (deficiency vs repletion) on drug transporter activity in CKD patients and healthy controls (HC).

Methods: ViD deficient (25(OH)D < 30 ng/mL) subjects with CKD stage I-III (n=15), CKD stage IV-V (n=8) and HC (n=9) were enrolled. The phenotypic probe drugs fexofenadine (FEX) and olmesartan (OLM) were used to assess P-glycoprotein (P-gp), organic anion transporter (OAT) and organic anion-transporting polypeptide (OATP) function, and endogenous N-methylhistamine (NMH) was used to assess multidrug and toxin extrusion proteins 1 and 2K (MATE1/2K) activity. FEX 60 mg and OLM 10 mg were orally administered at baseline (ViD deficiency) and after 12 weeks of oral therapy with ViD. 5000 IU daily and confirmed repletion (25(OH)D < 30 ng/mL). Serial blood and urine samples were collected for 48 hours. FEX, OLM, and NMH concentrations in plasma and urine were determined by LC/MS/MS and noncompartmental pharmacokinetic (PK) parameters were calculated.

Results: CKD IV-V subjects had 77% higher FEX systemic exposure (AUC 0-last of Gr3 1.22 and 1.90 folds, D 1.65 and 4.43 folds, P 0.99 and 1.57 folds, R 1.43 and 1.83 folds, M 2.19 and 2.68 folds, D 1.65 and 4.43 folds, P 0.99 and 1.57 folds, R 1.43 and 1.83 folds, and A 2.28 and 4.22 folds). AUC 0-last of Gr3 exhibited a doubling of AUC 0-12 (1.12 and 1.59 folds, P 1.22 and 1.90 folds, R 1.12 and 1.59 folds, and A 2.28 and 4.22 folds). AUC 0-12 of Gr3 was significantly increased when compared to Gr2 in D, P and A (2.69 (p<0.001), 1.59 (p<0.001) and 1.92 (p<0.001) folds, respectively). Cmax were significantly increased only in P and A (1.70 (p<0.001) and 1.94 (p<0.001) folds, respectively).

Conclusions: Independent of ageing, CKD itself further reduces the activity of drug transporters, suggesting that this information has to be taken into account when drugs that pass through these transporters are prescribed to CKD patients.

Funding: Government Support - Non-U.S.
**PO2366**

A Single Time Point Plasma Concentration of Mycophenolic Acid Predicts Enteric-Coated Mycophenolate Sodium Exposure in Thai Renal Transplant Recipients

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**Background:** Enteric-coated mycophenolate sodium (EC-MPS) is a salt form of mycophenolate widely used in renal transplantation. The area under the concentration-time curve (AUC) of an active form of EC-MPS, mycophenolic acid (MPA) of ≥30 μg/mL is highly associated with drug efficacy. However, this technique is impractical in clinical setting. Little is known regarding metabolites’ AUC. This study determined the relationships of a single time point of plasma MPA level and time to optimum MPA exposure. The full profile of active (7-O-MPA-glucuronide; MPAG) and inactive (acyl mycophenolic acid glucuronide; AcMPAG) metabolites, both free and total form are also measured and related to its AUC.

**Methods:** Twenty renal transplant recipients with EC-MPS were studied. On day 3 post transplantation, plasma samples were collected at 0, 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 6, 8, 10, and 12 hours post dose. Total and free form levels of MPA and metabolites were measured using a fully validated LC-MS/MS. Receiver operating curve (ROC) was calculated for each metabolite.

**Results:** The AUC of the MPA total form moderately correlated with a single time point plasma MPA concentration at Cmax (r2 = 0.50) with the concentration cut of 2.5 μg/mL (sensitivity 87%, specificity 80%, area ROC = 0.83). The AUC of the MPA free form poorly correlated with a single time point concentration. The AUCs of total and free forms of MPAG and AcMPAG highly correlated with a single time point concentration of C8 (r2 = 0.97) and C9 (r2 = 0.95) for MPAG and C8 (r2 = 0.59) and C9 (r2 = 0.81) for AcMPAG. High variability in metabolites concentrations were observed, suggesting inter-individual variability in drug metabolizing enzyme activity.

**Conclusions:** At the early stage post transplantation, in renal transplant recipients who received EC-MPS, a single time point of the total form plasma MPA concentration is best monitored at 4 hours post dose. The MPA level of ≥2.5 μg/mL at that time point predicts optimum AUC. Further studies required for the use of metabolites’ AUCs to assess drug efficacy and to evaluate a single time point concentration that predicts drug exposure.

**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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**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. The area under the concentration-time curve (AUC) of an active form of EC-MPS, mycophenolic acid (MPA) of ≥30 to 60 μg/mL, 34.3% of RTR achieved this range with 56.7% above this therapeutic exposure. There were 52.2% of RTR within the therapeutic tacrolimus AUC-12hr target of 120-200 ng.hr/ml with 46.1% below this range with no age relationship. Reduced tacrolimus CL/BMI was noted in elderly compared to middle age.

**Conclusions:** Tacrolimus and mycophenolic acid pharmacokinetics demonstrates age-related differences with lower clearances or exposures in the elderly. Tacrolimus and mycophenolic acid immunosuppression may require age-adjusted individualization to achieve therapeutic exposure.

**Funding:** NIDDK Support, Commercial Support - Novartis Pharmaceuticals, Astellas Scientific and Medical Affairs, Inc

**Tacrolimus and Mycophenolic Acid Pharmacokinetics by Age**

- Significant
- Trend toward significant

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**PO2368**

Pharmacokinetic Evaluation of Drug Interactions Between Vadadustat and HM-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 hyposulinemic-factor (HIF) 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 rosvastatin (20 mg; n=34), pravastatin (40 mg; n=34), simvastatin (40 mg; n=34), or statin-free (n=34). Changes in lipids were calculated from the PK parameters area under the curve (AUC) and maximum concentration (Cmax).

**Results:** Vadadustat was generally well tolerated by healthy subjects when taken alone or with statins. Exposure (AUC and Cmax) to rosuvastatin, a BCRP and OATP1B1 substrate, increased 2- to 3-fold in the presence of vadadustat. No change in exposure to pravastatin (an OATP1B1 substrate) was observed. The AUC for atorvastatin (a BCRP and OATP1B1 substrate) increased 1.4-fold, although no change in Cmax was noted; for simvastatin (a BCRP and OATP1B1 substrate), the AUC increased 2-fold and Cmax increased 1.6-fold in the presence of vadadustat.

**Conclusions:** There were no clinically significant interactions with pravastatin 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: Akebia Therapeutics, Inc.

**Funding:** Commercial Support - Akebia Therapeutics

**PO2369**

Impact of Renal Impairment and Dialysis on the Pharmacokinetics and Pharmacodynamics of Roxadustat

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**Background:** Roxadustat is an orally active hypoxia-inducible factor prolyl hydroxylase inhibitor for the treatment of CKD anemia. The objective was to evaluate the pharmacokinetics (PK), metabolic profile, pharmacodynamics, and safety of roxadustat in patients (pts) with varying degrees of renal function (RF).

**Methods:** In this phase 1, open-label study (EudraCT: 2015-002565-28), 16 pts were enrolled in one of four RF groups: normal (NRF; eGFR >90 mL/min/1.73 m2), mild (eGFR 60-89 mL/min/1.73 m2); moderate (eGFR 30-59 mL/min/1.73 m2) and severe (eGFR 15-29 mL/min/1.73 m2) RF. Following a 2-week run-in period with roxadustat, a single dose of 100-mg oral roxadustat on Day 1. Two treatment periods (P1/P2), separated by a washout period, were used for HD/HDF treatment periods (P1/P2), separated by a washout period, were used for HD/HDF

**Results:** AUC and Cmax increased 3.5- to 4.3-fold across RF groups (P1/P2), separated by a washout period, were used for HD/HDF
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 panthetinase Vanin-1 is highly expressed in tubular cells and is regarded as a key player in producing oxidative stress by inhibiting the replenishment of cellular anti-oxidative glutathione stores. The aim of this study was to elucidate whether pharmacological inhibition of Vanin-1 protects mice from acute or chronic kidney injury.

Methods: C57Bl6 mice undergoing ischemia reperfusion injury and Col4α3−/− (Alport syndrome) mice were treated orally for 1d and 3wk, respectively, with a potent and selective Vanin-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, Vanin-1 activity, oxidative stress level and tubular apoptosis were monitored.

Results: Oxidative stress levels were elevated in all models. Treatment with the Vanin-1 inhibitor resulted in ample systemic compound exposure and full inhibition of Vanin-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 in Vanin-1 inhibited mice.

Conclusions: Pharmacological inhibition of Vanin-1 is insufficient to protect kidneys from oxidative stress insults contributing to acute and chronic kidney injury. The biological relevance of pharmacological Vanin-1 inhibition for the treatment of kidney diseases remains to be proven.

Funding: Commercial Support - Bayer AG

PO2373
Evaluation of Veverimer Drug Interaction Potential for pH-Dependent Drugs
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Background: Veverimer, an orally administered, non-absorbed polymer that selectively binds and removes hydrochloric acid (HCl) from the gastrointestinal tract, is negative charge, with small size as a secondary determinant. Veverimer did not bind to any of the anionic probes and a panel of 16 drugs were used to define characteristics required for binding. Test drugs covered a broad range of size, charge, solubility and permeability characteristics across 14 drug classes. The magnitude and duration of veverimer’s effect on gastric pH was determined in fed and fasting healthy subjects via 24-h monitoring with an intragastric pH probe. Results from binding and gastric pH studies informed selection of drugs for human DDI studies.

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 zwitterionic drugs. Negatively charged drugs with pH-dependent solubility (warfarin, dabigatran) were limited to effects on absorption of other oral drugs via (1) direct binding (2) increases in gastric pH resulting from HCl binding.

Methods: Features important for binding to veverimer were determined in vitro. A set of anionic probes and a panel of 16 drugs were used to define characteristics required for binding. Test drugs covered a broad range of size, charge, solubility and permeability characteristics across 14 drug classes. The magnitude and duration of veverimer’s effect on gastric pH was determined in fed and fasting healthy subjects via 24-h monitoring with an intragastric pH probe. Results from binding and gastric pH studies informed selection of drugs for human DDI studies.

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 decreases the overall systemic acid-base neutrality.

Methods: Pharmacological inhibition of Vanin 1 is not protective in models of acute and chronic kidney disease. The panthetinase Vanin-1 is highly expressed in tubular cells and is regarded as a key player in producing oxidative stress by inhibiting the replenishment of cellular anti-oxidative glutathione stores. The aim of this study was to elucidate whether pharmacological inhibition of Vanin-1 protects mice from acute or chronic kidney injury.

Results: Oxidative stress levels were elevated in all models. Treatment with the Vanin-1 inhibitor resulted in ample systemic compound exposure and full inhibition of Vanin-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 in Vanin-1 inhibited mice.

Conclusions: Pharmacological inhibition of Vanin-1 is insufficient to protect kidneys from oxidative stress insults contributing to acute and chronic kidney injury. The biological relevance of pharmacological Vanin-1 inhibition for the treatment of kidney diseases remains to be proven.

Funding: Commercial Support - Bayer AG

PO2371
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, 9 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 46% 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 at least one actionable CKD risk variant. 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 genotype. 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

KBP-5074, a Nonsteroidal Mineralocorticoid Receptor Antagonist, Reduces Urinary Albumin-to-Creatinine Ratio and the Risk of Hyperkalemia in a Rat 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 uninephrectomized 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 Na+/K+ ratio and serum K+ were assessed following 14 and 27 days of treatment. Blood samples were collected on days 1 and 26 to determine 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%, 96%, and 99% respectively on day 14, and 59%, 86% and 99% 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, resulting in a therapeutic index (TI) against hyperkalemia of 24.24 for KBP-5074 vs 0.62 for eplerenone. Thus, the TI against hyperkalemia of KBP-5074 is 39-fold superior to eplerenone suggesting that the non-steroidal MRA, 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 USA Inc.

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Underline represents presenting author.

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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 single oral 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).

**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 heparinase. 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 H2 assays. The ESRD cohort was stratified into heparinized and heparin naïve groups.**

**Results:** ESRD group showed decrease in peak thrombin (107.1 ± 163.5 M) and AUC (589.8 ± 815.7 nM*min) with increase in lag time (2.9 ± 2.2 min) compared to NHP. Heparinase supplementation increase 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 ± 31.1 sec), anti Xa (0.21 ± 0.14 U/mL) and anti-IIa (0.27 ± 0.15 U/mL) decreased with heparinase 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 heparinase 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 possess 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 methicillin-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 CRCL 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 a decrease in creatinine elevation in conditions 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 anaphylactic injury. Clinicians are developing strategies to circumvent these problems. One strategy is the use of antibiotic slurry/paste applied to infected tissue. This has
traditionally not been associated with systemic vancomycin toxicity. We report here an incidence of vancomycin nephrotoxicity secondary to a sternal venacavum 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. The infecting agent was a vancomycin-resistant enterococcus and a trans-thoracic echo revealed a circumferential fluid collection around the aortic arch. He underwent a “redo” sternotomy, exploration and drainage. Plasma creatinine concentration (P_c) 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_c and vancomycin troughs are detailed in the figure. On POD2 serum vancomycin trough was 42 mg/L. Intravenous vancomycin was undetectable and P_c was 6.45mg/dL.

He was emergently dialyzed. After 5 rounds of dialysis, serum vancomycin concentration lowered to 8 mg/L and P_c to 2.77 mg/dL. Urine output improved to 1200 mL/day. He was discharged on POD14 on daptomycin and ceftriaxone. On POD21 at follow-up, serum vancomycin was undetectable and P_c was 1.08 mg/dL.

**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**

**Case Description:** We report a case of a 53-year old 50kg woman admitted for surgery for a 5 cm left carotid endarterectomy. Her medical history included ESRD, DM, HTN, atrial fibrillation, and peripheral vascular disease. She was hemodialysis dependent and was on IHD 3 times weekly. Her baseline renal function was GFR 15 mL/min. She was recently diagnosed with a transesophageal echocardiogram showing a 1.5 cm thick atrial myxoma,amenable to surgical resection. She had a history of chronic kidney disease stage 5 and 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 proctor 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. The first case was a 48-year-old female with a history of ESRD (HD X 3 times/week), HCV, DM, HTN and spinabps accessed 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 (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 non-healing heel ulcer. 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 arousal and GCS of 12/15, intact strength & sensation of both extremities, no ataxia, dysarthria, hemineglect or signs of proctor 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. **Conclusion:** Gabapentin toxicity is one of a number of first-line medications for the treatment of pain. It has multiple well-known side effects but less recognized is edema. We describe a case of Gabapentin induced edema, which was misdiagnosed as CHF exacerbation, resulting in significant diuretic use and stage 3 AKI.

**PO2381**

**Gabapentin Toxicity in Existing and Developing Renal Failure**

**Case Description:** 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. **Conclusion:** Here we report two cases of potential Gabapentin toxicity across the spectrum of renal insufficiency. The first case was a 48-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 Levetiracetam. 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 non-healing heel ulcer. 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 arousal and GCS of 12/15, intact strength & sensation of both extremities, no ataxia, dysarthria, hemineglect or signs of proctor 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. **Conclusion:** 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 underrecognized. In this case report, a 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.

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

Underline represents presenting author.

723
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 218 lbs and 2.7 mg/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
Gomerular Changes in Transplant Glomerulopathy
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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 μm sections were imaged. While for Airyscan, 1-3 microns, formalin fixed paraffin embedded (FFPE) sections were used. Samples were labeled with antibodies for Laminin α5, Integrin α8, Myosin IIA, Vimentin, Synaptopodin, Integrin β1, Fibronectin, and several collagen IV chains.

Results: STORM TG samples showed increased distance between Integrin β1 labeled membranes, indicating thickening of the GBM. Collagen α1α1α2(IV) did not change, while Collagen α1α2(IV) 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 αII-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 α1α2(IV) secreted from the endothelial side, while Collagen α1α2(IV) was unchanged at the GBM's endothelial aspect. 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 landmarks.

PO2385
Calcineurin Inhibitor Cyclosporine A but Not Tacrolimus Induces Proapoptotic Endoplasmic Reticulum Stress in Kidney Epithelial Cells
Duygu E. Yilmaz,1 Karin M. Kirschner,1 Hasan Demirci,1 Sebastian Bachmann,1 Kerim Mutig,2 1Charite Universitatsmedizin Berlin, Berlin, Germany; 1LM. Sechenov First Moscow State Medical University (Sechenov University), Moscow, Russian Federation.

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 landmarks.

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 spliced XBP1 (sXBP1) products. In contrast, Tac enhanced ER stress-induced, 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.

Conclusions: In summary, 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.

Funding: Government Support - Non-U.S.
Methods: Kidneys from MyD88 knock-out (KO) or MyD88 and Trif double knock-out (DKO) mice were harvested and stored in a cold preservation solution (UW) for 4 hours, and then transplanted into bi-nephrectomized syngeneic or allogeneic recipients. Graft survival, renal function, histology change, phenotype analysis, and expression of involved genes, were observed and/or determined. Primary RTECs isolated from B6 and BALB/c mouse kidneys were stimulated by lipopolysaccharide (LPS) and cytokines in supernatant were collected.

Results: C57BL/6 (B6) kidneys were more susceptible to IR injury following syngeneic transplant compared to BALB/c kidneys. Genetic ablation of MyD88 in B6 donors, but not BALB/c donors significantly reduced creatinine levels at post operation day (POD) 1-2, compared with wild-type (WT) kidneys. Moreover, compared with recipients of WT kidneys at POD 1-2, recipients of MyD88/Trif DKO kidney allografts showed improved graft function that was consistent with improved tissue integrity. Strikingly, MyD88/Trif DKO donor induced indefinite renal allograft survival and preserved intact renal allograft architecture at POD 100. In vitro study showed that levels of cytokines were increased by both B6 and BALB/c RTECs upon LPS (TLR4 agonist) stimulation, but BALB/c RTECs produced significantly higher levels of cytokines (including TNFα, IL-6, and IL-10) in a dose-dependent manner. Expression of Ki-1, a known biomarker for renal allograft rejection, were significantly increased by B6 RTECs co-cultured with that in BALB/c RTECs. These results suggest that kidney-intrinsic innate immunity, especially the TLR/MyD88 pathway, plays a critical role in the susceptibility to transplant IRI and DGF.

Conclusions: Kidney-intrinsic TLR/MyD88 signaling regulates the susceptibility of delayed graft function following kidney transplantation.

Funding: NIDDK Support

PO2389

Immunohistochemical and Molecular Characterization of Immune Cells in Pediatric Renal Allografts: Mononuclear Phagocytes Correlate with Rejection, Re-Transplantation, Graft Function, and Fibrosis

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Methods: Kidneys from MyD88 knock-out (KO) or MyD88 and Trif double knock-out (DKO) mice were harvested and stored in a cold preservation solution (UW) for 4 hours, and then transplanted into bi-nephrectomized syngeneic or allogeneic recipients. Graft survival, renal function, histology change, phenotype analysis, and expression of involved genes, were observed and/or determined. Primary RTECs isolated from B6 and BALB/c mouse kidneys were stimulated by lipopolysaccharide (LPS) and cytokines in supernatant were collected.

Results: C57BL/6 (B6) kidneys were more susceptible to IR injury following syngeneic transplant compared to BALB/c kidneys. Genetic ablation of MyD88 in B6 donors, but not BALB/c donors significantly reduced creatinine levels at post operation day (POD) 1-2, compared with wild-type (WT) kidneys. Moreover, compared with recipients of WT kidneys at POD 1-2, recipients of MyD88/Trif DKO kidney allografts showed improved graft function that was consistent with improved tissue integrity. Strikingly, MyD88/Trif DKO donor induced indefinite renal allograft survival and preserved intact renal allograft architecture at POD 100. In vitro study showed that levels of cytokines were increased by both B6 and BALB/c RTECs upon LPS (TLR4 agonist) stimulation, but BALB/c RTECs produced significantly higher levels of cytokines (including TNFα, IL-6, and IL-10) in a dose-dependent manner. Expression of Ki-1, a known biomarker for renal allograft rejection, were significantly increased by B6 RTECs co-cultured with that in BALB/c RTECs. These results suggest that kidney-intrinsic innate immunity, especially the TLR/MyD88 pathway, plays a critical role in the susceptibility to transplant IRI and DGF.

Conclusions: Kidney-intrinsic TLR/MyD88 signaling regulates the susceptibility of delayed graft function following kidney transplantation.

Funding: NIDDK Support

PO2387

Immunosuppression by Cyclosporine A Affects Proximal Tubular Homeostasis via Endoplasmic Reticulum Stress

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Results: Rats with CsA displayed a stimulated RAS and increased distal NaCl transporter activity along with decreased urine volume, GFR, FE, and COX-2 expression. Pathological changes in vasculature and glomeruli were inconspicuous, whereas early proximal tubular segments (S1, S2) revealed large lysosomal vacuoles with granular content, their abundance correlating with epithelial dedifferentiation, basement membrane thickening, and subepithelial collagen I accumulation. Protein endocytosis was diminished. Changes in UPR included enhanced pERF2α, pPERK, CHOP, and Bip levels. Parallel studies in cultured cells indicated sensitivity to chemical chaperones ameliorating proteostasis.

Conclusions: These results suggest a so far unrecognized role of proximal tubular homeostasis in long term CsA-induced nephropathy. Addressing UPR failure and restitution of proteostasis in proximal tubule may, therefore, have renoprotective potential.

Funding: Government Support - Non-U.S.
Fibroblast culture from CABMR patients were cultured to purity and to mimic this condition fibroblasts were pre stimulated with IL-6 (20ng/ml), IL-17 (50ng/ml), IL-6 plus IL-17 for 24 hrs and culture supernatent were collected for IL-6 ELISA to see synergistic activation. Serum IL-6 levels of CABMR and Non-CABMR patients were measured by ELISA. mRNA expression of pro-fibrotic genes; COL1A1, FN1, ASMA1, and anti-fibrotic gene; MMP2/TIMP was analyzed by real-time PCR. Student’s t-test was used for statistical analysis in SPSS 17 software.

**Results:** IL-6 in sera of CABMR patients was significantly higher (p<0.001) than non-rejection patients. In comparison to IL-6 and IL-17 alone these cytokines synergistically induced IL-6 production from renal fibroblasts(Fig 1). Together IL-6+IL-17 significantly increased the expression of COL1A1, ASMA1, Fibronectin and CCL2(MCP1) and reduced expression of MMP2 gene against GAPDH gene compared to alone IL-6, IL-17 and untreated fibroblasts.

**Conclusions:** CBMR is perpetuated by inflammation amplifier or synergistic induction of IL-6 and IL-17 which results in chronic inflammation and Allograft rejection. Anti-IL-6 may attenuate the CABMR related injury.

**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 (KT), 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. 83% of the patients were males and mean eGFR was 49±17 ml/min. B cells absolute counts were lower in latter phases post-transplant (R -0.4, 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 1.11 respectively, p>0.05) whereas the percentages of them were positively correlated with time post-transplant (R 0.40 and 0.56 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 cell subsets reveals that this reduction is due to an absolute decrease in naive B cells counts. Mature 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.

**Results:** 44 patients had side by side dd cf-DNA done using AS and Prospera for cause. There were 5 patients with either ACR 1a or 1b or AMR on biopsy. 6 patients had no rejection on biopsy. Please see image for statistical analysis.

**Conclusions:** There was no statistical difference between dd-cfDNA as measured by both commercial tests in all 44 patients, including 5 with ACR or AMR and 6 without rejection by biopsy. We acknowledge the number of patients who underwent biopsies were small. Prospera demonstrated larger measurements of dd-cfDNA in comparison to AS, but this was not statistically significant p>0.27. Side by side analysis showed AS had marginally better AUC but no significant differences between diagnostic test characteristics observed. AS had better specificity, PPV, and NPV, but this did not reach statistical significance.
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 (due 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 ccfDNA 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 ccfDNA level increased significantly for 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 ddcfDNA 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 ccfDNA with response to rejection therapy. We propose that the combination of tissue gene expression using the molecular microscope and blood-based ddcfDNA may add precision to traditional histology and could change future practice and treatment paradigms

PO2396
Elevated Donor-Derived Cell-Free DNA (dd-cfDNA) Attributed to Anti-Class II Type I Receptor Antibodies (ATIR-Ab) in Renal Re-Transplantation
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Introduction: Complications of renal transplants include graft rejection and failure. Noninvasive ddcfDNA 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 (DSAs) to human leukocyte antigens (HLA), non-HLA antibodies may also impact allograft outcomes. This series of re-transplantation patients with graft injury from ATIR-Ab (<10 U/mL) shows improvement in ddcfDNA levels with initiation of an ARB, 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. Antibody assessment showed negative DSA but positive ATIR-Ab at 16 U/mL. Post-transplant allograft function was excellent with nadir creatinine of 0.8 mg/dL. Non-invasive allograft surveillance was initiated with initial ddcfDNA (ALLOSURE, CareDx, Brisbane, CA) elevated at 1.8%. Antibody assessment was negative for DSA but positive for ATIR-Ab at 28 U/mL. Losartan was initiated with a sustained decrease in ddcfDNA 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 surveillance showed an acute rise in ddcfDNA 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 ATIR at 16 U/mL. Following Losartan initiation, ddcfDNA decreased to <1%, with continued excellent graft function.

Discussion: ATIR-Ab may be more prevalent in the re-transplant population and is a causative factor for accelerated allograft injury, chronic fibrosis, and graft loss. Early detection of kidney injury via ddcfDNA, prompt assessment of ATIR-Ab, and initiation of ARB therapy may lead to preserved allograft function, particularly in high immunologic risk patients.
Clinical Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (for each 1 y)</td>
<td>0.98 (0.96-1.01)</td>
<td>0.92 (0.95-1.02)</td>
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<td>Gender (female vs. male)</td>
<td>1.19 (0.87-1.64)</td>
<td>0.81 (0.58-1.14)</td>
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<tr>
<td>Ethnicity (other vs. Caucasian)</td>
<td>1.07 (0.66-1.74)</td>
<td>0.79 (0.48-1.34)</td>
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<td>Type of transplant (cadaveric vs. living)</td>
<td>0.66 (0.29-1.51)</td>
<td>0.33 (0.19-0.57)</td>
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<td>Time from Tx to dd-cfDNA (for each 1 year)</td>
<td>0.81 (0.57-1.11)</td>
<td>0.67 (0.43-1.01)</td>
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<tr>
<td>Serum creatinine (for each 1 mg/dl)</td>
<td>0.42 (0.27-0.64)</td>
<td>0.27 (0.20-0.35)</td>
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<td>Usual body weight/comet ratio (for each 1 g)</td>
<td>1.13 (0.96-1.32)</td>
<td>0.79 (0.64-1.00)</td>
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<td>Calculated Panel Reactive Antibody (PRAT, &lt;20%)</td>
<td>0.84 (0.62-1.17)</td>
<td>0.77 (0.61-0.97)</td>
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<tr>
<td>DSA category (vs. negative DSA)</td>
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<td>-</td>
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<tr>
<td>DSA MFI &lt;2500</td>
<td>1.81 (1.05-3.13)</td>
<td>1.17 (0.67-2.06)</td>
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<td>DSA MFI =2500-3000</td>
<td>8.16 (3.25-24.19)</td>
<td>0.47 (0.11-1.96)</td>
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<td>DSA MFI &gt;3000</td>
<td>11.80 (4.11-33.88)</td>
<td>&lt;0.001</td>
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<td>Induction ii (ITG vs. Basilime)</td>
<td>1.13 (0.53-2.38)</td>
<td>0.66 (0.37-1.17)</td>
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<tr>
<td>FK level (for each 1 ng/ml)</td>
<td>0.99 (0.87-1.12)</td>
<td>0.87 (0.77-0.99)</td>
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<td>Micophenolate dose (for each 1 mg)</td>
<td>1.00 (0.99-1.01)</td>
<td>0.39 (0.35-0.43)</td>
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PO2398

Case Series: Systemic Infection Alters Background Cell-Free DNA and Influences Rejection

Donor-derived cell-free DNA level by presence and titer of DSAs

<table>
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<tr>
<th>Variable</th>
<th>Multivariate analysis*</th>
<th>Multivariate analysis*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recipient age (for each 1 y)</td>
<td>0.90 (0.85-0.95)</td>
<td>1.00 (0.91-1.10)</td>
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<td>Type of transplant (cadaveric vs. living)</td>
<td>0.87 (0.55-1.37)</td>
<td>0.63 (0.39-1.02)</td>
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<td>Time from Tx to dd-cfDNA (for each 1 year)</td>
<td>1.75 (0.58-2.95)</td>
<td>0.84 (0.27-2.69)</td>
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<tr>
<td>Serum creatinine (for each 1 mg/dl)</td>
<td>0.94 (0.84-1.05)</td>
<td>0.94 (0.83-1.07)</td>
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<tr>
<td>DSA MFI &gt;3000</td>
<td>0.14 (0.03-0.65)</td>
<td>0.33 (0.07-1.52)</td>
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<td>FK level (for each 1 mg/ml)</td>
<td>0.72 (0.50-1.04)</td>
<td>0.60 (0.39-0.95)</td>
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PO2399

Donor-Derived Cell-Free DNA Identifies Patients with Antibody-Mediated Rejection and Strongly Correlates Histologically with Microvascular Inflammation


Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
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 follows: <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>
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<th>BMI (kg/m²) category</th>
<th>&lt;25</th>
<th>25-29.9</th>
<th>≥30</th>
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</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>19</td>
<td>29</td>
<td>21</td>
</tr>
<tr>
<td>Number of dd-cfDNA tests</td>
<td>60</td>
<td>98</td>
<td>61</td>
</tr>
<tr>
<td>dd-cfDNA % (mean ± SD)</td>
<td>0.63 ± 0.63</td>
<td>0.41 ± 0.27</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
Pichpouch Naisaisorarakorn, Het Patel, Martha Pavlakis, Amitul Aala, Nikiil 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 protocol (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 allograft recipients transplanted between July 2018- April 2020. Data collection was done at measurement of dd-cfDNA surveillance and included: dd-cfDNA (positive if ≥1% dd-cfDNA), elevated Cr (≥0.3 mg/dL from baseline), proteinuria (≥0.3 mg/dL from baseline), DSA (if available).

Results: 366 screening dd-cfDNA test results were reviewed from 84 patients. There were 123/366 positive dd-cfDNA tests in 8/84 patients. 5 of the 8 patients underwent a kidney biopsy which showed: 4 rejections (2 humoral, 2 cellular) (for 1 patient who had cellular rejection, dd-cfDNA test was the only surveillance test that was positive) and 1 ATN (dd-cfDNA test was borderline positive at 1.0%). The 3 remaining patients did not undergo a biopsy and repeat dd-cfDNA testing improved without intervention. In the 353/366 negative dd-cfDNA tests in 76 patients: 8 patients underwent a biopsy: 2 patients who had increased Cr showed borderline acute cellular rejection, 3 had recurrent disease (MPGN, DM, IgAN) and 3 showed ATN/Vascular disease/IFTA. In the 2 patients with borderline acute cellular rejection dd-cfDNA was <0.7%.

Conclusions: We found that the addition of surveillance dd-cfDNA testing to current surveillance testing algorithm was able to identify rejection in 1 patient, when others surveillance tests were negative. A negative result may obviate the need for biopsy, including protocol biopsies in centers who perform them.

Funding: Commercial Support - CareDx

PO2402
Successful Transplantation Outcomes Using Deceased Donors with AKI
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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 AKIN 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: 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 1.09, 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 dysfunction 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

PO2403
Combined Impact of Presensitization and Delayed Graft Function on Allograft Outcome in Deceased Donor Kidney Transplantation: Nationwide Cohort Study
Byung ha Chung,1 Haubi Lee,1 Yohan Park,1 Tae Hyun Ban,2 Sang Heon Song,2 Jaeceok Yang,1 Curie Ahn,1 Chul Woo Yang.1 Korean Organ Transplantation Registry Study group; 1Seoul Saint Mary’s Hospital, Seocho-gu, Seoul, Republic of Korea; 2Eunpyeong St. Mary’s Hospital, Seoul, Republic of Korea; 3Pusan National University Hospital, Busan, Republic of Korea; 4Seoul National University College of Medicine Department of Internal Medicine, Seoul, Republic of Korea.

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-reperfusion injury. We undertook analysis to determine combined association of pre-sensitization 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.

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Methods: In our prospective cohort study, between May 2014 and June 2019, 137 patients with deceased donor kidney transplants 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 were 137 (10.0%) patients and others (n=1233, 90.0%) were assigned to non-pre-sensitized group. Pre-sensitization-non-DGF subgroup was 21 (15.3%) and pre-sensitization-non-DGF group was 116 (84.7%). 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 to HLA.

PO2404
The Clinical Significance of Preformed C1q-Binding Donor-Specific HLA Antibodies in Kidney Transplantation
Sun Lee,1 Byung Ha Chung,2 Chul Woo Yang,2 Seoul National University Hospital, Jongno-gu, Seoul, Republic of Korea; 2Catholic 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 terms of 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 9.333). 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 significant difference 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 Kidney
Pablo Magrini,1 Sergio Hernandez-Estrada,1 Odette Del Carmen Diaz Avendano,1 Christian P. Flores,2 Benjamin Gomez-Navarro,3 Maria Guadalupe R. Ramirez,1 Jose H. Cano,1 Maria Concepcion Oseguera-Vizcaino,1 Daniel F. Ovando-Morga,1 Mayra M. Matias Carmona,1 Renal Transplant Unit, National Medical Center “20 de Noviembre”, Mexico City, Mexico; Renal Transplant Unit, Hospital Civil de Guadalajara Fray Antonio Alcalá, Guadalajara, Mexico; 3Centro Medico Nacional de Occidente, Guadalajara, Mexico.

Background: The use of the sum of EPTS and KDPI scales to predict the decline of eGFR in patients who received a deceased donor transplant. Assess the reproducibility of the Organ Assignment System of the USA in our country.

Methods: 128 deceased-donor kidney transplant recipients at two National Mexican Hospitals between 2015 – 2017, retrospective, observational cohort study over 36 months following transplant. We include age, gender, primary renal disease, sensitization events, peak panel-reactive antibody, cold ischemia time, dialysis type and vintage, KDPI and EPTS, DGF, PTDM, Acute rejection, eGFR and cause of graft failure P. outcome: Relationship between a decrease >30% eGFR and the different combined scores of the KDPI and EPTS scales.

Results: The sum of the scores of the EPTS and KDPI scales >81% had a sens. 76% and a spec. 84% to predict a >30% decline in eGFR. AUC 80.8% [95% [CI] 0.022 to 0.005; p < 0.001). Multivariable Cox proportional hazard model: the sum of EPTS and KDPI scores >81% was associated with a 9.9-fold increase in losing more than 30% eGFR over the 36-months follow-up ([adjHR] 9.9; 95% [CI] 1.85 to 53.6, p = 0.007). Acute rejection was associated with a 3.1-fold increase in losing more than 30% eGFR ([adjHR] 3.1; 95% [CI] 1.15 to 8.72, p = 0.02).

Conclusions: Observing the donor and the recipient as a sum can be a new tool that helps us to predict the decline eGFR in Deceased Donor Kidneys transplants.

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. Moothri, Michael T. Eadon, Jeanne Chen, Asif A. Sharifuddin. 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.

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Methods: A retrospective chart review was done on patients ≥18 years of age who required AVP post operatively after a DDKT over 5 years (2012-2017). Recipient, donor characteristics, intraoperative parameters, hospital/ICU stay, graft failure, patient survival, and hyponatremia during first 48 hours were reviewed.

Results: A total of 43 patients fulfilled inclusion criteria. Refer to Table for summary. Total of 5 patients (11.6%) required dialysis, 3 of whom received donation of kidney after cardiac death. There were 3 deaths during the first 12 months (6.9%). Mean cold and warm ischemia time were 32.5±12.9 hours and 39.2±10.2 minutes, respectively. Mean time to start AVP was 6.8 hours postoperatively and mean duration of AVP use was 43.2 days with a median of 30 hours. 72.1% of patient also required dopamine. Mean hospital stay was 14.5 days and length of ICU stay was 5.4 days. Mean creatinine at day 7 was 4.0 ± 4.2 mg/dl. There was no incidence of hyponatremia during the first 48 hours. Graft survival was 72% at median follow up time of 7.2 years.

Conclusions: Patient requiring AVP post DDKT have unique characteristics - fewer anti-HTN medications and longer time on dialysis prior to transplant. A longer than median hospital length of stay was noted. To our knowledge this is the first study reviewing AVP use post DDKT. Future studies are needed to compare characteristics and outcomes with patients’ who did not require AVP post DDKT.

Recipient Characteristics and Intraoperative BP (n=43)

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Intraoperative BP</th>
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<tbody>
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</table>

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 biosample 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-donorrecipient 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 T-test or Wilcoxon test for parametric and nonparametric data respectively.

Results: Interleukin (IL)-7, IL-15, 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 Calisik,1 Safak Mirioglu,2 Halil Yazici,2 Ahmet B. Dirim,2 Erol Demir,2 Ozgur A. Oto,2 John C. Edwards,1 Rosemary Ousph,1 Aydin Turkmen,2 Krista L. Lentine,1 Saint Louis University, Saint Louis, MO; 2Istanbul University, Istanbul, Turkey.

Background: Recent advances in precision medicine have provided new insights into the pathogenesis of kidney transplant (KTx) 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 KTx 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 graft failure. 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 rs893043-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 KTx rejection.

Funding: Private Foundation Support

Figure 1. Catheterized urine samples from recipients at time of transplant have higher levels of IL-9 than their donors
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 Lluis Guirado,4 Petra Glander,4 Stefan Meuer,4 Martin G. Zeier,4 Thomas Giese.4
1Nephrology, University Hospital Heidelberg, Heidelberg, Germany; 4Renal Transplant Unit, School of Medicine, Uchinada, Ishikawa, Japan.

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; II-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 (C0 and C1.5) 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 16±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 infectious 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 study, the 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 perinuclear region or on the basement membrane with cytokines and immunosuppressants. 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 (990 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 5.01; 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-DQ DSA and other DSAs (HLA-A, HLA-B, HLA-C, HLA-DR) had a tendency to interact with acute AMR, although no statistical significance (p = 0.05).

Conclusions: Preformed HLA-DQ DSA may be necessary to improve graft outcomes.

PO2411
The Clinical Impact of Preformed HLA-DQ Donor-Specific Antibodies on Graft Outcomes in Kidney Transplantation
Sua Lee,1 Chul Woo Yang,2 Byung ha Chung.3 1Seoul National University Hospital, Jongno-gu, Seoul, Republic of Korea; 3Catholic University of Korea, Seoul, Republic of Korea.

Background: Preformed 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-DQ DSA has been discussed. This study aimed to investigate the clinical impact of preformed HLA-DQ 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 (990 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 5.01; 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-DQ DSA and other DSAs (HLA-A, HLA-B, HLA-C, HLA-DR) had a tendency to interact with acute AMR, although no statistical significance (p = 0.05).

Conclusions: Preformed HLA-DQ DSA is associated with the development of acute rejection, especially acute AMR. Therefore, the identification of preformed HLA-DQ 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 (DDKT) over several years. We performed a single-center analysis of 1119 consecutive adult DDKT from 2016-2019. Our endpoints were Kaplan-Meier death-censored

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
PO2413
Could Individually Measured Creatinine Clearances Decrease the Discard Rate of High Kidney Donor Profile Index (86-100) Deceased Donor Kidneys?

Adnan A. Khan, Robert W. Steiner, Hannah L. Turner, Charles K. Wainaina, Ashley S. Hahn. University of California San Diego, La Jolla, CA.

Background: The Kidney Donor Profile Index (KDPI) guides center acceptance and allocation of deceased donor kidneys (DDKs). It uses donor factors such as serum creatinine (sCr), diabetes mellitus and hypertension to predict organ quality and corresponding longevity. Due to this higher KDPI kidneys are often discarded. KDPI offers "only moderate predictability" of long-term transplant function with a c statistic of 0.6.

Methods: As an unexplored, but direct measure of deceased donor kidney quality, we determined pre-recovery creatinine clearances (CrCls) in 260 deceased donor candidates (1/2015 -12/2018) using ICU urine collections (Uccols) and pre- and post-recovery serum creatinine (sCr) values. We used CrCl > 80 ml/min as the threshold of interest, as that defines acceptable kidney function for living kidney donor candidates. Donor creatinine production rates were calculated to assess the veracity of CrCls. Organ match sequence was reviewed for all denials and UNOS denial codes and corresponding reasons for denial were reviewed.

Results: Of the 134 kidneys available from 67 high KDPI donors, 32/67 donors had both kidneys transplanted, 7/67 donors had one kidney transplanted and 28/67 donors were not transplanted. Reviewing the 35/67 donors in whom either one or both kidneys were not transplanted; 10 of them had CrCl > 80. This amounts to about 28.6 % (10/35) of the non-transplanted donors with high KDPI, having a CrCl >80 ml/min. In the high KDPI group 28/67 candidates (~42%) had measured CrCl>80 ml/min. In the KDPI 21-85 group, 97/155 (63%) of donors had CrCl >80 ml/min; while 42/50 (84%) in the KDPI 0-20 group had measured CrCls > 80 ml/min. Lower CrCls did not correlate with higher KDPIWs within each subgroup. Donor creatinine production rates were 17.9 ± 9.1 mg/kg/day, within population expectations. UNOS denial codes for high KDPI organ offers were mostly 830 - donor age or quality or 837 - organ specific donor issue.

Conclusions: Our data suggests that about 28.6% of the non-transplanted high KDPI donors had CrCl>80 and these kidneys could have been potentially used and not discarded. Direct measurement of CrCl in deceased kidney donors is not difficult and deserves further study, as it may improve estimates of donor kidney quality and reduce inappropriate discards in a heterogeneous group.

Funding: Clinical Revenue Support

PO2414
Glomerular Blood Flow in Living Donor Kidney Transplant Recipients

Gio Kanazaki, Takaya Sasaki, Kotaro Haruhara, Rina Oba, Yusuke Okabayashi, Kentaro Koike, Akimitsu Kobayashi, Izumi Yamamoto, Nobuo Taibo, Takashi Yokoo. The Jikei University School of Medicine, Minato-ku, Japan.

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 nephron 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/Nglomer(-1-hematocrit/100) x10^6. We analyzed the GBF before and during a 1-month observation period after transplantation. The GBF ratio as a marker of change in GBF was calculated as follows: (GBF one-month post-transplantation) / (GBF before transplantation in donors).

Results: Prior to transplantation, the GBF in donors was 559 ± 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 ± 299.1 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 1 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.
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 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 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 and 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) mimetic, 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 <500cc 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.
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=0.0001). There was no difference in recipient sex, native kidney disease, primary immunosuppression, drug disruption or incomplete medical record. Kidney recipients transplanted abroad are at increased risk of acute cellular rejection; however, patient and graft survival rates remained excellent.

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.

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 a multi-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 every organ recovered at the center where the surgeons practiced, suggesting that surgeon 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.

Clinical and Immunologic Predictors of Post-Transplant Outcomes

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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; 95% CI, 18.6, 1984, p<0.001). Of the 18 patients with Mi, 2 died 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 potentially benefit long-term outcomes of kidney transplant recipients.

Funding: Commercial Support - CareDx, Clinical Revenue Support

Microvascular Inflammation Is the Main Determinant of Elevated Donor-Derived Cell-Free DNA in Kidney Transplantation

Poster

Conflict of interest: None.

The absolute level of dd-cfDNA and its correlation with rejection type and microvascular inflammation

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio (95% CI)</th>
<th>p-value</th>
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<tr>
<td>Mi lesions</td>
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<td>0.001</td>
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<td>ABMR Class II</td>
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</tbody>
</table>

Binary logistic regression analysis regarding variables associated with a high dd-cfDNA level (>1%)
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 NovoBio StatSensor®Xpreshed 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 (68%) male; Median eGFR 49 nls/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

Table 1

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 KTR.

Methods: Using the Wisconsin Allotransplant Recipient Database (WisARD), we identified 2919 KTRs 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 coefficients of variation based on a linear regression of eGFR from 1 to 2 years.

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.

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). Analyses: 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.
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 (EPTS) score. This score is used to determine allocation of kidneys in the kidney allocation system (KAS). The outcomes of candidates with an EPTS > 95% at the time of listing is limited.

Methods: UCLA kidney Transplant Program data of waiting list with EPTS > 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 EPTS a 95% compared with EPTS < 95%.

Results: A total of 124 patients were identified with an EPTS score > 95% at the time of listing during the study period. Of these patients 23 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=0.0001) and were more sensitized at the time of listing (34.3% vs. 11.8%, p=0.018). Compared to a group with an EPTS between 80-94% at time of listing (n=170) there were no differences in mortality (4.35% vs. 4.55%, 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 EPTS > 95% was older group, 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 EPTS >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 EPTS > 95% provides comparable outcomes to candidates with an EPTS 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 are 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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1University of California Los Angeles; 2University of California Los Angeles David Geffen School of Medicine; 3Washington University in Saint Louis School of Medicine, Saint Louis, MO.

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. Baseline on the age at which the GFR was measured we divided the cohort in to 3 categories (children <12 ys, Adolescents 12-17 yrs and young adults >18-21 yrs. We used Bland-Altman analysis to evaluate the bias, precision and accuracy between eGFR and mGFR.

Results: Pottel and BS performed well across pediatric and adolescent age groups with high 30% accuracy(figure). MDRD and CKD EPI performance improved in young adults ~18 years. 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 (β2M), 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 proteinuria was 5 (9, 12) mg/L, and the baseline eGFR levels were 31 ± 9 mL/ min per 1.73 m². The annual eGFR change was -1.6±2.0 mL/min per 1.73 m²/year. The median (IQR) urine levels of total protein, β2M, NAG, and L-FABP at baseline were 0.3 (0.1-1.1) 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 β2M 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 β2M, 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
Prince Singh,1 Aleksandra Kukla. Mayo Clinic Minnesota, Rochester, MN.

Introduction: Graft-versus-host disease (GVHD), a common complication after allogeneic 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 (KP) patient 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 globulin (ATG) was used to manage the acute rejection. The patient had a history of chronic hypertension and smoking. The patient developed acute renal failure 48 months post transplantation and was eventually put on non-cyclosporine immunosuppression. The patient was found to be sensitized for a new panel-reactive antibody (PRA) as per the laboratory protocol 2 years after transplantation. The patient had 15% PRA at that time. The patient was found to have chronic allograft dysfunction (CRAD) 2 years after transplantation. The patient had a creatinine of 1.3 mg/dL with a transplant vintage of 8 (5, 12) years, and the baseline eGFR levels were 31±9 mL/min per 1.73 m². The annual eGFR change was -1.6±2.0 mL/min per 1.73 m²/year. The median (IQR) urine levels of total protein, β2M, NAG, and L-FABP at baseline were 0.3 (0.1-1.1) 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 β2M 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 β2M, total protein appears to have greatest predictive value for eGFR decline among KTRs.

Funding: Commercial Support - Chugai, Kissei, Roche Diagnostic K.K.
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 chromatin 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. De-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.

PO2430
Association of the Rate of Kidney Transplant Function Decline with the Risk of Death After Graft Loss
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Background: Patients with failed kidney transplants are at increased risk of death after graft loss compared to transplant-naive counterparts. We hypothesized that in this high risk population, a faster decline in eGFR in the 2yr prior to graft loss is associated with death after graft loss.

Methods: We retrospectively reviewed all patients with death censored graft loss of eGFR from 1995-2018 at a single center. We collected demographic, clinical and transplant characteristics at time of transplant and graft loss. Rate of eGFR decline was expressed as eGFR slope, calculated from all SCR values obtained within 2yr prior to graft loss. Cox proportional hazards regression was used to determine the association between rate of eGFR decline and death while adjusting for age, gender, race, cause of ESKD, cause of graft loss, dialysis access at graft loss, and nephrectomy after graft loss.

Results: 333 patients with DCGL were included. Baseline characteristics were: median age 45y (IQR 35.57), 59% male, 43% black; 19% DM as cause of ESKD. CAN (65%) and acute rejection (29%) were the top causes of graft loss at a median time from transplant of 4.9y (IQR 2.5,7.9). Rate of eGFR decline (in ml/min/1.73m²) was -14.49 ± 13.24 (means±SD) and -11.73 (-18.72,-6.19) (median, IQR). At time of DCGL, 46% had a history of acute rejection and 54% had a permanent dialysis access. Of the 251 patients without missing data, 97 (40%) died and 68 (27%) underwent a nephrectomy after graft loss. Median time from graft loss to death was 3.1y (IQR 1.47,7.3). In multivariable analysis, there was a 0.6% increase in risk in death for every 1 ml/min/1.73m² increase in rate of eGFR decline though not statistically significant (HR 1.006, 95% CI 1.00-1.01). Exploratory analysis with non-linear modeling of eGFR slope showed that the risk of
death increases up to a rate of decline of 10 ml/min/1.73m²/y. DM as cause of ESKD was associated with an almost 2-fold increase in risk of death after graft loss compared to non-DM (HR 1.95, 95% CI 1.27-2.96).

Conclusions: In this single-center cohort of kidney transplant recipients with DCGL, a faster rate of eGFR decline in the 2y prior to graft loss was not associated with a higher risk of death after graft loss after adjustment for important clinical variables.

PO2432
Renal Recovery After Liver Transplantation Alone in Patients with Liver Cirrhosis and Severe CKD with Normal Kidney Size
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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 <9cm]-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 at >60 ml/min and 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 75% 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 (bilirubina10 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 and comparable (P=0.5 between group 2&3) outcomes. Survival was better in group 2&3 compared to those in group 4 (P<0.001) 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 Equity 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 partiallyameliorated 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 (dGF) 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, 1.46], and dGF 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.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
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 04/01/2011 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. Among unrelated donors <35, 35-49, and ≥50, white donors increased by 18%, 14%, and 27%; Hispanic donors <35 did not change but increased by 22% and 35% for 35-49 and ≥50; black donors <35 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
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 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(CKD – EPI(ml/min/1.73m2),24-hour creatinine clearance(Cr Cl) and Creatinine clearance by Cockcroft Gault(2CrCl(C/G)(ml/min)) between age, ethnicity, and gender. We also calculated the relative bias(mGFR-eGFR/mGFR), root mean square error and the accuracy(P30(eGFR between +30 and mGFR) of different eGFR equations.

Results: 422/423.32% males donors. 616(62%) Caucasian, 228(23%) South Asian. 114(11%) Afro Caribbean and 39(4%) of other ethnic groups(Arabic, oriental and mixed ethnicity). Mean mGFR was 100.08(SD 10.87). Mean mGFR for males and females were 105.77 ± 96.27, respectively(p=0.05). 63(6%) donors were >65 years. Mean mGFR comparing young and >65 years old donors were 103.44 ± 82.27, respectively(p=0.0028). As predicted, there is a linear decline in mGFR with increasing age. Cr Cl-C G has a tendency towards underestimating function in healthy living donors over 65 years old. GFR calculated by CKD-EPI formula was comparable to mGFR amongst all age groups, genders and ethnically diverse living donors. CKD-EPI performed better in terms of least bias and highest accuracy compared to MDRD for all donor subgroups(Table1).

Conclusions: mGFR declines with age and healthy older donors have significantly lower mGFR compared to younger donors. Cr Cl-C G overestimates kidney function and should be used with caution. eGFR by CKD EPI comes closest to compared to mGFR in all groups. It could be reliably used as first screening tool for assessing function of living donors pre donation, irrespective of age, gender or ethnicity.

Demographics & Comparative performances

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 different eGFR equations

Results: 153 donors were admitted, 34% without 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 106 ± 6 / 72.9 ± 5.4, BMI, 26.3 ± 3.2, proteinuria 124.6 ± 13.4, hemocrit 44.6 ± 4.9, albumin 4.1 ± 0.4, K 9.4 ± 0.6, Uric acid 5.4 ± 1.2, Total cholesterol 185.6 ± 34, triglycerides 156.5 ± 91.7, fasting glucose 91.6 ± 15.2, Creatinine 0.78 ± 0.14. The mean bleeding during surgery was 263.6 ± 447 mL, creatinine after surgery was 1.21 ± 1.8, upon release from hospital it was 1.13 ± 0.27. 72% of donors presented acute kidney injury (AKI) after surgery, with an average of 1.56 ± 1.8 days with AKI, 30% of donors released from hospital with AKI. More than 25% of kidney donors had 2, 3 and 4 CRFs. Figure 1 presents the comparison between groups (AKI vs No AKI) of creatinines at baseline, 3 months and 6 months.

Conclusions: A higher presence of CRFs is associated with higher AKI events after kidney donation. AKI patients during renal donation show a further deterioration of renal function at 3 and 6 months of follow-up. Timely interventions prior to donation could improve the evolution of this group of patients.
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(-); n=116) and HCV Ab negative and NAT positive (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-HCVAb(+)/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 African 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<0.011) 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(-) recipients. HCVAb positive, but NAT negative donor kidneys should not be allocated as HCV positive kidneys.

PO2443
Transplantation of Kidneys from Hepatitis C-Infected Donors to 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 IRB 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 sclerotic glomeruli, 14/16 (88%) had minimal interstitial fibrosis, and 15/16 (94%) had no arteriolar sclerosis. 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.

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.

PO2444
Transplantation of Kidneys from Hepatitis C-Infected Donors to Hepatitis C-Negative Recipients: 1-Year Renal Allograft Outcomes
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Background: Transplant centers in United States are increasingly willing to transplant kidneys from HCV infected donors to hepatitis C negative recipients. Long-term renal outcome data of a non-prophylactic HCV treatment approach outside clinical trials is missing.

Methods: We examined 65 HCV negative recipients who received a HCV infected kidney transplant (HCV+) and 59 HCV negative recipients who received a HCV non-infected kidney transplant (HCV-) during 2018 in a single transplant center. We compared estimated glomerular filtration rate (eGFR), cumulative results of per-cause and surveillance protocol biopsies, development of de novo donor specific antibodies (DSAs), co-infection rates and patient and graft outcomes up to 1 year post-transplant between HCV+ versus HCV- groups.

Results: The mean±SD age of recipients was 52±11 years, 43% were female, 19% and 80% of recipients were Caucasian and African-American, respectively. Baseline characteristics were similar between the HCV+ and HCV- groups. The delayed graft function rate, estimated GFRs at post-transplant 3, 6, 9 and 12 months, cumulative rejection rate, development of de novo DSAs and co-infection rates were not statistically significantly different between the HCV+ and HCV- groups (Table).

Conclusions: Recipients of HCV-viremic kidneys have similar renal allograft function, incidence of rejection in the first year after transplantation compared to those who received HCV-non-viremic kidneys.

Renal graft and patient outcome of all kidney transplant recipients

Human Herpesvirus 8-Associated Kaposi Sarcoma Developing in a Kidney Allograft from a Hepatitis C-Positive Donor
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Introduction: Kaposi Sarcoma (KS) is an endothelial malignancy caused by the oncogenic virus Human Herpesvirus-8 (HHV-8) and transmission during kidney transplantation can occur. We describe two cases of donor-to-recipient transmission of HHV-8, with one recipient developing KS in the kidney allograft causing acute kidney injury (AKI).

Case Description: Donor: The donor died from complications of IV drug use and had known hepatitis C (HCV) at the time of organ donation. Recipient 1: 64-year-old male with ESRD, induction with basiliximab. He tested positive for HCV on post-transplant day 2 and was treated with sofosbuvir/velpatasvir for 12 weeks. Two months post-transplant, he developed encephalopathy and was found to have HHV-8 viremia during his workup. Immunosuppression was decreased, HHV-8 PCR levels were monitored and eventually were undetectable. He did not develop KS. Recipient 2: 71-year-old male with ESRD, induction with anti-thymocyte globulin. He was treated pre-emptively for HCV with glecaprevir/pibrentsvir. Five months post-transplant he was admitted for rising creatinine. Initial allograft biopsy was of poor quality but was suggestive of Banff IA

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
rejection; IV methylprednisone and anti-thymocyte globulin were administered. Repeat biopsy at 1 year of transplant revealed increased interstitial inflammation and tubulitis. A biopsy from a control kidney revealed metastatic KS. Immunosuppression was discontinued and he underwent allograft nephrectomy. He died at home 2 months later. Retrospective testing of samples prior to transplantation revealed the donor was HHV-8 PCR positive at the time of death and both recipients were HHV-8 antibody and PCR negative.

Discussion: We describe donor-to-recipient transmission of HHV-8 during kidney transplantation. HHV-8 associated post-transplant KS is well described but rare in the US. Post-transplant KS typically presents with classic skin lesions and kidney allograft involvement. This is the only case reported in the literature. Future interest is needed into this population to determine if post-transplant HHV-8 PCR monitoring or adjustments in immunosuppression are needed for kidney transplant recipients of HHV-8 increased risk groups.

PO2445

John Cunningham Virus (JCV) in Renal Allograft Recipients (RAR)

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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) resulting in graft dysfunction. She received a 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 350659 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 RAL nephrectomies with pathologic 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.cr of 1.6 mg/dl. He was on Myfortic, Sirolimus and Prednisone for IS. He presented with rising s.cr 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 2630 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 JCVN. Early diagnosis and reduction in IS are critical. Cidofovir may be of utility.

PO2446

Disseminated Adenovirus Treated with Brincidofovir in a Kidney Transplant Recipient

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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 in immunosuppression. She presented one day of gross hematuria and right flank pain, as well as 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 in urine (420,000 IU/ml) 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 q48h alternating with IVIG 500mg/kg q48h. She received 4 doses of cidofovir and IVIG, with resolution of hematoma 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 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 adenovirus level in urine. Although she received hydration before and after cidofovir, creatinine rose to 2.04 mg/dl.

Discussion: The most commonly used adjunctive treatment to reduced immunosuppression in management of adenovirus infection is cidofovir. However, cidofovir is nephrotoxic and rarely 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.

PO2447

Early Ganciclovir-Resistant Cytomegalovirus Infection in a Kidney Transplant Recipient: Could We Avoid It?


Introduction: Although uncommon, ganciclovir-resistant cytomegalovirus (GR-CMV) can lead to a therapeutic challenge given drug nephrotoxicity. Here we report a case of GR-CMV infection during early post-kidney transplant (KT).

Case Description: A 41-year-old woman with ESRD received the second KT in February 2019 with rATG induction. She also received rituximab one dose for pre-KT donor specific HLA antibodies. Maintenance immunosuppression are tacrolimus, mycophenolate sodium (MPS), and prednisone. Serum creatinine slowly trended down to the baseline of 1.3mg/dl at 3 month post-KT. CMV IgG serostatus was D+/R-. She received a 6-month CMV prophylaxis with a renally-adjusted dose of valganciclovir 450 mg twice weekly for 1 month, which was increased to 450 mg twice daily for 5 more months. 4 months after the CMV prophylaxis was completed, she developed asymptomatic CMV viremia with a titer up to peak of 47,643 IU/ml. Valganciclovir 900 mg twice daily was started and MPS was decreased. CMV PCR slowly decreased to 440 IU/ml after 1 month of therapy. Despite continuation of valganciclovir, CMV PCR became rapidly increased to 3,349 IU/ml [Figure]. A CMV genetic resistance test revealed a UL97, but not UL54 resistance. Flow cytometry was started and CMV PCR was decreased. Allograft function has been at the baseline.

Discussion: Our patient has several risk factors for GR-CMV including high-risk CMV serostatus, prolonged exposure to low-dose oral valganciclovir prophylaxis, and intensified immunosuppression including rituximab. Given current treatment for GR-CMV remains limited with drug toxicity, adequate dose of CMV prophylaxis is critical to avoid GR-CMV. Pattern of CMV PCR after initiation of therapy should also raise a suspicion for GR-CMV and genetic CMV resistance testing is paramount in early diagnosis. Novel preventive and therapeutic options may mitigate the risk of GR-CMV and drug-induced renal allograft toxicity.
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.

PO2449

BK Polyomavirus Nephropathy After Kidney Transplantation from HCV-Infected Donor to HCV-Uninfected Recipient

Faisal Abdulameer,1 Hisham N. Abu Farsak,1 Barry M. Wall,1,2 Miklos Z. Molnar,1 The University of Tennessee Health Science Center; Memphis, TN;2 VA Medical Center, Memphis, TN.

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. This case report demonstrates the clustering of BKPyV DNAemia/nephropathy and severe BKPyV DNAemia/nephropathy, supporting the previous finding that transplantation from HCV-infected donors to uninfected recipients may be a risk factor of BKPyV DNAemia/nephropathy.

Case Description: A 62-year-old HCV negative African American male received a cadaveric kidney transplant from an 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 peginterferon (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 >3,000,000 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/velpatasvir/voxilaprevir and ribavirin for a total of 12 wk, achieving SVR at 12 wk. His BKPyV DNAemia slowly responded with 1,257,789 copies/mL at 6 wk of DAA treatment and 7,378 copies/mL at 12 wk. Serum creatinine gradually improved to 2.04 mg/dL. His 1 year protocol biopsy still showed tubulointerstitial inflammation, rare positive SMA staining, proliferative GN with improving monoclonal IgG deposits, indicating Banff borderline acute cellular rejection. His immunosuppressive regimen was intensified and graft function has remained stable.

Discussion: Our case report with close proximity of HCV treatment failure and severe BKPyV DNAemia/nephropathy supports the previous finding that transplantation from HCV infected donor kidneys to uninfected recipients may be a risk factor of BKPyV DNAemia/nephropathy.

PO2450

Cytomegalovirus-Associated Collapsing Glomerulopathy in a Renal Transplant Recipient

Chirag Lavani, Alexander J. Gallan. Division of Nephrology Medical College of Wisconsin, Milwaukee, WI.

Introduction: Cytomegalovirus (CMV) is a cosmopolitan virus that has long been recognized as a common cause of disease in transplant recipients. It can cause a variety of complications leading to impairment of renal allograft function. There are several possible manifestations of CMV nephropathy including interstitial nephritis, positive staining for CMV inclusions in glomerular cells, and collapsing focal segmental glomerulosclerosis. CMV nephropathy is an uncommon complication of CMV viremia following renal transplant but should be considered in the differential diagnosis of patients with CMV viremia and AKI.

Case Description: A 73 year old Caucasian male with history of ERUS due to collapsing glomerulopathy (CG) is a glomerular disease presenting with nephrotic syndrome and acute kidney injury (AKI), and showing collapse and sclerosis of glomerular capillaries with hypertrophic and injured podocytes on kidney biopsy. CG is most often seen in association with HIV infection and APOL1 nephropathy; however, CG can be associated with non-HIV viral infections. We describe a case of CMV-associated CG in a renal transplant patient.

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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

Won-Hye Cho,1 Su Woong Jung,1 Ju young Moon,1 Yang gyun Kim,2 Kyung hwan Jeong,3 Sangho Lee.1 Kyung Hee University Hospital at Gangdong Department of Orthopedic Surgery, Seoul, Republic of Korea; 2Kyung Hee University Hospital at Gangdong, Seoul, Republic of Korea.

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 posttransplantation.

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 posttransplantation and then decreased. Multivariable-adjusted Cox regression showed that urinary exosomal bkv-miR-B1-5p makes its predictive ability for biopsy-proven BKVN superior to that of plasma BKV DNA at 2 weeks posttransplantation.

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

<table>
<thead>
<tr>
<th>Group</th>
<th>Biopsy-proven BKVN</th>
<th>Presumptive BKVN</th>
<th>Non-BKVN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Age</td>
<td>45±10</td>
<td>50±15</td>
<td>47±12</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Diabetes</td>
<td>Hypertension</td>
<td>Kidney Disease</td>
</tr>
<tr>
<td>Duration</td>
<td>3 months</td>
<td>6 months</td>
<td>9 months</td>
</tr>
</tbody>
</table>

Discussion: BKVN 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 BKVN. 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 BKVN and supports that crescent formation can be caused by viral infection of the parietal epithelial cells.

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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 tubulointerstitial inflammatory reaction to the virally infected tubular epithelial cells, there are few reports of glomerular viral tropism. We present unique histopathological 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.
PO2455
A First-in-Human Study of MAU868, a Novel Neutralizing Antibody Against BK Virus
Steven J. Kovacs,1 Johanna R. Abend,1 Xiaoying Xu,2 Sachin Desai,2 Amanda Nguyen,2 Laura M. Sterling,1 Michael R. Hodges,1 Peter Pertel,1 Novartis Institutes for BioMedical Research Emeryville, Emeryville, CA; Novartis Institutes for BioMedical Research East Hanover, East Hanover, NJ; Celerion Inc, Lincoln, NE; Amplyx Pharmaceuticals, Inc, San Diego, CA.

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 d with routine safety monitoring and PK assessments. Ex vivo neutralizing activity of serum was measured before and 4 w 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 (ecchymosis 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·hr/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
Ali M. Zebi, Aria Ghahramani, Mujahed M. Dauleh, Nastrollah Ghahramani. Penn State College of Medicine, Hershey, PA.

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 leucopenia, CMV infection, and BKV 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 transplant recipients with routine safety monitoring and PK assessments. We compared the association between induction with thymoglobulin and alemtuzumab on the risks of leucopenia, CMV infection, and BKV virus nephropathy.

Results: Study cohorts included 220 patients (mean age: 57 ± 15) in the thymoglobulin group, and 160 patients (mean age: 54 ± 19) in the alemtuzumab group. Leukopenia occurred in 50 patients in the thymoglobulin group and in 70 patients in the alemtuzumab group (RR: 0.52; CI: 0.39 to 0.76; p<0.0001). CMV infection occurred in 80 patients in the thymoglobulin group and in 20 patients in the alemtuzumab induction group (RR: 1.45; CI: 0.89 to 2.39; p = 0.14). BKV virus nephropathy occurred in 20 patients in the thymoglobulin group and in 20 patients in the alemtuzumab induction group (RR: 0.72; CI: 0.41 to 1.31; p = 0.29).

Conclusions: Induction therapy with thymoglobulin is associated with a lower risk of leukopenia compared with alemtuzumab induction. The risks of CMV infection and BKV virus nephropathy are not statistically different in the two induction therapies.

PO2457
Effects of Early Conversion to mTOR Inhibitors on Viral Infections in Renal Transplant Recipients: Eight-Year Single-Center Experience
Waleed Hassan,1 Hisham Mostafa,2 ‘The University of Tennessee Health Science Center College of Medicine, Memphis, TN; ‘Minia Nephrology and Urology University Hospital, Minia, Egypt.

Background: Mammalian target of rapamycin inhibitors (mTORis) may decrease cytomegalovirus (CMV) and BK infection in renal transplant recipient. long-term effect of rejection rate deserves follow up.

Methods: This is a retrospective analysis of all patients who underwent living unrelated donor kidney transplantation at Nasr city Insurance and Nile Badrawy Hospitals from 2011 to 2018, panel reactive antibody zero and no donor specific antibody. Uni- and multi-variant 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 rejection 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.

Funding: Commercial Support - Novartis

Underline represents presenting author.

PO2458
The Utility of Procalcitonin in the Management of Kidney and Pancreas Transplant Recipients with Suspected Infection
Sarah Gilligan, Fuaad S. Shihab, Divya Raghavan, Laith Al-Rabadi, Josephine 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.

Table (2) comparison between mTOR and CNI in the incidence of BPAR

<table>
<thead>
<tr>
<th>Year</th>
<th>Total number</th>
<th>(BPAR) Rejection N(%)</th>
<th>Total number</th>
<th>(BPAR) Rejection N(%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>50</td>
<td>12(24%)</td>
<td>98</td>
<td>8(8.2%)</td>
<td>0.158</td>
</tr>
<tr>
<td>2012</td>
<td>64</td>
<td>4(6.3%)</td>
<td>122</td>
<td>12(9.8%)</td>
<td>0.407</td>
</tr>
<tr>
<td>2013</td>
<td>65</td>
<td>10(15.4%)</td>
<td>170</td>
<td>14(11.7%)</td>
<td>0.473</td>
</tr>
<tr>
<td>2014</td>
<td>105</td>
<td>10(9.5%)</td>
<td>151</td>
<td>13(8.6%)</td>
<td>0.615</td>
</tr>
<tr>
<td>2016</td>
<td>98</td>
<td>4(4.1%)</td>
<td>67</td>
<td>1(1.5%)</td>
<td>0.041</td>
</tr>
<tr>
<td>2017</td>
<td>124</td>
<td>7(5.6%)</td>
<td>79</td>
<td>12(15.2%)</td>
<td>0.017</td>
</tr>
<tr>
<td>2018</td>
<td>107</td>
<td>7(6.6%)</td>
<td>111</td>
<td>5(4.5%)</td>
<td>0.298</td>
</tr>
</tbody>
</table>

Overall time 638 (272.4±1.4) 800 (111.9±1.4)

• Chi square test for qualitative data between the two groups
• * Significant level at P value < 0.05

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PO2459

Infection Rate at 1 Year of Deceased Donor Kidney Transplant in the Elderly

Wina Yousman, Nicole Low, Wei Xiang Wong, Venkatesh Kumar Ariyamuthu, Bekir Tanriver. 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 DDKT (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 cPRA.

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 (0.3% vs 51.3% p=0.11, 20.6% vs 11.5% p=0.10, 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, cPRA, and CMV mismatch) did not show increased odds of all types of infection among older recipients.

Conclusions: The infection rate of elderly versus non-elderly who received DDKT were similar.

Table 1: Baseline Characteristics and Outcomes of Elderly vs. Non-elderly

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. In an additional patient reported as “borderline”, the 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

Luz E. Liriano-Ward, Yorg Al Azzi, Cindy T. Pynadath, Maria Ajaimy, Pablo Lorette Campos, Purna Bindu Nandigam, Enver Akalin. Montefiore Medical Center, Bronx, NY.

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: Out 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

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Underline represents presenting author.
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 patients were more often with 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.

<table>
<thead>
<tr>
<th>Clinic location</th>
<th>Patients age &lt; 65</th>
<th>Patients age &gt; 65</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Results:** The number of matched 7,462 subjects (total 22,386) were included to each 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 3.39 (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.

**PO2464**

**Risk of Active Tuberculosis Infection in Kidney Transplantation Recipients: A Matched Comparative Nationwide Cohort Study**

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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. We 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 incidence of complications >3- to 8-years post-KTx, according to 3xs Regimen and HCQ Use (7-12 mos).

**Conclusions:** HCQ is an inexpensive immunomodulatory agent that may be used safely in selected KT recipients as an alternative or adjunct to standard immunosuppression.

**PO2465**

**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 the COVID-19 pandemic, although safety is controversial.

**Methods:** We examined a novel database linking national transplant registry identifiers for kidney transplant recipients (KTs) to records from a large U.S. pharmaceutical claims warehouse (2008–2017) and Medicare claims to study HCQ use among Medicare beneficiaries with kidney failure due to SLE or scleroderma (N=2,550). We compared 3 groups based on immunosuppressive regimen 7–12 mos. post-KTx: 1) Tac+HCQ+MPA+Pred; 2) Tac+HCQ+Pred; and 3) Tac+HCQ+MPA+Pred. Associations of regimen with graft failure, death and clinical cardiovascular complications captured in Medicare claims >1-to-3 yrs post-KTx were examined with multivariate Cox regression, adjusted for baseline factors in the registry.

**Results:** Among the study sample, 18.3% received Tac+HCQ+MPA+Pred; 7–12 mos. post-KTx, while 1.7% received Tac+HCQ+Pred. Use of HCQ containing regimens was more common in women (vs men), and Black and Hispanic (vs white) recipients; use of Tac+HCQ+MPA+Pred was more common in younger patients (vs older) patients (Table). The unadjusted incidence of adverse events did not differ across the 3 groups (Fig A); risks also did not differ with covariate adjustment (Fig B).

**Conclusions:** HCQ is an inexpensive immunomodulatory agent that may be used safely in selected KT recipients as an alternative or adjunct to standard immunosuppression.

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

Underline represents presenting author.

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globulin induction, and maintenance tacrolimus, mycophenolate, and prednisone. Two months later, he presented with diffuse violaceous papules (Figure 1A). Biopsy of a papule with Wartthin-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 doxcycline with resolution of symptoms. BH and BQ Immunglobulin 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 without recent exposure. Allograft 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 angiomatous-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) Wartthin-Starry stain showing bacteria (arrow).
PO2469

National Trends in Kidney Transplantation Among Patients with ESKD from Plasma Cell Dyscrasias

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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 Sharing1/ Organ Procurement and Transplantation Network (UNOS/OPTN) database. Patients 18 years or older, BMI >15 or <45 kg/m2 not having a preference for organ type, with plasma cell dyscrasia (PCD) were included. 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.

Results: A total of 160,966 patients received a first kidney transplant. Among these, 487 (0.3%) had ESKD and 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 patients 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 (No.)</th>
<th>Total plasma cell dyscrasia (No.)</th>
<th>Multiple myeloma (No.)</th>
<th>Amyloidosis (No.)</th>
<th>Monoclonal gammopathy (No.)</th>
<th>Survival (%)</th>
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<tr>
<td>2006</td>
<td>20,342</td>
<td>33 (0.2%)</td>
<td>13 (0.1%)</td>
<td>10 (0.1%)</td>
<td>10 (0.1%)</td>
<td>73.0 (33.0)</td>
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<td>27,571</td>
<td>40 (0.2%)</td>
<td>18 (0.1%)</td>
<td>10 (0.1%)</td>
<td>12 (0.1%)</td>
<td>73.0 (33.0)</td>
</tr>
<tr>
<td>2008</td>
<td>27,679</td>
<td>50 (0.2%)</td>
<td>20 (0.1%)</td>
<td>10 (0.1%)</td>
<td>20 (0.1%)</td>
<td>73.0 (33.0)</td>
</tr>
<tr>
<td>2009</td>
<td>27,422</td>
<td>54 (0.2%)</td>
<td>20 (0.1%)</td>
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<td>21 (0.1%)</td>
<td>70.0 (33.0)</td>
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<tr>
<td>2010</td>
<td>27,490</td>
<td>58 (0.2%)</td>
<td>21 (0.1%)</td>
<td>13 (0.1%)</td>
<td>24 (0.1%)</td>
<td>68.0 (33.0)</td>
</tr>
<tr>
<td>2011</td>
<td>27,385</td>
<td>56 (0.2%)</td>
<td>21 (0.1%)</td>
<td>13 (0.1%)</td>
<td>22 (0.1%)</td>
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<td>2012</td>
<td>27,394</td>
<td>58 (0.2%)</td>
<td>21 (0.1%)</td>
<td>15 (0.1%)</td>
<td>22 (0.1%)</td>
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<td>52 (0.2%)</td>
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<td>2014</td>
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<td>22 (0.1%)</td>
<td>15 (0.1%)</td>
<td>21 (0.1%)</td>
<td>68.0 (33.0)</td>
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<tr>
<td>2015</td>
<td>27,394</td>
<td>58 (0.2%)</td>
<td>22 (0.1%)</td>
<td>17 (0.1%)</td>
<td>23 (0.1%)</td>
<td>68.0 (33.0)</td>
</tr>
<tr>
<td>2016</td>
<td>27,404</td>
<td>59 (0.2%)</td>
<td>22 (0.1%)</td>
<td>16 (0.1%)</td>
<td>21 (0.1%)</td>
<td>68.0 (33.0)</td>
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<tr>
<td>2017</td>
<td>27,399</td>
<td>57 (0.2%)</td>
<td>22 (0.1%)</td>
<td>17 (0.1%)</td>
<td>22 (0.1%)</td>
<td>66.0 (33.0)</td>
</tr>
</tbody>
</table>

Conclusions: Despite improvement in 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

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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 diagnostic dilemma with a retroperitoneal hemorrhagic cystic tumor turned out to be an adenocarcinoma of pancreaticobiliary origin.

Case Description: A 57-year-old woman with PMH of ESRD x/p kidney transplant (D+/R-, E-), with chronic ChEI of 30-40% presented with paroxysms 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 vasogenic 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. Myectomy was stopped and oral steroids started with mild improvement in symptoms. Choice of systemic chemotherapy was limited due to reduced ChEI and risk of graft failure. She received modified regimen with re-titrated high dose Methotrexate, Vincristine and Rituximab for 6 cycles with partial remission and then Tenozolomide for 7 cycles with complete remission.

Discussion: The incidence of PTLD ranges from 1 to 25% with 90% of cases being EBV driven. PTLD is a monoclonal cell neoplasms. PCNs-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 is the preferred imaging and shows multifocal, ill defined, ring enhancing lesions usually in supratentorial and lobar regions. Positive 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.

PO2471

Secondary Malignancy in Kidney Transplant Recipients: University of Southern California Experience

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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 ATG (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 celacipt 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

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Background: Cancer is an important cause of morbidity and mortality in kidney transplant recipients. Despite being described as a critically important outcome by patients, caregivers and health professionals, inconsistency in how cancer outcomes are defined and reported in trials of 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.

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Underline represents presenting author.
Acute Rejection and Graft Failure in a Kidney Transplant Recipient with Malignant Melanoma and Treated with Pembrolizumab: A Case Report

Annalise M. Panthofer, Kurtis 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 high risk of rejection. Immune checkpoint inhibitors increase 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 cell 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 of graft rejection. Prevention and management of rejection in a transplant recipient with an aggressive melanoma such as ours is not clear.

PO2474
Renal Transplant Recipients Suffer Significantly More Complications After Breast Cancer Surgery but Benefit from Treatment at Transplant Centers

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1The University of Toledo Medical Center, Toledo, OH; 2Westchester Medical Centers, New York, NY; 3Miami, Miami, FL

Background: Breast Carcinoma has the highest incidence of any cancer in adult females. The impact of kidney transplant (KT) on breast cancer surgery has not been examined. Our objective was to evaluate the influence of a previous KT on the short-term outcomes of mastectomy or lumpectomy.

Methods: A retrospective analysis was conducted using Nationwide Inpatient Sample (NIS) data between 2005 and 2014. Population included adult females with kidney transplant and surgically treated for breast malignancy. Weighted multivariate regression models were employed to compare outcomes at transplant and non-transplant centers.

Results: 598 women met the inclusion criteria. There was a greater proportion of African-American (p<0.001), and Hispanic women (p=0.01) compared to the cohort. KT recipients had more comorbidities and higher Eluxhauser Comorbidity Index scores (p<0.001). We noted longer length of stay (p<0.001), higher expenditure (p<0.001), and complications (p<0.001). Specifically, rates of hematoma (p=0.041), acute renal failure (p=0.001), blood transfusion (p=0.001), fresh frozen plasma transfusion (p=0.001), cardiovascular (p=0.001), and other complications (p=0.012) were increased. There was no mortality among transplant recipients. Weighted multivariate analyses highlight that rates of complication (p<0.001), and length of stay (p<0.001) are lower at transplant centers.

Discussion: Cancer is one of the most important outcomes for patients post-transplantation, but cancer outcomes are very poorly defined and highly variable in KT recipients. 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: National Cancer Institute - U.S.

PO2475
Local Renal Graft Irradiation as Salvage Treatment for Renal Graft Rejection Secondary to Checkpoint Inhibitor: A Case Report

Edgar A. Acuna-Morn, Oscar A. Garcia Valencia, Javier Pagan, University of Miami, Miami, FL.

Introduction: Graft rejection after treatment for malignancies with checkpoint inhibitors targeting the CTLA-4 and the PD-L1 pathways has been a growing interest in recent years since the rates of graft rejection are high as 33.3% with a median time to rejection of 8 days. To the best of our knowledge, there are no prior case reports of a renal transplant patient with stage IV gastric adenocarcinoma treated with pembrolizumab (a PD-1 inhibitor) who developed graft rejection and required local irradiation.

Case Description: This is a 65-year-old male with history of ESRD secondary to IgA nephropathy, chronic Hepatitis B and related donor kidney transplant who was diagnosed with gastric malignancy with peritoneal carcinomatosis and outlet obstruction after 12 years of transplantation. Gastric adenocarcinoma was HER2 equivocal, FISH negative, MMR deficient, PD-L1 positive. Initial therapy included discontinuation of Tacrolimus, steroid monotherapy. Initial chemotherapy included 2 cycles of FLOT followed by ramucirumab. After finding disease progression at 6 months, he received a salvage chemotherapy with pembrolizumab. Two weeks after, presented to the ED with anuria AKI. A Mag-3 scan demonstrated good perfusion and a kidney biopsy showed cortex coagulative necrosis. High dose steroids and sirolimus were given with no response and required initiation of hemodialysis. In the following weeks, presented to the ED complaining of gross hematuria and clots. Cystoscopy with bladder biopsy was performed and showed no bladder injury and normal mucosa. The hematuria was found to be secondary to kidney graft rejection and he was started on high dose of steroids with mild improvement. Nephrectomy was not an option due to poor nutritional status and overall health condition. Palliative radiation therapy to the kidney was the only option for immunosuppression. He received local graft irradiation of 7.5 Gy in 5 fractions with resolution of hematuria.

Discussion: The case illustrates first, that the use of checkpoint inhibitors in patients with kidney transplant convey a high risk of severe irreversible allograft rejection and can occur after only one dose. Second, the viability of palliative radiation as a non-surgical option for acute kidney graft rejection causing symptomatic hematuria resistant to conventional immunosuppressant therapy.
A Rare Presentation of Disseminated Nocardia in a Kidney Transplant Recipient
Ruchi Haik, Saed Shawar, Heidi M. Schaefer, Vanderbilt University Medical Center, Nashville, TN.

Introduction: Nocardiosis is a very rare infection caused by the Nocardia asteroides bacterium. It most commonly involves the lungs but can spread to other areas of the body 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.

Case Description: Patient is a 58 year old African American man with a history of ESRD due to hypertension and reduced kidney mass status post right radical nephrectomy for renal cell carcinoma in 2001. He underwent deceased donor kidney transplant in May 2017 after being on dialysis for 13 years. He received alemtuzumab and methylprednisolone prednisone for induction followed by maintenance immunosuppression with Tacrolimus, mycophenolate mofetil and prednisone. In January 2020, he presented to the orthopedic clinic with a 10-day history of pain in a soft tissue mass of the right scapula and was diagnosed with a parascapular muscle tear. One week later he presented to an outside hospital with fevers and CT of chest showing pulmonary nodule with satellite lesions in the RUL concerning for malignancy. He was transferred to our hospital where PET CT scan showed multiple intensely FDG avid masses in the lungs, brain, cecum and soft tissue inferior to the right scapula concerning for malignancy. Core tissue biopsy from the right scapular region was negative for bacterial or acid-fast bacilli stain but showed gram positive beaded rods identified as Nocardia. He was initially treated with intravenous sulfamethoxazole/trimethoprim and intravenous meropenem and then based on susceptibility transitioned to intravenous ceftaroline and oral sulfamethoxazole/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 one should have a high suspicion in patients who present with fever and disseminated lesions on imaging with plan for biopsy and culture of tissue early. In most cases, Nocardia can be treated successfully with appropriate antibiotics.

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 later converted to alternative therapy); patients 1 and 2 were also given intravenous fluids and calcitonin specifically for treatment of their hypercalcemia. Patient 6 was initially thought to have aspiration pneumonia but was hypercalcemic on presentation. Because of our experience with the previous patients, when we noted elevated 1,25 dihydroxyvitamin D (1,25(OH)2 VitD) and low PTH level, and his sputum was positive for PJP by DNA PCR.

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 1-alpha-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>Case</th>
<th>Age</th>
<th>Gender</th>
<th>Disease</th>
<th>PJP Progression</th>
<th>1,25(OH)2 VitD Level</th>
<th>PTH Level</th>
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<tr>
<td>1</td>
<td>49</td>
<td>M</td>
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Calcium trend
PO2479

Effect of UNOS Kidney Allocation System on Transplantation Rates for Veterans Waitlisted at Veterans Affairs Transplant Centers

Nidhi Aggarwal,1,2 Sankar D. Navaneethan,1 Jingbo Niu,1 Jenny S. Pan,1,2 Chandan Vangala,1,2 Ronald T. Cotton,1,2 Venkat Ramanathan,1,2 Michael E DeBakey VA Medical Center, Houston, TX; 3Baylor College of Medicine, Houston, TX.

Background: Impact of new Kidney Allocation System (KAS) on kidney transplantation (KT) rates for Veterans 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 waitlisting. Odds ratio (OR) was calculated adjusting for demographic factors, comorbidities, calculated Panel Reactive Antibodies (cPRA) and Estimated Post-Transplant Survival (EPST) 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 EPST (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 transplant listed in this early waitlisting period. But waitlist was longer 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 EPST score. Early benefit of KAS seen in non-VATC’s 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

<table>
<thead>
<tr>
<th>Center Type</th>
<th>Time Period</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>VATC</td>
<td>Pre-KAS</td>
<td>1.301 (0.77, 2.23)</td>
</tr>
<tr>
<td>VATC</td>
<td>Post-KAS</td>
<td>0.94 (0.57, 1.51)</td>
</tr>
<tr>
<td>Non-VATC</td>
<td>Pre-KAS</td>
<td>0.76 (0.47, 1.27)</td>
</tr>
<tr>
<td>Non-VATC</td>
<td>Post-KAS</td>
<td>0.41 (0.24, 0.70)</td>
</tr>
</tbody>
</table>

*p<0.01

PO2480

Lend Me Your Ear: An Unusual Presentation of a Transplant Complication

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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 y 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 obtained 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 cryptococci (Figure B). Patient was admitted to the hospital and further testing revealed positive CSF cryptococcal antigen, CT chest with nodular opacities, leading to a diagnosis of disseminated cryptococcal infection. She was treated with amphotericin B and fluconazole and eventually transitioned to oral fluconazole.

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

Abdul A Abdellatif,1 Lin Zhao,2 Paul M. Pelosso,2 Katya Cherny,2 Brad A. Marder,2 John D. Scandling,1 Kenneth G. Saag,3 Baylor College of Medicine, Division of Nephrology, Houston, TX; 2Horizon Therapeutics plc, Lake Forest, IL; 3Stanford School of Medicine, Division of Nephrology, Stanford, CA; 4University of Alabama at Birmingham, Division of Clinical Immunology and Rheumatology, Birmingham, AL.

Background: Gout is common and more severe in US kidney transplant (KT) recipients, with prevalence >10x 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 (NCT04807720) to examine pegloticase use in KT recipients.

Methods: Patients with uncontrolled gout (sUA ≥7 mg/dL, intolerance of or contraindication to ULT, and a1 of the following: tophi, chronic gouty arthritis, a2 flares in past yr) and functioning KT graft (eGFR ≥15 mL/min/1.73m2) were included in this trial. 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 studies, 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. 12 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

Serum uric acid (sUA) and kidney function parameters

PO2482

Minoxidil-Induced Chylous Asciates 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 (Halaz et al J Clin Med 2019;8:466). 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 y 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, amiodarone, lasix minoxidil, prednisolone, MMF, Tacrolimus, insulin, 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 transjugular 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 miopladine 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.
He also underwent diagnostic laparoscopy which also ruled out TB or any malignancy. This resulted in 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 vasodilation 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 atramatic drug induced chylous ascites.

PO2483
COVID-19 in Kidney Transplant Recipients: Experience from a Large Health System in Louisiana
Aldo E. Torres Ortiz, Joseph B. Walker, Juan Carlos Q. Velez, Jorge C. Garces. Ochsner Nephrology Ochsner Health System, New Orleans, LA.

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 11 March 2020 and 20 December 2020. We compared them with affectees who were not 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 < 0.002). 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. After 3 new relapses occurred (anemia and anemia 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 viral serum 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 KTR, 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.

PO2485
Adjusted Donor Age Score: Validity and Influence on Deceased Donor Offer Decisions
Christoph F. Mahler,1,2 Emma. Morganti,1 Dhirri Dosani,1 Anamika Adwaney,1 Rupert B. Bright,1 Damien Ashby,1 West London Renal and Transplant Centre 1Imperial College London, London, United Kingdom; 2Ruprecht Karls Universität Heidelberg, Heidelberg, Germany.

Background: Although a number of donor factors are known to affect outcome following deceased donor kidney transplantation, many units have no clear criteria for acceptance. Existing donor scoring systems, such as KDRI, perform poorly in the modern comorbid donor pool, and are difficult for patients to understand. Adjusted Donor Age (ADA) is a patient-friendly scoring system in which donor age is modified according to the presence or absence of a number of risk factors, as categorised by ADA decade (using cut-offs at 50, 60, 70 and 80 years) into quintiles (A – E) representing increasing donor risk (A – C: favourable, D: marginal, and E: unfavourable).

Methods: All deceased-donor kidney offers at a single centre were analysed over a 3 month period (beginning after the September change in UK organ allocation) during which ADA was optionally available to clinicians at the time of considering the offer. The effect of ADA on acceptance decisions and outcome in those transplanted were analysed.

Results: Out of 230 offers median(IQR) ADA was 67(56–76). Kidneys were transplanted in 24%, declined due to concern over donor risk in 44%, with recipient and other factors responsible for non-transplantation in 32%. In those identified as favourable by ADA (quintiles E – C, with exclusion factors), organs were rejected due to donor risk in 28/104 offers (27%), compared to 50/186 (27%) in the 2018 cohort. In those identified as unfavourable by ADA (quintile E) organs were transplanted in 0/38 offers (0%), compared to 10/66 (15%) in the 2018 cohort. At 1 month post-transplantation (N=55, from quintiles A – D only, since no organs from quintile E were accepted) one recipient remained dialysis dependent (from quintile D). In those with functioning transplants (N=54) recipient GFR was strongly correlated with ADA (R=0.52, p<0.001) and was seen to reduce across quintiles A – D (74, 55, 43 and 36 ml/min/1.73m2).

Conclusions: ADA is a patient-friendly score, calculated from donor age but adjusted for 12 potential risk factors, which can be used to guide acceptance decisions. At this early stage of familiarity, clinicians appear to be more persuaded by an unfavourable ADA quintile, than a favourable one. In this validation cohort, ADA strongly predicts early post-transplant outcome.

PO2486
Kidney Offer Calculator: The Risk of Accepting an Offer vs. Waiting for a Better Offer
Shan Shan Chen,1 Igor Litvinovich,2 Ashish Kataria,2 Yiliang Zhu,2 Christs Argyropoulos,2 Yue-Harn Ng,1 1University of Washington, Seattle, WA; 2University of New Mexico, Albuquerque, NM.

Background: Currently, no tools exist to facilitate patients with decisions to accept or refuse an offer. Using the scientific registry of transplant recipients database, we formulated a risk calculator for allograft failure and patient mortality risk (if offer accepted) vs. mortality risk if the patient refused.

Methods: Using a multi-state model approach, we created multiple competing risk models for: 1) first kidney offer or dying on wait-list without any offer; 2) if offer is refused, the probability of a) receiving a transplant vs. b) death and 3) if an offer is accepted, the probability of a) allograft failure vs. b) death. All models were adjusted for 12 potential risk factors, which can be used to guide acceptance decisions. At this early stage of familiarity, clinicians appear to be more persuaded by an unfavourable ADA quintile, than a favourable one.

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

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PO2487

Racial-Ethnic Disparities in Preemptive Kidney Transplantation Among Incident ESKD Adult Patients, 2006 to 2018

Navya Baranwal,1 Rebecca Thorsness,2 Shailender Swaminathan,1,3 Rachel E. Patzer,4 Rajnish Mehrotra,4 Amal Trivedi,5,6 *Brown University Warren Alpert Medical School, Providence, RI; 2Brown University School of Public Health, Providence, RI; 3Providence VA Medical Center, Providence, RI; 4Harborview Medical Center, Seattle, WA; 5Division of Transplantation, Department of Surgery, Emory University School of Medicine, Atlanta, GA.

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 kidney 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 white, blacks, Hispanics and Asians, adjusting for clinical, geographic, socioeconomic, and access factors.

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 Asian: 2.4 to 2.9%) (Figure). In age-sex adjusted analyses, whites had 3.9, 3.2, and 1.7 percentage point higher rates of PKT compared to blacks, Hispanics, and Asians, respectively. These differences persisted after adjusting for clinical, geographic, SES, and pre-ESKD nephrology care (Table). Among patients aged 19-44, whites had 8.0, 6.3, and 3.3 higher rates of PKT, compared to blacks, Hispanics, and Asians.

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.

PO2488

Lower Prevalence of Kidney Transplant Waiting List Among Smaller Facilities in Non-Metropolitan Areas

Eric D. Weinhandl,7 H. E. Hamilton,1 Loren S. Dalrymple,1 *Fresenius Medical Care, Waltham, Anguilla; 2Chronic Disease Research Group, Minneapolis, MN.

Background: The Percentage of Patients Waitlisted (PPPW) measures the percentage of patients at a dialysis facility who are 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

Michael Spiegel,1 Morenike Bello,1 Melanie Paris,1 Lisa Vo,2 Silas Norman,2 *American Kidney Fund, Rockville, MD; 2University of Michigan Transplant Center, Ann Arbor, MI.

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
plans reduce out-of-pocket spending on healthcare services by almost 50%, spending on hospital visits 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 adequate insurance 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 (HIPPP) 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 premiums on a plan that recipients were more likely to be a 65 (24%), more likely to be African American (38% vs. 34%), and had lower median incomes ($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

Catherine Butler,1 Aaron G. Wightman,1 Janelle S. Taylor,1 Claire Richards,1 Chun-fen Liu,1,2 Ann M. O’Hare.1,2 1University of Washington, Seattle, WA; 2VA Puget Sound Health Care System, Seattle, WA; 3Seattle Children’s Hospital, Seattle, WA; 4University of Toronto, ON, Canada.

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 intrusive and placed substantial demands on patients’ family members; 2) psychosocial valuation: the psychosocial transplant assessment could be subjective and invasive and placed substantial demands on patients’ family members; 3) surveillance over compliance: clinicians monitored patients’ adherence to a wide range of medical recommendations; 4) dispensemom 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 a lengthy, demanding, opaque evaluation process 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. Scar 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 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 discussed. Using a backward logistic regression, the presence of the nephrologist on the surgeon 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<0.001, 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<0.001; 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.

Funding: NIDDK Support, Clinical Revenue Support

PO2492

Predictors of Kidney Transplant Evaluation Non-Attendance

Christopher G. Ford,1 Eric Kruger,1 Yuridia Levy,1 Yiliang Zhu,1 Kellee Reynolds,2 Emilie J. Crockett,2 Mury Poo,2 M. Puttarajappa,2 Mark L. Unruh,1 Yue-Harn Ng,1 Larissa Myaskovsky.1 1University of New Mexico Health Sciences Center, Albuquerque, NM; 2University of Pittsburgh Medical Center, Pittsburgh, PA; 3University of Washington Medical Center, Seattle, WA.

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, health literacy), and knowledge (e.g., knowledge of KTE). We used latent 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, 95% CI 1.17-3.24).

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 FA VORIT 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

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

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PO2494

Patient Barriers to Kidney Transplantation on the Mexican American Border


Background: Hispanics are the largest minority group in the United States and are more likely to develop end-stage renal disease (ESRD) compared with non-Hispanic whites. However, Hispanics with ESRD are less likely to receive a deceased donor kidney transplant. We reviewed data from clinics on the Mexican American border to evaluate barriers to transplantation.

Methods: We gathered data from three dialysis clinics in Laredo, Texas, a city on the Mexican American border. It has a population of approximately 250,000 inhabitants of which 73% are white, 15% Hispanic, and 12% of other races. A number of patients were scheduled for living donor transplantation was evaluated. We also determined the number of patients that were referred but not listed and those that were not referred at all and investigated reasons for non-referral.

Results: A total of 285 patients were included in the analysis. 52 patients (18.2%) were waitlisted or denied for living donor transplantation. An additional 91 patients (31.9%) were referred but not yet waitlisted nor scheduled for living donor transplantation. A total of 140 (49.1%) were not referred. Of those not referred, the most common reasons included: deceased donor unacceptably heavy weight (4.2%), asynchronous donors, no organ offer and/or waitlisted (1.6%), peripheral vascular disease (1.0%). The most common reasons for referring patients were: patient's strong preference (1.4%), patient's advanced age (1.1%), and patient's health status (1.1%). In this analysis, 49% of the patients received a living donor transplant offer and 46% of those referred were waitlisted or scheduled for living donor transplantation. This is lower than previous studies showing a greater percentage of referred patients as waitlisted (up to 66% in some studies). Major barriers to referral included age, immigration status, and transportation limitations. The latter two barriers are likely more of a factor in a Mexican American border town than in other areas of the United States. Identifying these barriers highlight areas for improvement in access to renal transplantation for Hispanics.

Funding: NIDDK Support

PO2495

The Strength of Weak Ties and Living Donor Offers: A Multi-Site Social Network Analysis of Hemodialysis Patients

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Background: Increasing the rate of living donor kidney transplantation is crucial. Little is known about hemodialysis patients’ social networks and the members who offer to donate yet are never evaluated.

Methods: We administered a REDCap social network survey in an urban (Philadelphia) and suburban (North Brunswick) hemodialysis clinic. We asked participants to identify their strongest and weakest network members, who offered to donate, whose offers were accepted, and who got tested. We analyzed the associations between living donor offers and the size and strength of the connections in the networks. Strongly connected members are those connected to greater than 2/3 of the other network members.

Results: A total of 105 patients participated. Their mean age was 60 +/- 13 years. Half (54%) identified as male and 75% identified as black. Half were on the waiting list and unsure of receiving a kidney (50%). Half of the 527 network members identified, 133 offered to donate, 43 of these offers were accepted with 12 being evaluated for donation. Most (83%) network members were strongly interconnected within the participants network, however, a greater proportion of weakly interconnected network members offered a kidney donation compared to strongly connected members (31% vs. 19%, p = 0.02). Participants accepted a greater proportion of offers from weakly connected members than strongly connected members (56% vs 33%, p = 0.03). Although a greater proportion of strongly connected members were evaluated compared to weaker connected members this was not significantly different (36% vs. 17%, p = 0.16).

Conclusions: Weakly connected social network members tend to offer to be living donors more frequently than those of other degrees of connectedness. Unfortunately, most (89%) social network members who offer to donate never make it to the transplant center. Future interventions should focus on patients accepting living donor offers as well as identify methods to increase testing of interested donors especially those weakly connected in the network.

Funding: NIDDK Support

PO2496

Association of SNAP Benefit Use by Inner-City Kidney Transplant Recipients with Poorer Graft Function, Lower Fruit and Vegetable Intake, and Increased Psychosocial Stress

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Background: Longterm 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±9.9 yrs, 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=0.014) and eGFR 37.9±3.8 vs 38.8±3.8 mg/dl (p=0.06, min-p=0.003). SNAP+ did not differ for race, 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 medical problems (16% 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(<11.1±3 vs 16±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. 3...They also reported feeling less control over their health and less ability to handle daily stress. 4. These finding suggests that special attention should be paid to this population who have issues with social determinants that may affect kidney function.

Funding: None
Table 1. Adjusted outcomes for paired recipients of AA donor kidneys with white American recipients as reference

PO2498

Cardio-Metabolic Risk Factors in Kidney Donors at a Third-Level Hospital of Care in Mexico

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Background: 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% IC. 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. 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 42.7 ± 10.7 years; the mean BMI 26.3 ± 5.4, with a mean GFR 101.9 ± 13.4 (61-136) ml/min. 28% of donors smoked, 7% had SBP risk and 27% DBP risk, 60% had BMI> 25, 4% had anemia and 13% hypobulinemia; 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 1 to 4 CRFs with frequencies to 126-34%.

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 pleiotropic effects including anti-cancer properties and may prevent the development of post-transplant malignancy (PTM). Whether this association is due to inflammation, iron overload or combination of the two.

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 vs <10.5 g/dL) and to either cholecalciferol 1000 IU/day or control. PTM was a prespecified secondary outcome.

Results: Patients were 51±12 years, 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 in the cholecalciferol group after Month 6 whereas it did not change in the control group throughout the study period. A total of 7 PTMs developed 2 years of the follow up; 2 lung cancers, 1 breast cancer, 1 gastric cancer, 1 testicular cancer, 1 renal cell carcinoma, and 1 myelodysplastic syndrome. There was no between-group difference in the incidence of PTM in the hemoglobin target arm (i.e., n=3 [4.1%] vs. [5.1%] in the high vs low Hb target groups, respectively; P=0.77). In the cholecalciferol arm, all 7 PTMs developed in the control group while none was observed in the cholecalciferol group (i.e., 9.1% vs 0%, respectively; P=0.007).

Conclusions: The incidence of PTM was not increased by aggressive anemia correction with ESA and was reduced by cholecalciferol supplementation among KTRs. Large clinical trials with a long-follow up period are needed to validate these findings. Registered at ClinicalTrials.gov (NCT01817699).

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 post transplantation have 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 ferrite value during the first year post transplantation. Ferritin and transferrin were logarithm transformed and serum ferritin was also analyzed as a dichotomous variable with 500 ng/ml as a cutoff value. Primary outcome was the composite of graft and patients’ survival. Secondary outcomes included death censored graft loss. Univariate and multivariate Cox models 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, and post-transplantation delayed graft function. By univariate Cox analysis, ferritin level above 500 mg/ml was 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). By extensive 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). The results were similar when ferritin was evaluated as continuous variable. In contrast, transferrin saturation was not associated with overall death and censored death graft survival. High ferritin 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 Backward, Symbol Digit Modalities Test, Trail Making Test-A) and executive functioning (Trail Making Test-B, Digit Span Backward). 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 <100 μg/L or ≥100 μg/L with transferrin saturation (TfS) ≥20%. We used multivariable linear regression analysis 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/1.73 m²). ID was present in 289 (73%). ID and iron neurocognitive scores are presented in the table. Conclusions: ID, low ferritin and low TfS 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.

PO2502

Anemia and Decreased Muscle Mass and Muscle Strength in Kidney Transplant Recipients

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Background: Anemia is highly prevalent in kidney transplant recipients (KTRs). It is known that anemia impairs quality of life, especially physical functioning. Although surmised, data about the latter in KTRs specifically are scarce. Hence, we aimed to investigate the association between anemia and muscle mass and muscle strength in KTRs.

Methods: In a prospective study among KTRs participating in the TransplantLines Biobank and Cohort study, we used KTRs >1 yr post-transplant with data on hemoglobin (Hb) levels and muscle mass. Muscle mass was assessed in two ways: by using 24-hour urinary creatinine excretion and with bioelectrical impedance analysis (BIA). Muscle strength was determined by means of hand grip strength using a dynamometer. The mean overall hand grip strength was calculated out of three attempts of both hands with 30 seconds recovery time in between. Anemia was defined as an Hb <12 g/dL for women and <13 g/dL for men, according to WHO definitions. We used multivariable linear regression analyses to assess associations between anemia and muscle mass and strength.

Results: We included 824 KTRs (age 56±13 years, 60% males, eGFR 52±18 mL/min/1.73 m², serum HB 13.5±1.8 g/dL). Anemia was present in 30% of KTRs. Hb levels were associated with creatinine excretion, independent of age, sex, eGFR, BMI, hs-CRP, smoking status, alcohol use and the use of RAAS-inhibitors, statins, calciuminhibitors, proliferation inhibitors or prednisolone (β<0.01). Similarly, the presence of anemia was independently associated with a lower creatinine excretion (st.β=-0.14, P<0.001). Similarly, the presence of anemia was independently associated with a lower creatinine excretion (st.β=-0.09, P=0.021). Hb levels (st.β=-0.20, P=0.001) were also independently associated with muscle mass, estimated using BIA resistance measurements. In line with muscle mass parameters, Hb (st.β=-0.18, P=0.001) and anemia (st.β=-0.01, P=0.005) were associated with handgrip strength independent of potential confounders as well.

Conclusions: Low hemoglobin levels and anemia are both strongly associated with lower muscle mass and muscle strength in KTRs, likely impairing physical functioning. Future research is needed to address whether correction of anemia improves physical performance in KTRs.

PO2503

Sevelamer-Associated Gastrointestinal Complications in Kidney Transplant Recipients

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Introduction: Sevelamer (SV) is a resin based oral phosphate binder used commonly in chronic kidney disease (CKD) patients. Clinical trials performed for approval for clinical use showed mild to moderate gastrointestinal (GI) intolerance in a minority of patients. In general clinical use of SV in CKD patients, there have been case reports of more serious GI problems than were reported in original trials, including GI bleeding and colonic complications including colitis and perforation. The majority of patients receiving kidney transplants have required long term oral phosphate binders at the time they are transplanted, often using SV. Delayed graft function (DGF) early post transplant may require ongoing use of oral phosphate binders to control hyperphosphatemia.

Case Description: We report 3 cases of significant GI morbidity in association with SV occurring in transplant recipients within the first 2 weeks after kidney transplantation. In one patient, the post transplant course was complicated by sepsis due to perforated colonic diverticulum in the context of preexisting diverticulitis disease; surgical intervention showed SV crystals associated within the area of bowel perforation. Two patients had severe upper GI symptoms and abnormal findings on upper endoscopy, including severe esophagitis and esophageal ulceration. SV crystals were found in the biopsies of abnormal areas. Both patients had long-term use of SV prior to transplantation, whereas one patient was treated with SV for a short time only after transplantation. All had required more than one phosphate binder for long-term control of hyperphosphatemia; two required cinacalcet for management of secondary hyperparathyroidism.

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 (KTRs) 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 death). Both cFGF23 and iFGF23 concentrations were significantly higher in patients who had adverse outcome than without adverse outcome (24.59 [11.43-87.83] vs. 10.67 [5.99-22.73] pg/mL; p<0.0001 and 82.24 [18.63-159.0] vs. 29.04 [15.23-60.65] 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=0.02) 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.

Figure 1. Multivariable-adjusted Cox regression analyses of composite endpoint: graft loss or all-cause mortality. Model 1: adjusted for eGFR; Model 2: adjusted for eGFR, age, sex, time on dialysis, pre-donation smoking, donor age, donor sex, donor family history of cardiovascular disease, recipient race, recipient BMI, recipient age, recipient Systolic BP, recipient smoking status, recipient body mass index and preemptive. HR: Hazard Ratio; 95% CI: 95% Confidence Interval; p-value: p-value for the HR.

PO2505

The Time Is Now: Reducing Waiting Times in Minority Populations


Background: A significant limiting factor to transplantation resides on waiting time based on blood type. Historically candidates in blood groups B and O experience higher waiting times for kidney transplantation. Our center has worked to increase the rate of acceptance in kidney donors that would have previously been discarded to try to maximize the donor pool for these blood groups.

Methods: We retrospectively analyzed 1287 consecutive deceased donor kidney transplantations from 2015 to 2019. This cohort was chosen to ensure baseline was after allocation system changes, so the change is a result of change in practice at our center. Average waiting time to transplantation and renal transplantation rates were analyzed based on ABO stratification as well as ethnicity to compare longitudinal disparities.

Results: We observed a decrease in waiting time across all blood types (Figure 1) over the 5 year period of this study. There was a substantial benefit in blood type B recipients with a 6.4 year decrease in average waiting time from 2015 to 2019. Waiting time in
PO2506
Ethnic Disparities in Hospitalization After Deceased Donor Kidney Transplantation
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Background: The cause of disparities in hospitalization after deceased donor kidney transplantation (DDKT) is unknown. In a prior study, we found that African American (AA) recipients were more likely than European American (EA) recipients to have hospitalizations after DDKT. Here we evaluate the contribution of two possible factors: (1) donor factors (mortality, preservation, and pre-morbid factors) and (2) recipient factors (medical comorbidities) to hospitalizations after DDKT.

Methods: We reviewed the records of 9,068 patients who received a DDKT from 2006-2015. Using logistic regression, we evaluated the contributions of donor and recipient factors to hospitalizations after DDKT, adjusting for transplant era (2001-2005, 2005-2010, after 2010), the kidney donor index risk (KDR), estimated post-transplant survival (EPS), donor- and recipient age, sex, recipient insurance, prior employment status, delayed graft function (DGF) and cold ischemia time.

Results: HRs were higher among recipients of kidneys from AA donors compared to EA donors (odds ratio 1.41, 95% CI 1.29-1.52) after adjusting for the donor mortality (KDR), estimated post-transplant survival (EPS), donor- and recipient age, sex, recipient insurance, prior employment status, delayed graft function (DGF) and cold ischemia time.

Conclusions: HRs for the DRPs have increased over time with higher rates among recipients of AA DD kidneys. Additional donor-level factors may contribute to the hospitalization rate after DD kidney transplantation.

Funding: Clinical Revenue Support

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 ViD (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 ViD group and 95 in Placebo group. Dropout during this study were 3 KTRs in Vitamin D group and 2 in Placebo group. In ViD 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 were 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.

PO2508
Effects of Arteriovenous Fistulas on Outcomes of Kidney Transplant Recipients
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Background: Arteriovenous fistulas (AVFs) may exacerbate cardiovascular events (CVE) after kidney transplantation (KTx). We aimed to investigate the long-term effects of AVFs on KTx outcomes.

Methods: Prevalent 168 recipients were categorized at median 2yr. after KTx: recipients with functioning AVF (n=73), recipients with non-functioning AVF (n=62) and recipients without AVF (n=33) on pre-KTX peritoneal dialysis or underwent preemptive KTx. Baseline characteristics, echo findings and endothelial function were compared. During a median 11yr. follow-up after enrollment, CVE were defined as acute coronary syndromes or cerebrovascular accidents; additional outcomes included eGFRs at baseline and end of follow-up, graft failure and death.

Results: Demographic, clinical, laboratory and echo characteristics and endothelial function at enrollment were not significantly different across all groups (Table 1). During follow up, CVE occurred in 9 (12.3%), 5 (8%), and 0 (12.1%) patients in IAVF, nIAVF and noAVF groups, respectively. Groups were comparable regarding graft and patient survival rates (p=0.70). During follow-up, CVE rates were not significantly different across all groups in the period from D1 to D11, as well as from D11 to D23. Groups were comparable regarding graft and patient survival rates (p=0.13 and p=0.87, respectively). During follow-up, functioning AVFs thrombosed in 5 (7%) and were surgically closed in 20 (27%) patients in IAVF group. CVE rate was similar in patients with thrombosed (20%), closed (5%) and still functioning (15%) AVFs (p=0.47). Patient and graft survival rates were significantly lower in recipients with still functioning IAVFs (77% and 73%, respectively) compared to IAVF patients with thrombosed (100% and 100%, respectively) and closed (100% and 95%, respectively) AVFs (p=0.05 and 0.03, respectively).

Conclusions: Long-term CVE rate is similar in KTx recipients with and without patent AVFs. In a subgroup of KTx recipients with functioning AVFs, closure and thrombosis of AVFs may be associated with higher rates of patient and graft survival.
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, 602 (53%) required dialysis, and 867 (76%) received living donor KTx. After a median follow-up of 74 months there were 229 (20%) deaths and 217 (19%) CV events, of which 92 (40%) were cardiac, 86 (39%) were vascular, 39 (18%) had both. 119 patients had an isolated CV event and 98 had recurrent CV events (median 3 (range 2,4)). Multivariate analysis revealed the following independent significant predictors of CV events: older age, prior history of CV event, diabetes, hypoalbuminemia and measured GFR. Compared to recipients with no CV events and those with an isolated event, recipients with recurrent CV events had increased: mortality (15% vs 38% vs 45%, p<0.0001) and graft failure (14% vs 26% vs 40%, p<0.0001). Hazard ratio for mortality associated with isolated CV events was 2.66 (1.90-3.73) compared to a HR 3.06 (2.18-4.29) for recurrent CV events, (14% vs 26% vs 40%, p<0.0001). [Figure 1]. Predictors of multiple CV events included measured GFR and age, prior history of CV event, diabetes, hypoalbuminemia and measured GFR. Compared to recipients with no CV events and those with an isolated event, recipients with recurrent CV events had increased: mortality (15% vs 38% vs 45%, p<0.0001) and graft failure (14% vs 26% vs 40%, p<0.0001). Hazard ratio for mortality associated with isolated CV events was 2.66 (1.90-3.73) compared to a HR 3.06 (2.18-4.29) for recurrent CV events, (14% vs 26% vs 40%, p<0.0001). [Figure 1].

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.
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 excess 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±33 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

PO2513
Abstract Withdrawn

PO2514
Median Waiting Time of Kidney Transplant Candidates with Initial Estimated Post Transplant Survival Score >90% According to Organ Procurement Organization Waiting Time
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Background: The kidney allocation system (KAS) and the estimated Post Transplant Survival (EPTS) score were introduced in the United States in December 2014. The transplant rate among very high EPTS candidates (>90%) may be impacted by lack of KAS priority, geographic factors based on the living donor procurement organization (OPO), and/or differences in waitlist mortality/delisting. Here we study the impact of new KAS among the candidates with EPTS>90%.

Methods: The Organ Procurement Transportation Network/United Network for Organ Sharing (OPTN/UNOS) data of all first-time transplants have been collected from 2015-2018 were included. Individuals listed for multiple organs, at multiple centers, and age >18 years were excluded. The outcomes included median waiting time to transplant, transplant rate, death rate and delisting rate among candidates with EPTS>90% compared to those with EPTSe<90%. Median waiting time was calculated by Kaplan-Meier model with censoring for still waiting candidates.

Results: A total of 114,870 candidates were included. Candidates with EPTSe>90% (9.74%) had a lower rate of overall transplant compared with EPTSe<90% (30.3% vs. 45.9%, p<0.001), higher rate of deceased donor transplant (87.6% vs. 60.9%, p<0.001), lower rate of living donor transplant (12.8% vs. 39.1%, p<0.001), higher death rate (8.5% vs. 5.73%, p<0.001) and higher delisting rate (22.9% vs. 13.3%, p<0.001). Overall median waiting time to transplant was 444 days (range 188-1,042 days among OPOs) compared to 1,025 days (range 160-1,633 days among OPOs) in those with EPTSe<90% (p<0.001).

Conclusions: Candidates with EPTSe>90% had a longer median waiting time compared to total waitlisted in all but one OPO. Median waiting times were heavily influenced by the lower overall rate of kidney transplantation and living donor transplantation in this group.

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 parental 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.
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-transplant PDC exit-site infections has been reported. In the US guidelines for PDC 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 PDC 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, 16had a deceased donor, and 2 underwent 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 PDC 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.

PO2517
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 ± 0.26±0.25 kg). The other 15 (37.5%) patients achieved post-HD weights higher than their usual targets (+0.72±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 set target dry weight before transplantation when feasible.

PO2518
Trends in Time to Graft Loss by Dialysis Exposure
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Background: Preemptive transplantation is believed superior to transplantation after dialysis initiation, and transplantation after shorter dialysis exposure is better than with longer exposure. Considering recent registry reports of improved survival on dialysis, we examined temporal trends of graft loss by time on dialysis prior to kidney transplantation.

Methods: Using the US Renal Data System, we identified adults who underwent first kidney transplant between January 1, 1995 and July 31, 2017. We excluded recipients of simultaneous multiorgan transplants. We used an adjusted Cox model to examine the association between dialysis exposure prior to transplantation (categorized as preemptive, ≤6 months, 6 months-1 year, 1-3 years, 3-5 years, and >5 years) and graft failure within 3 years of transplant. Our model was adjusted for donor and recipient demographic factors, donor type, cause of ESKD, BMI, panel reactive antibodies, diabetes status, and cardiovascular disease status. We organized patients into the following transplant era groupings: 1995-2001, 2002-2006, 2007-2011, and 2012-2017.

Results: A total of 277,158 transplant recipients were studied and 38,364 had graft loss within 3 years. In each era, the hazard ratio for graft loss was lower for preemptive transplant recipients (referent group) compared to all other dialysis exposures except for the group that received less than 6 months of dialysis in the 2012-2017 era (HR 1.06 (95% CI 0.91-1.24)). Those exposed to more than 5 years of dialysis exposure had the highest risk for graft loss within 3 years in all eras, with over 2 times the hazard compared to the referent group in the most recent eras (figure).

Conclusions: Although preemptive transplantation offers the best graft survival across the study period, those transplanted within 6 months of dialysis initiation had similar 3-year graft survival to those transplanted preemptively in the most recent era. The negative association between the longest duration of pre-transplant dialysis and post-transplant survival persists.

Funding: NIDDK Support
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 patterns given lack of consensus surrounding many aspects of pre-transplant workup. The differences in national practice patterns related to transplant eligibility assessments have not 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 begun, 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.

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PO2520

Post-Transplant Diabetes Mellitus in a Single Pediatric Kidney Transplant Center: Risk Factors, Outcomes, and Characterization of Clinical Course
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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 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
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.
PO2525

Health System Encounters in Kidney Transplant Recipients Converted from Immediate-Release Tacrolimus Capsules to Extended-Release Tacrolimus Tablets

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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 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 in an ER-TAC financial assistance program. Median (IQR) time since transplant was 333 (211-1,483) days. KTRs converted to ER-TAC for: 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. Closer follow up may be beneficial for these KTRs. Future research should determine if reasons for conversion resolved with 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 trajectories, ACGL, and mortality by 1-year pre-KT weight change, defined as stable 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 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.

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 post-KT weight gain and intentional weight loss. Those with post-pre-KT 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 (HR 2.31 [1.24,3.3], p<0.008) and ACGL (HR 2.62 [1.24,3.3], p<0.005) relative to stable weight.

PO2527

Incidence, Risk Factors, and Outcomes of Post-Transplant Erythrocytosis After Kidney Transplantation

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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 called 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 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 to 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-heart-beating transplant. 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), higher BMI (HR: 0.97, 95% CI 0.93-0.99, p<0.05) was less likely to develop PTE, while pre-emptive 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

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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 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.

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 post-KT weight gain and intentional weight loss. Those with post-pre-KT 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 (HR 2.31 [1.24,3.31], p<0.008) and ACGL (HR 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.

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PO2520

Obesity and Poorer Renal Allograft Function: Analysis of Longitudinal Data

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Background: Obesity is associated with worsened allograft function, but its effect on allograft function after established baseline allograft function at a 12-week post-kidney transplant (KT) is unclear.

Methods: All 105 KT recipients were divided into obese (BMI ≥ 30 kg/m^2) 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 m^2 (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 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 m^2 for every 1 week after KT. Posterior expected median eGFR at 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 vs. 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. donors without 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
Table 1. Hazard ratios of death-censored graft loss according to BMI and presensitization status

<table>
<thead>
<tr>
<th>Low BMI (non-sensitized)</th>
<th>Reference</th>
<th>Adjusted BMI (65-69)</th>
<th>P-value</th>
<th>Adjusted BMI (&gt;69)</th>
<th>P-value</th>
<th>P-value for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unadjusted HR (95% CI)</td>
<td>Reference</td>
<td>Adjusted HR (95% CI)</td>
<td></td>
<td>Adjusted HR (95% CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>1.00</td>
<td>1.00 (0.90-1.12)</td>
<td>&lt;0.01</td>
<td>1.00 (0.86-1.16)</td>
<td>0.85</td>
<td></td>
</tr>
<tr>
<td>High BMI-sensitized</td>
<td>2.30</td>
<td>2.30 (1.73-3.07)</td>
<td>&lt;0.001</td>
<td>2.30 (1.57-3.32)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>High BMI non-sensitized</td>
<td>1.69</td>
<td>1.69 (1.30-2.19)</td>
<td>0.002</td>
<td>1.69 (1.28-2.23)</td>
<td>0.02</td>
<td></td>
</tr>
</tbody>
</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.

Methods: KT recipients with suspected oxalosis due to any of the following: inflammatory bowel disease, bariatric surgery, or pancreatic insufficiency from 2015 to 2019 were included. At our institution, pre-KT serum oxalate>30mcmol/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 years (median) prior to KTx. 39% had history of nephrolithiasis. Median peak serum oxalate (SOx) pre-KTx was 24mcmol/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>30mcmol/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-KTx. The median duration of dialysis after KTx was 13.5days. After median follow up of 27.9 months, MD showed significantly lower serum calcium and phosphorus (GFR) was 47.6±1.21mL/min/1.73m2 and 68% of patients had GFR <60. One-year GFR was 48.4±2.4mL/min/1.73m2 which is lower than expected 1-year GFR for our Transplant Center (mean GFR 58±2.06mL/min/1.73m2). RYGB patients (n=24) had lower GFR vs patients with other EH causes (n=7) (1 year: 48.7±2.04.4±5.6±4.9; last follow-up 47.3±2.11 vs 57.5±14.4 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±2.83 mL/min/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 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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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 MCV 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 (MCV 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±17 years old, 74.3% male, 91.4% white, 22.9% with diabetes, and 91.4% with hypertension. Controls were 54.2±20 years old, 74.3% male, 80% white, without diabetes, and 14.3% with hypertension. Baseline MCAV was similar in the two groups, but the response during moderate intensity exercise differed; CVR for KT recipients was 8.12±0.8 cm/s compared to 12.9±1.4 cm/s for controls (p=0.003) and target workload for KT recipients was 84.1±2.8 watts compared to 123.1±5.3 for controls (p=0.001) (Table 1).

Conclusions: KT recipients have a blunted middle cerebral artery hemodynamic response to exercise compared to healthy controls. This may be due to vascular disease and can explain the higher white matter disease, dementia, and stroke in this population.

Funding: Other NIH Support - Grant K23-AI055666, Commercial Support - Veloxis and Novartis

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.

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

Underline represents presenting author.
PO2535

Longitudinal Physical Performance Following Kidney Transplantation
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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 dialysis vintage was 7 years. 49% had diabetes mellitus, 18% had coronary artery disease, 5% had cerebrovascular disease, and 10% had peripheral arterial disease (PAD).

Conclusion: 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.

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 included. 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 only 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 = 0.10) nor mortality (0.48) among recipients with vs. without FD.

Conclusion: 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 assess 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%) receiving first KTx, 41 (75.9%) required dialysis, and 17 (30.9%) had stone event prior to KTx. Twenty one (37.5%) had at least 2 stones in the allograft, median 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 a 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 (17.6%), 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.

Conclusion: 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 Research 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 calculated exposure time for each drug level interval during the first year following transplantation, defined as the cumulative number of days at each interval. This measure
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 interval level of 5-6ng/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 5ng/ml (HR 1.56, p<0.001). These results remained consistent in an extensive multivariate analysis (HR 1.44, p<0.001) and were not significantly changed when we analyzed for death-related 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 levels above 6ng/ml was significantly associated with increased risk of graft loss in most studied subgroups including age, gender, donors with high immunologic risk recipients, except for the subgroup of recipients with diabetes. **Conclusions:** Prolonged exposure time to TAC trough level between 5-6ng/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 6ng/ml during high immunologic risk recipients, except for the subgroup of recipients with diabetes.

**PO2539**

High Intraepithelial Variability of Tacrolimus in Pediatric and Adolescent Renal Transplant Recipients Is Associated with Worse Graft Outcomes

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**Background:** High intra-patient variability (IPV) in tacrolimus (TAC) levels has been associated with the development of de novo donor-specific antibodies. The degree of TAC IPV in relation to poor graft outcomes in pediatric kidney transplant patients is unknown.

**Methods:** Patients 0-25 years who were on TAC from 01/2010-01/2018 at a single center were considered for inclusion. Minimum required follow-up time was 12 months. Primary outcomes were formation of C1q+ de novo DSAs (dnDSAs) and high, dnDSAs were identified by routine screening or at investigation of allograft dysfunction. TAC IPV was defined using the mean coefficient of variation (CV) over the immediate 6-month time period prior to each TAC level. All available TAC levels were included in the analysis. Mean CV was calculated using CV from 10 months post-transplant until end of follow-up. Patients were followed until 01/03/2019 or until graft loss. Analyses were performed using descriptive statistics and the Mann-Whitney U test.

**Results:** 225 pediatric kidney transplant patients met inclusion criteria. Median age was 12.5 years (range 15 mo.-21 yrs.). 46% were female, and 24% received a living donor transplant. 51 formed C1q+ dnDSAs and 174 did not. Among patients who formed C1q+ dnDSA, 13/51 (25.5%) lost their graft, compared to 2/174 (1.1%) in patients who did not form dnDSA by C1q. C1q+ dnDSA forms were found in 12 patients; 4 patients did not form dnDSA by C1q (median CV 33.9% vs 26.1%, p=0.0001), including when stratified by age subgroups of 0-12 years (p=0.0217) and 13-25 years (p=0.0001). Patients with graft loss had higher mean CVs compared to those who did not have graft loss (median CV 39.0% vs 25.8%, p=0.0006).

**Conclusions:** High tacrolimus IPV was associated with C1q+ dnDSA formation and graft loss. Tacrolimus IPV is a potential prognostic tool for optimizing transplantation outcomes.

**PO2540**

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-transplant. 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 regimen were collected. According to KPSS, RTRs were classified according to time of transplantation 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 were important novel determinants of functional capacity post-transplant and merit considerations during transplant selection and subsequent immunosuppressive therapeutic planning.

**PO2541**

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 favoring 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 121 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 preconception to the third trimester level was slightly different (~3.1% in CNI+ vs 2.2% in CNI-, p=0.05). In both groups, a postpartum on discharge were collected according to 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.

**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.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
PO2542
The Natural History of Waitlist Candidates in the United States
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Background: Estimates of time to deceased-donor transplantation (DDKTX) generally fail to take into account the competing risks of mortality. Understanding the natural history of KT registrants - their chance of DDKTX/LLKT/mortality based on individual characteristics - can inform referrals for transplantation, counseling for transplant candidates, and allocation policy.

Methods: Using SRTR data on 186,174 waitlist registrants 12/2014-12/2019, we modeled time to DDKTX, LLKT, or waitlist mortality in a competing-risks framework, overall and for clinical and demographic 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 DDKTX/LLKT/mortality based on candidate characteristics.

Results: Among all candidates, 5-year cumulative incidence of DDKTX/LLKT/other removal was 17.3%/34.4%/15.7%/18.1% respectively. 85% of DDKTX recipients received LLKT within 2 years of listing. Pediatric registrants had substantially higher incidence of DDKTX than waitlist mortality (61.7%/vs 1.1%), but adults had higher combined of waitlist mortality/other removal DDKTX, particularly patients above age 65 (44.4%/vs 32.3%) (Figure). Center-level 5-year incidence of DDKTX (DDKTX) 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 organ pool.

Funding: NIDDK Support

PO2543
Unusual Cause of Calcium Oxalate Nephropathy in a Renal Allograft
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Introduction: Crystalline 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 homozgyote 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 crystalization consistent with oxalate. Her particular mutation responds very 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.

Diagnosis: Hyperoxaluria type 1 (PII 1) 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 PI 1 is 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 PI 1 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 reported in 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. The vitals were unremarkable on admission and was anemia was noted. Lab findings showed Na 139, K 5.5, Cl 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 972 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 MMF levels must be checked and MMF dose should be adjusted accordingly.

PO2545
Prophylactic Use of Eculizumab and Graft 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 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.
PO2547

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 12/2016 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 level 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 mg/dL, Mg level 1.5 - 1.8 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.

Funding: Private Foundation Support

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 ≥50%) 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-PXM, 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.

PO2549

Reassessing RenalTransplantation in Light-ChainDeposition 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.

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

Underline represents presenting author.
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 the 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 several cases.

Case Description: A 29 year old female with history of living donor kidney transplant due to Henoch Schönlein 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; however, given risk of nephrotoxicity, was ultimately deferred after response to conservative treatment.

Discussion: Recurrence of HSP was in the broad differential given the initial presentation. Given its rarity, a paucity of cases and epidemiologic literature exists in illustrating allograft failure due to adenovirus nephropathy. Further research is not only needed to expand awareness of its presenting features and characteristic biopsy findings, but also, to limit more familiar culprits in masquerading as the elusive adenovirus infection, particularly in light of indeterminate therapeutic modalities.

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. Plasma levels should be monitored post treatment to ensure resolution. This approach allows performing biopsy to confirm diagnosis and initiate therapy expeditiously. PLA2R Ab levels should be monitored to direct care: decreasing 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 titer 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 treatment to ensure resolution. This approach allows stratification and directed therapy of patients with MN undergoing transplantation and avoids over treatment.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
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-cell mediated rejection (2, I2) 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*01:03. 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 dexamethasone, 10 sessions of PLEX and intravenous immunoglobulin (IVIG), and Rituximab. Her Cr improved to 1.2 mg/dL but DSA remained positive. Later on he was restarted on Etanercept which was withdrawn 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 intravenous immunoglobulin (IVIG), and Rituximab. Repeat DSA showed reduction in A2, but no change in DQ7. Her 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 withdrawn in transplant recipients.

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 of ≥3 or ≥4 and sub grouped per interstitial inflammation (i score=0 and >0)and compared to biopsies with both c i t c v c v ≥ 3 and r o=0.

Results: Biopsies were done at a median 12.5 months after kidney transplantation. The histopathological diagnoses were as follows: 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 (10.8%), 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), c i t c v ≥ 3 (p=0.0485), c i t c v ≥ 3 with interstitial inflammation > 0 (p=0.0001), microvascular inflammation (p=0.0052), C4d positivity (p=0.008), serum creatinine at time of the biopsy (p=0.0001), and spot urine protein/creatinine (<0.0001). In the multivariate analysis c i t c v ≥ 3 with i>0 has the highest hazard ratio followed by c i t c v ≥ 3 with i=0, c i t c v ≥ 3 with i=0, black race, creatinine, and proteinuria.

Conclusions: Interstitial inflammation is the best predictor for allograft loss after clinically indicated kidney biopsy regardless of the severity of chronic allograft injury.

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 creatinine (Cr) from baseline of 1.3-1.5 mg/dL associated with de novo donor specific antibodies (DSA) to DR11 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. Her 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 withdrawn in transplant recipients.

PO2556

Molecular Analysis of Renal Graft Biopsies: Comparing the Edmonton 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 pathology by NanoString analysis, which was developed for formalin-fixed paraffin-embedded-derived (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 the development of 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,
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 outcomes.

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 regions in the number of biopsies performed (region 5 vs. region 9, p = 0.2). 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 regions in the number of biopsies performed (region 5 vs. region 9, p = 0.2). 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 Québec, the Hôtel-Dieu de Québec 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.

PO2559

Outcomes of Biopsy-Proven Acute Rejection (BPAR) in ABO-Incompatible Kidney Transplants (ABOi KTx) Compared with a Propensity-Matched Cohort of ABO-Compatible Transplant Recipients (ABOc KTx)

Background: Although available outcome data is equivocal for its non-inferiority compared to ABOc KTx, the data on graft survival after an BPAR episode are scarce in ABOi KTx.

Methods: Single centre, retrospective study, ESRD patients transplanted between 2014 and 2019 were included. Among 100 ABOc KTx, 37 had BPAR and were included. A matched cohort of 37 ABOi KTx with BPAR were identified as controls from 680 ABOc KTx by propensity score matching (nearest neighbour matching) using recipient age and sex, donor age and sex, donor GFR, HLA match and induction agent used as matching covariates. Rejection rates, BANFF score, response to antirejection treatment, overall graft survival, post rejection graft survival were compared between both the groups.

Results: The hazard ratio for BPAR was 1.4 in ABOi KTx, compared with ABOc KTx. Overall graft survival at 1, 3 and 5 years were 86%, 72% and 50% in ABOc KTx; 97%, 91% and 79% in ABOi KTx, respectively. The post BPAR graft survival at 1 and 3 years were 80% and 63% in ABOi KTx; 92% in both 1 and 3 years in ABOc KTx. ABMR was more common in early period in ABOi KTx and ACR was predominant in late period in both the groups. The response to anti-rejection therapy were similar between two groups, no response group (NR) in the ABOc KTx had the poorest graft outcome, complete response group (CR) in the ABOi KTx had the best graft survival. Between CR, PR (partial response) and NR groups, no histopathological parameters were found significant in ABOc KTx, whereas in ABOi KTx, T1 scores were higher in PR compared to NR group.

Conclusions: The graft survival after an acute rejection depends upon response to antirejection therapy. After an episode of acute rejection, the overall post rejection graft survival was inferior in ABOc compared to ABOi KTx.

Kaplan-Meier curve of 5-year allograft survival for pediatric kidney transplant patients by donor kidney glomerular sclerosis (GS)
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 (DFG). 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 KF 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 (N=16) and No Cardiac Arrest (No-CA, N=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 APOL1-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 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 C/W collapsing FSGS. If negative, including CMV and C4d. Donor tested for and found to be homozygous for APOL1 G1 mutations conferring donor derived APOL -1 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 RAA5 blockade, antivirals & immunosuppression. He cleared his CMV Viremia promptly. However, EBV viremia worsened. Eventually, in May 2019, received Rituxinab with resolution of EBV viremia. He is 18 months out from 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 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 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 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 his CMV Viremia promptly.
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 subependymal 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. Semi quantitative 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.

Renal ultrasound with Doppler (left), renal angiography (middle), post-coiling (right)

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.
Discussion: Renal artery stenosis is a correctable cause of hypertension and graft dysfunction in KTx. Graft renal artery kinking is rare, even more so in association with stenosis, worsening its prognosis as kinking makes 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.
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 kidneyTx, 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 where 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.

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). Graph 1.

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.

Graph 1. Creatinine and Creatinine Clearance Levels (Means±SEM)
PO2571
Patient and Graft Outcomes of Kidney Transplant Recipients with Anti-Human Neutrophil Antigen Antibodies

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, 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 (PKCD) 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 (f/u), 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, PKCD 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 NLGN 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.

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 fistulae 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 into 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 lateAMR. The objective was to determine the effect of TPEonGFR at 0, 1, and 3 months postTPE.

Methods: Retrospective study that included patients with a renal transplant of the CMN“November 20”in Mexico City, from 2016-2019, undergoing membrane TPEforAMR. 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 HLAClass II DSA(66%), specifically vs DQandDR (57.2% and 28.8%). There was a significant difference between preTPE GFR and at the end of treatment(Δ=0.015, r=0.53), and no significant differences between preTPE GFR, with 1or3 monthGFR(p=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.
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 flow cross-match compatible kidney transplant between December 2014 and May 2020. We excluded patients who underwent pretransplant desensitization, simultaneous multi-organ transplantation, or received 0-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 d/dNDSA 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 highly sensitized 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.

PO2578
Risk Factors and Outcomes of Acute and Chronic 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 survival (DCGS), we performed Cox proportional hazards analyses including AMR as a time-dependent covariate.

Results: Among 3131 kidney and kidney-pancreas transplant recipients, there were 194 with biopsy proven T-Cell Mediated Rejection (TCMR) in the first post-transplant year. 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.

Conclusions: While the causes of death, early allograft loss and dysfunction were diverse, TCMR was the most dominant cause for allograft dysfunction. 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.

PO2579
Allograft Loss and Patient Death Among Kidney Transplant Recipients: Is Therapy Nonadherence the Underlying Perpetuator?
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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.

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
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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 causes (41%), Cardiovascular (CV) disease (29%) and malignancy (12%), a significant proportion of whom were African American. 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.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
PO2581
Assessing Cumulative Immunosuppressive Drug Exposure: Metrics, Outcomes, and Implications for Kidney and Non-Kidney Transplant Patients
Cavizhajian Skanthan, Emily Nguyen, Lakindu Somaweera, Madhumitha Rabindranath, Olusegun Famure, Joseph Kim. University Health Network, Toronto, ON, Canada.

Background: Immunosuppressive drugs are used in the long-term management of post-transplant patients to prevent rejection of transplanted organs. Lacking a 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. We measured 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. We also compared baseline characteristics and measures of drug exposure (e.g., trough and area-under-the-curve) in patients who received fludrocortisone with those who did not.

Results: Pre and post-fludrocortisone serum concentrations for potassium were 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 ± 12.0/9.9 mmHg and 129/70 ± 8.6/6.6 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.

Conclusions: Fludrocortisone corrected 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
Juan A. Medina,1 Charat Thongprayoon,2 Napat Leepaephorn,3 Javier A. Neyra,4 Pradeep Vaitla,1 Franco H. Cabeza Rivera,1 Michael A. Mao,5 William C. Oliver, Jr.1 1Division of Nephrology and Hypertension, Department of Medicine, Mayo Clinic, Rochester, MN; 2Department of Medicine, Mayo Clinic, Jacksonville, FL; 3Division of Nephrology, Department of Medicine, University of Kentucky College of Medicine, Lexington, KY; 4Renal Transplant Program, University of Missouri-Kansas City School of Medicine/Saint Luke’s Health System, Kansas City, MO.

Background: α-klotho protein 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. Study results were pooled and analyzed utilizing random-effects model.

Results: 10 cohort studies with a total of 431 KTx patients were identified. After KTx, there was significant increase in serum klotho levels at (4 to 13 months post-KTx) with mean difference (MD) of 243.11 (3 studies; 95%CI 67.41 to 418.81). Although KTx patients had lower serum klotho level with MD of = -234.50 (5 studies; 95%CI -444.84 to -42.16) compared to healthy volunteers, a study demonstrated comparable klotho level between KTx patients and eGFR-matched controls. Two studies demonstrated high serum klotho levels in deceased donors as prognostic marker for good allograft function within 1 year after KTx (p<0.05).

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.

PO2584
Braving the Storm: Cytokine Release Syndrome with Rabbit Antithymocyte Globulin Therapy after Kidney Transplant
Himmat S. Brar, Franco H. Cabeza Rivera. University of Mississippi Medical Center, Jackson, MS.

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 ago experienced the rejection of transplanted kidney 1 year back. Her home immunosuppression included Tacrolimus, MMF and Prednisone. She underwrote a kidney transplant from a living donor. The induction immunosuppression consisted of rabbit anti-thymocyte globulin (ATG), methylprednisolone and MMF. Two hours after the rATG infusion (1.5 mg/kg) on day 1 of transplant; she developed breathing difficulty, temp of 102.7 R, RR of 25, 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 negative for DVT. The patient was quickly diagnosed to have CRS and instead of giving fluids and causing pulmonary decompensation, she was given Solumedrol, Henarudy and TYLENOL. RATG was discontinued. Cultures were obtained that resulted negative. She improved within a couple of hours with stabilization of vitals. We suspect that the CRS following ATG infusion caused the patient’s acute decompensation, given the temporal following ATG infusion caused the patient’s acute decompensation, given the temporal relationship, rapid recovery following withdrawal and lack of proven infectious etiology. She was finally premedicated and given ATG at a slower rate over 12 hrs and tolerated it well.

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 decompensation. 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 hypotension leads to pulmonary edema.1,2 The patient responded to corticosteroids 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.

PO2585
Proton Pump Inhibitor Prevalence and Documented Indication in a Small Kidney Transplant Program
Abdulrahman Alkandari, Frances Macleod, M. Khaleed Shamseddin. Queen’s University, Kingston, ON, Canada.

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 hypomagnesemia 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 GERT 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 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.

PO2586
Unexpected Recurrence of Undiagnosed ANCA-Associated Vasculitis in a Kidney Transplant Recipient
Ruchi H. Naik, Heidi M. Schaefer, Saed Shawar. Vanderbilt University Medical Center, Nashville, TN.

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 almentuzumab 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 pan-immune crescentic GN. Her serology workup was positive for ANA, ANCA with high titers 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 titers 3.5 years back, suggestive 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 is needed to answer the question whether the ANCA positivity at the time of transplant is.
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 with reports of kidney transplantation curing the disease. We report the case of a patient who had previously undergone kidney transplantation and developed PCT after transplant.

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-sulfamethoxazole (TMP-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 elevate heptacarboxyl, hexacharboxyl and pentaclecarboxyl porphyrins with normal coreporphyrin I and III consistent with PCT. Additional workup was notable for a ferritin of 978 ng/mL, hepatitis A, B and C titers inconsistent with current or past infection and HFE gene testing showing the absence of mutations C282Y, H63D and S65C. Patient’s kidney injury resolved with cessation of TMP-SMX and fluid resuscitation. Patient was treated with therapeutic phlebotomy and erythropoiesis stimulating agents along with counseling on sunscreen use and wearing sun protective clothing.

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.

PO2588

Recurrent Focal Segmental Glomerulosclerosis After Kidney Transplantation: A Single-Center Experience

Muhammad Ajmal Panezai, Priya Yenebere, John K. Guirguis, Dennis P. Mishler, Oluwafisayo O. Adebiyi, Muhammad S. Yaqub, Tim E. Taber, Asif A. Sharifuddin. Indiana University School of Medicine, Indianapolis, IN.

Background: Recurrent FSGS (rFSGS) after Kidney Transplantation has a high risk of graft loss. However, the natural history, clinical predictors, and response to treatment remain unclear.

Methods: We retrospectively reviewed all transplant patients at our institution from 2000-2019 with a diagnosis of FSGS and identified and sub-analyzed all cases of recurrent FSGS cases (r-FSGS).

Results: Out of 198 transplants, there were 22 (11.1%) events of biopsy proven r-FSGS. Demographics of the rFSGS cases are described in the Table. 27% of cases had recurrence within 1 month of transplant. Treatments given for r-FSGS included ACE/ARB (100%), Therapeutic Plasma Exchange (40.9%), Rituximab (36.3%), conversion to Cyclosporin (36.3%) and Steroids (27.2%). 65% of cases had either a partial or complete remission. Median proteinuria decreased and mean eGFR was improved at 1 year of recurrence (p<0.05). Over a median follow up period of 4.6 years, there was a 59% graft loss with no patient deaths. 31.8% of patients were re-transplanted after initial graft loss of which 42% had recurrence in their re-transplant. As compared to the cases without any recurrence, cases with rFSGS had a significantly lower long-term graft survival (p<0.001). Figure.

Conclusions: Recurrent FSGS continues to be a high risk for graft loss despite a multitude of therapies available.

Demographics & Outcomes of Recurrent FSGS Cases

<table>
<thead>
<tr>
<th><strong>Demographics</strong></th>
<th><strong>Recurrence</strong></th>
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<td>Gender M/F</td>
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<td>Race Other</td>
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<td>Re-Transplant</td>
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<tr>
<td>Primary Graft</td>
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<tr>
<td>Mean Proteinuria</td>
<td>3.97 ± 1.35</td>
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PO2589

What Is the Safe Anti-A2 Titer for a Successful A2-Incompatible Kidney Transplantation?

Yory Al Azzi, Pablo Loarte Campos, Gayatri D. Nair, Maria Ajaimy, Luz E. Liriano-Ward, Cindy T. Pynadath, Purna Bindu Nandigam, Enver Akalin. Montefiore Medical Center, Bronx, NY.

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 less than 1/16.

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 intravenous immunoglobulins.

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 transplant 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 titer 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

Gaurav Agarwal,1,2 Darnell Mompoint-Williams,1,2 Song C. Ong,1,2 Jayne E. Locke,1,2 Vinenca Kumar,1 University of Alabama at Birmingham 1The University of Alabama at Birmingham, Birmingham, AL; 2The University of Alabama at Birmingham Comprehensive Transplant Institute, Birmingham, AL.

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 post 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 transplant 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 transplant. A Kaplan Meier analysis was performed for patient survival and the combined endpoint of graft and patient survival.

Results: Total of 717 deceased donor kidney transplants were performed during the study period, of which 106 HS KTR were identified. 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 post KAS era are unknown.

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

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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 (DGCL) 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 DGCL 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 DGCL 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, 86% on 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 DGCL, 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). Older age had a trend for decreased risk of nephrectomy (HR 0.98, 95% CI 0.95-1.0, p=0.06) 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 be warranted. Strategies and interventions to reduce the need for nephrectomy warrant further study.

PO2592
Contraceptive Use Among Women with Kidney Transplants in the United States
Silvi Shah, Kathleen Harrison, Annette Christianson. University of Cincinnati, Cincinnati, OH.

Background: Kidney transplant improves reproductive function in women with end-stage kidney disease (ESKD). Little is known about contraceptive use in women with history of kidney transplants.

Methods: Using the United States Renal Data System (2005-2014), we evaluated for each calendar year women with kidney transplantation who were aged 15-44 years with Medicare as the primary payer and linked data from the United Network for Organ Sharing, for up to three years after the date of transplantation. We determined rates of contraceptive use and used multivariable logistic regression to identify factors associated with contraceptive use.

Results: The study cohort included 13,150 women and represented 26,624 person-years (PY). The rate of contraceptive use in women with kidney transplant was 9.5% of person-years. Figure 1 shows the rates of types of contraceptive use from 2005-2013. Compared to women aged 15–24 years, contraceptive use was lower in women aged 30–34 years (OR, 0.67; CI, 0.58-0.77), 35–39 years (OR, 0.36; CI, 0.31-0.43), and 40–44 years (OR, 0.23; CI, 0.19-0.28). Compared to white women, contraceptive use was higher in black women (OR, 1.26; CI, 1.10-1.43) and Native American women (OR, 1.52; CI, 1.02-2.26). Women had lower rates of contraceptive use in the second-year post-transplant (OR, 0.87; CI 0.79-0.94) and third-year post-transplant (OR, 0.69; CI 0.62-0.76) than in the first-year post-transplant. Women with a history of diabetes had a lower likelihood of contraceptive use (OR, 0.80; CI, 0.65-0.99).

Conclusions: Among women with kidney transplants, contraceptive use remains low at 9.5%. Factors associated with a higher likelihood of contraceptive use include younger age and black and Native American race/ethnicity; second- and third-year post-transplant and history of diabetes are associated with a lower likelihood of contraceptive use. The study highlights the importance of counseling for contraceptive use in women with kidney transplants.

Funding: Private Foundation Support
Reproductive Health in Kidney Transplant Recipients

Andrea G. Kattah, Fernando G. Cosio, Vesna D. Garovic. Mayo Clinic Minnesota, Rochester, MN.

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=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 pre-transplant. 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 post-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

Buffy Coat Methylation Is Representative of Methylation Patterns in White Blood Cell Types in Normal Pregnancy

Rabinie Ghannawi,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 heterogeneous 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 normotensive 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 normotensive 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 sea 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 - NIH

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 unwarranted 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 stated median age of 45 (IQR 40-52) years. Cyclophosphamide use was reported by 70% (135/192) of women. 80% (154/192) had a history of transplantation, 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 post-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. 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

Menstrual Cycle Length and Cessation Of Menses By Age Group

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 and pregnancy outcomes.

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, 3.63-9.80 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 delivery (OR, 2.21; 95% CI, 1.50-3.27), and 2-fold higher...
PO2598

Pregnancy Following Kidney Transplantation: Experience of a Tertiary Renal Obstetric Service Between 1996 and 2020

Sarah Gleeson,1 Michelle Willicombe,1,2 Seva Hassan,1 Daniel Christiadi,1 Philip Webster,1,2 Liz Lightstone,1,2 Imperial NHS Healthcare Trust, London, United Kingdom; Imperial College London Faculty of Medicine, London, United Kingdom.

Background: Compared with dialysis, fertility & pregnancy outcomes are more favourable following transplantation. However, pregnancies post kidney transplant are associated with a higher 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 duration of pregnancy was 39±2.5 weeks. Of the 52 pregnancies it was was 48 & 52.9 m/dL. 1 graft was lost during pregnancy (pre-eclampsia eGFR 25, PCR 150); None were lost in the year postpartum. 5 women(12%) have subsequently lost their graft(mean of 4 years postpartum). 1 woman was provisionally treated for rejection during pregnancy; 2 were treated for rejection within 1 month post-partum. 6 others(14%) had a rejection episode - mean time of 38.6±4.2 months post-partum. There were no maternal deaths. 3/19 women checked for Donor Specific Antibodies(DSA) postpartum had a DSA-1 present pre pregnancy & 2 de novo. The mean gestational age was 35±1.3 weeks. 26% were born <33% pre-term & 5 <34 weeks). 18 women(37%) developed preeclampsia. There was one intrauterine death. 66% delivered by caesarean section.

The mean birth weight was 2400±588 grams; 24% were ≤10 percentile.

Conclusions: Pregnancy outcomes in patients with transplants are better compared with those on dialysis(PMID. 27083278). However, 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 renal obstetric clinic.

PO2599

Does Nephrologist Involvement Improve Aspirin Prescribing in Pregnant Women with CKD?

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Background: Since 2014, the U.S. Preventative Services Task Force has recommended the use of aspirin beginning at 12 weeks gestation in women at high risk for development of preeclampsia including those with chronic kidney disease (CKD). A prior study at the authors' institution revealed overall low prescribing rates for women with CKD with only 50.5% taking aspirin according to the recommended guidelines.

Methods: The authors reviewed data from pregnancies with delivery 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 (including solitary kidney); 2.the majority of patients with PE, are healthy before pregnancy and return to well-being after delivery; 3.the familial recurrence of PE and the increased PE recurrence risk in subsequent pregnancies; 4.the increased risk in PE patients with a history of hypertension and CKD later in life; 5.the association between intrauterine poor environment, reduced nephron mass and risk of hypertension and CKD.

Conclusions: In this study, we observed slightly improved placental perfusion and lower fetal demise following prepartum BD treatment; however, the anti hypertensive effects of BD were not sustained through late pregnancy when supplementation was stopped at mid-pregnancy. No improvements in renal function were noted.

PO2600

Low Renin Endorphin and Pregnancy-Related Renal Maladaptation in the Pathogenesis of Preeclampsia

Silvia Oddo,1 Alessandro Forni,2 Giulia Genzone,2 Eugenio Ragazzi,2 Valentina Capone,1 Erich Cosmi,2 Gianluigi Ardissino,1 Pediatric Nephrology, Dialysis and Transplantation, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milano, Italy; 1Dept. of Women's and Child's Health, Obstetrical and Gynecological Clinic, University of Padova, Padova, Italy; 2Dept. of Pharmaceutical and Pharmacological Sciences, University of Padova, Padova, Italy.

Background: Pre-eclampsia (PE), whose pathogenesis is still unclear, complicates 2%-8% of pregnancies and is responsible of significant maternal and/or perinatal morbidity and mortality. Given the following facts: 1) the incidence of PE is significantly higher in women with chronic renal diseases and hypertension (including solitary kidney); 2) the majority of patients with PE, are healthy before pregnancy and return to well-being after delivery; 3) the familial recurrence of PE and the increased PE recurrence risk in subsequent pregnancies; 4) the increased risk in PE patients with a history of hypertension and CKD later in life; 5) the association between intrauterine poor environment, reduced nephron mass and risk of hypertension and CKD.

Conclusions: In conclusion, we observed slightly improved placental perfusion and lower fetal demise following prepartum BD treatment; however, the anti hypertensive effects of BD were not sustained through late pregnancy when supplementation was stopped at mid-pregnancy. No improvements in renal function were noted.

PO2601

Hypotenremia in Preeclampsia: A Diagnostic and Therapeutic Challenge

Nay Seif, Anand Srivastava. Northwestern University Feinberg School of Medicine, Chicago, IL.

Introduction: A 32-year-old female at 35-weeks gestation with twin pregnancy was admitted for hypertension, proteinuria, and hyponatremia (Figure 1A).

Case Description: She complained of nausea, bilateral vision loss, and pain. Physical exam revealed 3+ generalized edema. Her blood pressure improved with conservative management, and medications controlled her nausea and pain. Figure 1B shows her hospital serum sodium trend. The physical exam, serum and urine studies suggested

Conclusions: Hypotension complicated by hypertension and preeclampsia is rare and may be a sign of severe preeclampsia. This case demonstrates the importance of early recognition and prompt treatment.
hypoventilatory hyponatremia due to nephrotic syndrome. She was placed on fluid restriction. Repeat serum sodium and 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 vasodilatation, 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 SIAH. 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.

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 2/7 weeks gestation by in vitro fertilization was admitted for hypertension (HTN), proteinuria, and acute kidney injury.

Case Description: She reported no home medications other than prenatal vitamins. 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 there was no indication in this patient. At 22 weeks gestation, serum was tested for sFLT-1 and PlGF ratio >3 and >2 folds of ULN respectively whereas serum lipase (921 U/L) and Amylase (492 U/L) were raised >3 and >2 folds of ULN respectively. As serum lipase >3 times of the ULN range 64%-100% and 99%-100% respectively. More than 3-folds rise of serum lipase above the ULN can also be seen in a variety of other conditions including acute renal failure. Even in 15% cases of HG with normal renal function, serum Lipase can rise by 5-folds. Therefore, clinical and biochemical co-relation is necessary to rule out acute pancreatitis in pregnancy.

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

789

PO2604

Hyperelemesis Gravidarum-Induced Acute Tubular Necrosis: A Case with More Than Fivefold Rise in Serum Lipase Level Above the Upper Limit of Normal

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Introduction: Hyperelemesis 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-incidently 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/day) with FeNa+>31 mmol/L and UPCR = 118 mEq/L and 4.4 g/g creatinine. Repeat serum sodium and urine protein 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: Patients presenting with nephrotic syndrome and hypertension ≥ 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.
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 Bonniphop Boonpheng,4 Maria Lourdes Gonzalez Suarez,1 Jasmina Craici,1 Vesna D. Garovic,1 1Mayo Clinic Minnesota, 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 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

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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 24th percentile, head circumference in the 2nd percentile, and biparietal diameter (BPD) in the 33rd percentile. Therefore, the patient started daily dialysis with longer sessions to optimize fetal outcomes. A repeat ultrasound two weeks later revealed interval growth with a fetal weight in the 24th percentile and BPD in the 45th percentile but with abnormal umbilical artery Doppler findings, an absent end-diastolic flow, and a high velocity in the umbilical artery. The patient returned to the hospital with hypoxic respiratory failure due to parainfluenza virus infection. Further serologic investigation revealed elevated anti-GBM antibodies. A kidney biopsy was performed which demonstrated 100% cellular crescents on light microscopy and negative for mesangial deposition. Further immunofluorescence confirmed 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 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 nephrologists in the care of these patients is imperative to ensure the best possible outcomes.
POSTCONGRESS SESSIONS

PO2609
Identification of Renal Disease in Women with Hypertensive Pregnancies
Hayley Martin,1 Henry A. Kibble,2 Kieran R. Palmer,3 Emmanouil Koutroutsour,1 Amanda M. Holloway,1 Kate Bramham,1,2 Katherine R. Clark.2,1 King’s College Hospital NHS Foundation Trust, London, United Kingdom; 2 King’s College London School of Life Course 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 ongoing renal abnormalities. We aimed to determine prevalence of renal disease in postpartum women with chronic hypertension, pregnancy induced hypertension or pre-eclampsia in a previous or current pregnancy.

Methods: Women with singleton pregnancies seen in a specialist clinic for hypertension with estimated GFR (CKD-EPI) below 90mls/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 185 (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>
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<tr>
<th>Chronic Hypertension (N=341)</th>
<th>Preeclampsia (N=208)</th>
<th>Proteinuria (N=208)</th>
<th>History of CKD (N=208)</th>
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<td>BP (mmHg)</td>
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PO2610
Sexenenes Markers in Women with Preeclampsia Pregnancies
Sonja Suyakovic,1 Ranine Ghamrawi,1 Hai-tao Tu,2 Wendy White,2 Natasa Milic,1 Joseph P. Grande,3 Vesna D. Garovic.1 Mayo Clinic Minnesota, Rochester, MN; 2 The 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 (316.95±163.95 vs. 207.53±84.78, p=0.047), TNFa (2.79±1.08 vs. 2.06±0.64, p=0.043) and Pai1 (58.03±18.85 vs. 38.12±20.86, p=0.023). Similarly, significant increase in senescence markers was found in preeclamptic pregnancies for MCP1 and TNFa. 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

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

Underline represents presenting author.
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 Navdeep Taniguchi,3 Yuri Stavov,4 Dawn Parsell,5 Elizabeth Li,6 Gerrit Klarenbeek,7 David A. Bushinsky,8 Mathur Consulting, Woodside, CA; 4Baylor Scott & White Health and Wellness Center, Dallas, TX; 1University of Manitoba, Winnipeg, MB, Canada; 2Tricida, Inc., South San Francisco, CA; 3PharmaStat LLC, Fremont, CA; 4University 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 acidotic 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 mg/E. 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 the 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.

PO2613
Dietary Magnesium Intake, Risk of Kidney Stone, and Survival in the Women's Health Initiative (WHI)
Harshitha Kota,1 Xuering Wen,2 Chao Chen,2 Jie Tang,3 1Brown University, Providence, RI; 2University of Rhode Island, Kingston, RI; 3University of Florida, Gainesville, FL; 4Brown Urology Brown Physicians Inc, Providence, RI.

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 included free of history of kidney stone history at baseline. 83% were Caucasian, mean age was 63. Among them, 6024 (4%) developed incident kidney stone from 2.6 to 3.1 mg/dL. RPGN was suspected and kidney biopsy was performed that showed acute interstitial nephritis or pyelonephritis, due to presence of neutrophils in clumps. His AM cortisol level was 3 ug/dL (10-20). Because of hypotention, polyuria and natriuresis, hydrocortisone and fludrocortisone were started. His serum K level decreased and fludrocortisone was stopped. Over next few days, he became normotensive and his hypotension improved with increasing dose of hydrocortisone. Hypokalemia slowly resolved with potassium supplements.

Conclusions: 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.

Funding: Clinical Revenue Support

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, presented to the ER with dizziness, bradycardia and hypotension. He was weak, fatigued, and unarousable. In the ER, he 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 acute interstitial nephritis or pyelonephritis, due to presence of neutrophils in clumps. His AM cortisol level was 3 ug/dL (10-20). Because of hypokalemia, polyuria and natriuresis, hydrocortisone and fludrocortisone were started. His serum K level decreased and fludrocortisone was stopped. Over next few days, he became normotensive and his hypotension 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.

PUB002
Lymphoma of a Normal Kidney Size
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Introduction: Renal injury has been reported in the setting of hematolymphoid neoplasms. The kidneys can be affected by a variety of mechanisms such as acute tubular necrosis (ATN), paraneoplastic glomerulopathy, and lymphocytic infiltration of kidney parenchyma (LKP). Diagnostic evaluation is important in differentiating mechanism of kidney injury, which will affect management and prognosis. LKP is suggested with clinical findings of bilateral kidney enlargement, acute kidney failure (AKI), or proteinuria.

Case Description: 50-year-old male with new diagnosis of high-grade lymphoma found to have severe kidney failure. Initial work up was unable to explain the underlying process of kidney failure. The patient was managed with volume replacement to alleviate the pre-renal component. Kidney ultrasound had no evidence of enlargement. Kidney function worsened over days and a decision to initiated dialysis was determined. After establishing dialysis access, kidney function demonstrated an improvement trend without dialysis initiation. Kidney biopsy revealed infiltration by atypical lymphoid cells consistent with the Double-Hit Diffuse Large B-Cell Lymphoma (DLBCL). Patient’s kidney function spontaneously recovered. Patient was discharged with plan to start chemotherapy as an outpatient.

Discussion: Our patient was diagnosed with DLBCL. This type of lymphoma accounts for approximately 25 percent of all Non-Hodgkin Lymphomas in the developed world. Clinical presentation of renal involvement includes AKI, proteinuria, or enlarged kidneys on imaging studies. Location of lymphocytic infiltration determines the extent of renal injury and whether interstitial or glomerular. Renal involvement incidence is 2% at time of diagnosis. Extramedullar renal involvement is diagnosed either by biopsy or imaging. Renal involvement can be diagnosed by imaging in 65% of patients. Cases presenting with AKI of interstitial type of lymphomatous infiltration show bilaterally enlarged kidneys 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.

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

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Metabolic Encephalopathy due to AKI in a Patient with Recent Infusion of Intravenous Immunoglobulins (IVIg)
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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 mm Hg 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. AIN due to IVIg and/or IVIg induced osmolyte 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 dialytic removal of sucrose from the circulation. To make a diagnosis, serum creatinine must be followed for at least 6 months. An association with nephrotic syndrome may 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 rate of administration (<3 mg sucrose/kg/min) of IVIg.

A Patient with a Record High Blood Urea Nitrogen Value Surviving Without Dialysis
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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 only drinking coffee. Patient was not being confused by family. No history of analogistic 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 metabolic acidosis with serum bicarbonate of 10 mEq/L, anion gap of 33 mEq/L, lactate acid of 40 mEq/L. Creatinine kinase level was 253 U/L. Urine studies showed no proteinurina, mild hematuria, without crystals. Urine electrolytes showed sodium of 23 mEq/L and chloride of less than 20 mEq/L. Corona virus disease 2019 (COVID-19) was negative both by polymerase chain reaction and antibody test. All the sepsis work up, urine toxicology and blood alcohol level were negative. Renal ultrasound showed 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: CKD patients are susceptible to infection, dehydration and develop multiple episodes of acute on chronic renal injury, subsequently resulted in end stage renal disease. Our patient was taking metoprolol, lisinopril and hydrochlorothiazide for hypertension which could also have prompted her into hypovolemic state without adequate hydration. BUN easily be confused by family. No history of analogistic or herbal supplements usage was present. 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.

Cholesterol Crystal Embolism with End-Stage Renal Failure and Refractory Gastric Ulcers After Abdominal Angiography
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Introduction: Parkinson’s disease is a progressive neurodegenerative disease with diverse motor and neuropsychiatric manifestations. At the urological system level, it can cause neurologic dysfunction of the bladder but to our knowledge, no dysfunction of the upper collecting system has been described so far.

Case Description: A 67-year-old Lebanese female with a PMH of Parkinson’s disease, HTN, DL, DM II, HF, CKD (1.7), Hypothyroidism, recurrent pyelonephritis and chronic kidney disease stage 3b, stage 3 obesity with a body mass index (BMI) 37.7. she presented with marked increase in blood pressure requiring addition of four new anti-hypertensive medications by discharge. She complained of anemia, 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 ischemia, 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, capsuleotomy 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, diabetes mellitus, and a history of interventional pulmonary disease was diagnosed as hepatocellular carcinoma by transfemoral 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 1.17 to 5.87 mg/dL with eosinophilia (440/40/L) 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 clefts. He was diagnosed with tubular basement membrane 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 atheroembolic plagues at the level of celiac artery. Cholesterol clefts 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 endovascular surgery but also interventional transfemoral angiography. We need to consider cholesterol crystal embolism when acute kidney injury and refractory gastric ulcers after transfemoral angiography. Although PSL is administered.

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). The little about the associated factors and 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 our 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±13.9 years. 58.4% were men. Charlson comorbidity index (CCI) was 7.16±2.7 points. The mean of drugs ingested daily was 7.81±3.66 and the length of stay was 12.25±11.69 days. In view of the Etiology of AKI, 69.5% of perirenal AKI and 30.5% non-perirenal 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 CCI. 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) + (0.10 x CCI). 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 over 2 years, 2 patients survived. Kaplan-Meier analysis showed a significant difference (Log Rank (Mantel-Cox): p=0.001) between patients with hyperK and patients that did not present it.

Conclusion: HyperK occurred in just over half of our patients. The potassium level was significantly associated with previous comorbidity, 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.

A Case of Anti-Tubular Basement Membrane Antibody-Associated AKI

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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 5.31 mg/dL), he was transferred to our hospital on the 2nd day after admission. Physical examination revealed mild hypertension (130/80 mmHg) and a prominent distended abdomen. Laboratory examination revealed a significant increase in creatinine (baseline 1.5 mg/dL), 2,7 points. The mean of drugs ingested daily was 7.81±3.66 and the length of stay was 12.25±11.69 days. In view of the Etiology of AKI, 69.5% of perirenal AKI and 30.5% non-perirenal 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 CCI. 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) + (0.10 x CCI). 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 over 2 years, 2 patients survived. Kaplan-Meier analysis showed a significant difference (Log Rank (Mantel-Cox): p=0.001) between patients with hyperK and patients that did not present it.

Conclusion: HyperK occurred in just over half of our patients. The potassium level was significantly associated with previous comorbidity, 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.

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 fungi belonging to the order Zygomycetes. It is an azo-glucovascular 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 bilaterally smooth tapered distal ends of the renal arteries with non-perfused enlarged kidneys. These findings were consistent with the diagnosis of Zygomyccosis which has angio-invasive nature. Bilateral nephrectomy was done and diagnosis was confirmed on histopathology. 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.

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. The patient had severe renal abnormal nephrologic findings prior to the episode. The patient had been given baclofen 10 mg x 2 doses for back pain within 24 hours of her acute change in mental status. She was non-verbal but opening eyes and withdrawing to pain. The initial presenting signs of infection had been improving with cefotaxime and tazobactum. Serum creatinine time was 4.2 mg/dL on admission and had improved to 2.2 mg/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.
Light Chain Cast Nephropathy in an African-American Woman with Waldenström Macroglobulinemia

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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 chain casts/LPF. Serum immunofixation revealed IgA-kappa in the beta region and a faint IgA-cappa monoclonal protein in the gamma region. Autoimmune and infectious serologic work-up negative. Dapsone was stopped on day 5 and renal biopsy was performed due to ongoing rise in Cr on day 8. Biopsy confirmed diffuse interstitial nephritis with prominent eosinophilic inflammation along with low grade membranous nephropathy favoring secondary, PLA2R negative. Patient started on IV solumedrol followed by oral prednisone taper over 6 weeks. Creatinine improved to 1mg/dL at 3 month follow-up.

Discussion: DI-AIN was attributed to dapsone. Despite withholding this medication, the Cr continued to rise prompting renal biopsy. Studies suggest that early corticosteroid initiation is associated with better outcomes and be considered in patients with no prior kidney dysfunction. In patients with suspected DI-AIN where a biopsy cannot be performed, a trial of empiric steroid therapy may be considered. The finding of secondary membranous nephropathy (MN) was unexpected as to date there has not been any reports of renal disease and EDD. We report a case of secondary MN in a patient with EDD now undergoing a full malignancy investigation.

AKI from Tubular Bleeding from Rivaroxaban (XARELTO)

AKI: Aamir Zuberi, Fatima Zuberi, Nabiha A. Syed, Marisa L. Henderson, Safi Ahmad, Hafsa Zuberi, Aamir Zuberi MD PA, Decatur, TX; University of Texas at Austin, Austin, TX; University of Texas Southwestern Medical Center at Dallas, Dallas, TX; Wake Forest University, Winston-Salem, NC; Texas Tech University System, Lubbock, TX.

Introduction: Anticoagulation induced acute kidney injury

Case Description: A 68-year-old male with history of 7kg weight gain in the preceding 4 wks. & fatigue. History of CAD, COPD and Pulmonary Embolism treated with Rivaroxaban Exam essentially negative except for edema Creatinine 8.4, ultrasound negative, previous creatinine normal, UA positive for blood & protein Dialysis initiated. All serologies negative IVC filter was placed, anticoagulation stopped, and kidney biopsy performed Biopsy showed diffuse intratubular red blood cells, red cells casts, acute tubular epithelial injury, mild interstitial fibrosis, few eosinophils and negative for crescents or vasculitis (images shown below) On follow-up, Pt regained kidney function in 2 months and creatinine remained normal at 1 year.

Discussion: Warfarin related nephropathy is a rare but well-recognized phenomenon, which has also been reported with other anti-coagulation like Dabigatran (Pradaxa), however has not been reported with Rivaroxaban (Xarelto). Warfarin related nephropathy (WRN) and acute kidney injury is sometimes caused by excessive anticoagulation. A biopsy is needed to confirm this condition. Pathogenesis of anticoagulant related nephropathy is glomerular injury, obstruction of renal tubules by RBC casts, and tubular epithelial injury. Histologically, WRN and the biopsy from the patient receiving Rivaroxaban appeared very similar.
**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. Pericapodial necrosis 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). Given the concern for vasculitis, a kidney biopsy was performed. Her biopsy was significant for global glomerulosclerosis, glomerular 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 hypertensive. 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.

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

**Underline:** represents presenting author.

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**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 (0-48h), with blood and kidneys harvested at each timepoint for subsequent analyses. Plasma and kidney tissue were analyzed for gene expression via clinical chemistry.

The expression of 100 mRNA transcripts surveying genes across apoptosis, kidney injury, and inflammation/repair pathways were measured by Quantigen.

**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 a2hr post-reperfusion, indicating the initiation of programmed cell death. Last, pro-fibrotic 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 later phase, in line with exacerbated renal function. Our novel statistical method identified “high information” genes/parameters that can serve as reliable, mechanistic indicators of AKI in future studies.

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**PUB016**

**AKI, Diplopia, and Altered Psyche: One Rare Case of Extrapulmonary Sarcoidosis**

**Hillary DeRose-Caldwell. Western Reserve Health Education, Youngstown, OH.**

**Introduction:** Sarcoid 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 nephrocalcinosis on normal screening. Renal parenchymal involvement is typically granulomatous tubulointerstitial nephritis. Neuro-sarcoid 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 nax 28 (490/mL), Ser Calcium 8.6 (9.2 mg/dL) ACE 73 UI/L, Alc 5.4. Given the worsening CKD IV; the following were drawn: ANA-IFA: positive, speckled pt 1.640, UA bid 10, ion cast 0-5, crs gran cyst 0-5, ur prot rad 24. Renal biopsy demonstrated nonaseating granulomatous interstitial nephritis, numerous nonaseating granulomas with giant cells. He was referred to Cleveland Clinic Sarcoid Clinic and started on 40mg prednisone for renal sarcoid. CXR with prior nodules, no hilar or parenchymal changes. CC Ophthalmology clinic’s fundus exam revealed peripheral hypo-pigmented 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 sarcoid. 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.

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**PUB018**

**Antioxidant Ameliorates Pulmonary Renal Injury in an Experimental Model of COVID-19 Organ Failure**

**Firoozeh Farahmand, Saint Louis University, Saint Louis, MO.**

**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 curvedol 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 wet/dry 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 were removed for histology.

**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 GSHPs in the lung and the 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.

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**PUB019**

**SRP14 Regulated Renal Tubular Apoptosis Induced by Ischemia-Reperfusion Injury via Interaction with RPS7**

**Yun Tang, Yanmei Li, Guisen Li, Yi Li. Department of Nephrology, School of Medicine, Sichuan Academy of Medical Science and Sichuan Provincial People’s Hospital, University of Electronic Science and Technology of China, Chengdu, China.**

**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 LFQ proteomic analysis in HK, renal tubular epithelial cells and human kidney (Hep2) cell line. After finding SRP14 as candidate 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. In particular, the SRP14 could mediate the MDM2-p53 loop through RPS7 in renal tubular epithelial cells to regulate apoptosis of renal tubular epithelial cells induced by IRI. The AUC value of SRP14 (AUC [Cmax] = 0.774) was close to serum creatinine (AUC [Cmax] = 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
Sitalakshmi J. Iyer,1,2 Clay A. Block,3 (NYU Langone Health, New York, NY; 1VA New York Harbor Healthcare System, Manhattan, NY; 2Dartmouth College Geisel School of Medicine, Hanover, NH.

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 5 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.

Discussion: AKI defines AKI by an absolute rise in Cr >0.3mg/dl within 48 hrs, a relative rise in Cr >50% within 1 week, or reduction in UO to <0.5mL/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 in an attempt to increase her 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 sarcoenia, 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
George Boutsalis,1 Sigit D. Trier,3 Chris Allen,1 Jay B. Wish.2 (1Medscape LLC, New York, NY; 2Indiana University School of Medicine, Indianapolis, IN.

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 3-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), Neph assessment completers (n=122)

Results: At baseline, 20% of Neph (n=122) answered all 3 questions correctly, increasing to 61% (P < .001) post-assessment. An average of 61% of all responses were increasing to 61% (< .001) post-assessment. An average of 61% of all responses were ± 0.5 mg/dL of the actual PTH value. The MAE for the 1-, 2-, and 3-month calcium predictions is 0.410, 0.458, and 0.496 mg/dL, respectively. In addition, for the 1-, 2-, and 3-month predictions, 71%, 65%, and 63% of the predictions, respectively, lie within ±0.5 mg/dL of the actual calcium value.

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

PUB022
Predicting PTH and Calcium Trajectories for ESKD Patients on Intravenous Calcinimetics
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Background: Patients with End-Stage Kidney Disease (ESKD) often experience secondary and tertiary hyperparathyroidism leading to increased fracture risk, vascular calcification, and increased cardiovascular risk. Traditional pharmacotherapy includes phosphorus binders, Vitamin D analogues, and oral calcimimetics. Despite this, many ESKD patients still have elevated parathyroid hormone (PTH) levels. Etelcalcetide is an intravenously delivered calcimimetic approved to treat hyperparathyroidism. Advantages include a long half-life and IV administration which guarantees drug delivery. Despite this, response of PTH and calcium levels to etelcalcetide remains difficult to predict. A predictive algorithm could assist clinicians in assessing the potential effect of a given dose. As a first step in developing a dosing decision support tool, we present a predictive model that forecasts the 1-, 2-, and 3-month PTH and calcium values for patients receiving etelcalcetide.

Methods: We used tree ensemble (RandomForest) models for their ability to model the data non-linearities. Model inputs were historic data (calcimimetic dosing, labs, dialysis records, demographics, and phosphorus binder orders) and future calcimimetic dosing.

Results: The Mean Absolute Error (MAE) is 205, 227, and 249 pg/mL for the 1-, 2-, and 3-month PTH predictions, respectively. In addition, for the 1-, 2-, and 3-month calcium predictions, 70%, 65%, and 59% of the predictions, respectively, lie within ±25 pg/mL of the actual PTH value. The MAE for the 1-, 2-, and 3-month calcium predictions is 0.410, 0.458, and 0.496 mg/dL, respectively. In addition, for the 1-, 2-, and 3-month predictions, 71%, 65%, and 63% of the predictions, respectively, lie within ±0.5 mg/dL of the actual calcium value.

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
Michael Chang, Gary Dellacerra, Deep Sharma, Joshua M. Stern, Peter Nauka, Wei Chen. Montefiore Medical Center, Bronx, NY.

Introduction: Staghorn calculi are usually unilateral and typically occur in women. Chronic obstruction and infection of staghorn calculi can cause xanthogranulomatous pyelonephritis (XGXP), 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 nuclei 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 (urine pH ≥6.5), 100% carbonate apatite (dahilite) 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 1,25D, 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

Bei Hou,1 Bing Tang,1 Yong Xu,2 Yuanning Li,2 Ninxin Liu,1 Xiang yijia Doctor Group 1Jewel Hospital, Changsha, China; 2Xiang yia Hospital Central South University, Changsha, China.

Introduction: Exploration of parathyroid hyperplasia with single explosive growth

Case Description: A 46.5O Asian man with ESRD has been undergoing regular hemodialysis for 20 years due to glomerulonephritis. The patient has had bone 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 alkaline phosphatase were 2.46mmol/L, 2.44mmol/L and 380U/L, respectively, and serum iPTH was 2205pg/ml in this admission examination. The ultrasonography showed two hyperplastic parathyroid glands. They are 1.3*2.0mm on the right lower side of thyroid gland and 43*18mm on the left lower side. Parathyroid needle 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 help of the local anesthesiologist in May 15, 2020. Four parathyroid 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.

Acute Changes in Plasma Phosphate After Phosphorus-Standardized Meals in Peritoneal Dialysis: A Randomized Cross-Over Trial

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Background: Hyperphosphatemia is associated with increased morbidity and mortality in patients with chronic kidney disease. The aim of this study was to assess whether a meal with high phosphorus content affects plasma phosphate in the hours following such a meal among subjects with end-stage kidney disease on peritoneal dialysis.

Methods: This was a single-blinded randomized cross-over trial of 12 subjects on maintenance peritoneal dialysis, in which subjects were randomized to consume a meal with either high or low phosphorus content on two separate trial days. On each trial day plasma phosphate was measured immediately before consumption of the standardized meal, and after one, two, three and five hours.

Results: The mean fasting plasma phosphate at baseline was 1.69 ± 0.22 mmol/L. Plasma phosphate was similar between the two meals at baseline, as well as at one, two, three, and five hours after consumption. The largest observed difference in plasma phosphate between the two meals was 0.15 mmol/L, which occurred five hours after consumption (high phosphorus meal 1.75 ± 0.32 mmol/L versus low phosphorus meal 1.60 ± 0.14 mmol/L (p = 0.06)). Using summary analyses for repeated measures we observed a significant difference in the plasma phosphate between the two meals (p = 0.03).

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
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
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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, calciphylaxis & pruritus.

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 3519pg/mL, phos 6.7mg/dL, Ca 10.9mg/dL & ak phos 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 & sarcum, wide erosion of sacrailc joints bilaterally & calcified atherosclerotic disease of abdominal aorta & bilateral interiliac 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: Parathyroidectomy 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 other indicators like hypercalcemia, refractory hyperphosphatemia, bone pain/fractures & our case has majority of the above mentioned indications. Various other factors including immigration, insurance issues and post-operative intensive care requirements complicated the potential for parathyroidectomy 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
Yelvzyaveta Prysvazhnyuk, Isha Puri, Jic 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 G3a is divided into G3a (GFR 45–59 ml/min/1.73m2) and G3b (30–44 ml/min/1.73m2) 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 were presented as means+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: 93.9). 259 (80.6%) 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/1.73m2 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), 3.8 (1.6-9.1; 0.003) and 194 (8.7-43.0; <0.005) respectively. When adjusted for age and BMI, risks of progression to G5 were: RR=1.3 (1.6-3.0; 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?
Omar T. Ashour,1,2 Christine A. White,1,2 Eduard A. Iliescu.1,2 Queen's University, Kingston, ON, Canada; ‘Kingston Health Sciences Centre, Kingston, ON, Canada.

Background: Current guidelines for the evaluation of chronic kidney disease (CKD) in Canada do not include routine screening with serum and urine protein electrophoresis to detect for light chain deposit disease (M-spike). We postulated that CKD-chronic kidney disease; AA- African American; BMI- body mass index


PUB030
Is Yakima County a CKDu Hot Spot? A Case Series of CKD in Latino Agricultural Workers
Mark D. Baldwin, Katherine Ackerman, Tara L. Kronen, Polly Wiltz, Lizzie Lamb. PNWU CKDu Investigative Task Force Pacific Northwest University of Health Sciences College of Osteopathic Medicine, Yakima, WA.

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 presented in relatively young men without any of the traditional risk factor associated with renal disease. The common feature amongst cases was strenuous work in extremely hot 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, with detection costs of $ 553.28 per M-spike and $ 1,521.25 per myeloma cost. 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 costs of $ 59.13 per MGUS, $ 153.25 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. AlHwesh et al. J Am Soc Nephrol 2003 14:295A. 2. Chew et al. Am J Kidney Dis. 1999 Jul;34(1):135-9.
northern regions. At 46.602°N latitude, Yakima is closer to the North Pole than the Equator, and much farther north 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

Takahiro Kuragano, Takeshi Nakanishi. Hyogo college of Medicine: Kidney and dialysis, Nishinomiya, Japan.

**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 clarified.

**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), f2microglobulin (MG), HCO3−, and intact-parathyroid hormone (iPTH), in addition to urinary sodium, potassium, calcium, phosphorus protein, and i2MG 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=0.006), and higher i-PTH (β=0.334, P<0.001), urinary phosphorus (β=0.328, P=0.001), urinary i2MG (β=0.225, P=0.031) and urinary protein (β=0.280, P=0.02) levels were selected as significant predictors of decline of estimated glomerular filtration rate (eGFR) or 1/ creatinine(Cr) 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, the phosphate binder or vitamin D analogs were administrated appropriately, CKD-MBD factors were associated with progression 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.

**Figure one** shows the crude and the multivariable Cox proportional hazard models using anion gap as tertiles.

**PUB032**

Association of Anion Gap with the Risk of CKD Progression

Ashish Verma,1 Jing Liu,2 Maria Clarissa Tio,1 Ankit B. Patel,1 Sushrut S. Waikar,2 'B Brigham and Women's Hospital, Boston, MA; 'Boston University Medical Campus, Boston, MA.

**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 prospective cohort study assessed 4131 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 4131 participants [mean (SD) age, 60.48(10.21) years; 1788 (43.28%) female]. During 26673.46 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.

**Figure one**}

**PUB033**

Childhood Risk Factors for Adulthood 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.

**Figure one**

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

Underline represents presenting author.
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,2 Elani Streja,1 Kamary Kalantar-Zadeh,1 Csaba P. Kovetsy,1 1The 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 further clinical trials, and to offer race-specifically 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

Karim R. Masri,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 α36% 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 renal or hepatic disease may not be as restricting with leflunomide. This study examined pegloticase response rate in patients co-treated with pegloticase and leflunomide.

Methods: This chart review included uncontrolled gout patients treated with pegloticase (biweekly 8 mg infusions) and oral leflunomide (20 mg/day). Patient, disease, and treatment parameters were examined, along with safety data. Patients receiving ≥12 pegloticase infusions with a serum uric acid level (sUA) ≥6 mg/dL at infusion 12 were considered responders.

Results: 10 patients were identified and included (5 men, 72.7±12.5 years, pre-therapy sUA: 7.1±4.2 mg/dL). Common comorbidities were CKD (90%), hypertension (70%), diabetes mellitus (60%), obesity (60%), congestive heart failure (50%), and coronary artery disease (20%). 7 patients (70%) met responder criteria (26.6±14.0 infusions, sUA at infusion 12: 6.9±1.5 mg/dL). 3 patients were lost to follow-up or discontinued therapy. Gout flare (1 patient, 3 flares), weight loss (1 patient, before pegloticase infusion, deemed unrelated), worsening of kidney/cardiac issues (1 patient, deemed unrelated to treatment), and mild, transient ALT/AST increases (2 episodes, 1 patient) were observed. All treatment-related AEs were known effects of pegloticase or leflunomide.

Conclusions: These findings suggest that leflunomide/pegloticase co-therapy can increase the proportion of pegloticase responders, likely due to attenuation of ADAs. While methotrexate has been shown to increase pegloticase response rates, many gout patients have advanced CKD and leflunomide potentially represents an alternative option for minimizing ADAs.

Funding: Commercial Support - Horizon Therapeutics

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

Natarajan Ranganathan,1 Usha N. Vyas,1 Pari Ranganathan,1 Anthony Irvin,1 Alan D. Weinberg,2 2Kibow Biotech, Newtown Square, PA; 3Mount Sinai Health System, New York, NY.

Background: CKD patients experience poor quality of life due to high levels of uric acids in the blood. Renal®P, a Pro/Prebiotic dietary supplement has been in the market since 2010. It is proven to reduce several uric acids 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 metabolic markers. 2. Improvement in any of the basic blood creatinine (CR) or creatinine clearance (CC); 3. Reduction in C-Reactive Protein (CRP) levels. 4. Percent change from baseline in rating scale (Modified SF36 QOL questionnaire) at the end of 6 and 12 month. Tertiary (IN FEW SELECTED SITES): Blood levels of Kidney Injury Molecule (Kim)-1, Neutrophil Gelatinase Associated Lipocalin (NGAL), gut microbiome derived uremic toxins: Indoxyl Sulfate (IS), para-cresyl sulfate (pCS) and Trimethylamine-N-Oxide (TMAO).

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 removable, 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: ranganan@kibowbiotech.com

PUB037

Effects of Tolvaptan on Long-Term Prognosis in CKD Patients

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Background: Tolvaptan is a novel diuretic agent used for the treatment of intractable edema and SIAOH 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 variables. The endpoints were a decline 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 Tarone-Ware. The p-value for the statistic in (A) was 0.015.

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, 15 cases of diabetes and 6 cases of nephrosis. The normal patient group matched to these cases 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 variables. The endpoints were a decline 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 Tarone-Ware. The p-value for the statistic in (A) was 0.015.

Conclusions: Tolvaptan was administered after hospitalization, with an 82.1% increase in urine output and a weight of -4.2% at discharge. The tolvaptan group showed significantly lower eGFR levels when compared to the control group. However, there was no significant difference in the incidence of introduction of dialysis and death between the two groups. Further studies are needed to confirm these findings in a larger population.

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

Underline represents presenting author.
Serum Calcium Changes and Renal Function: A Dual Path Track
Julia Lauer, Tiago E. Costa, Giovanni G. Nascimento Santos, Rosa M. Moyse, 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 > 65pg/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 significantly 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. Olanye,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 in 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,2 Saurabh Bansal,3 Girish Singhania,1
1CHI Saint Vincent Health System, Little Rock, AR; 2Mount Carmel East, Columbus, OH; 3University 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 3.28mcg/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 diabetes. 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.
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-presential 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>
<thead>
<tr>
<th></th>
<th>2018 (N)</th>
<th>MEAN ± SD</th>
<th>2019 (N)</th>
<th>MEAN ± SD</th>
<th>2020 (N)</th>
<th>MEAN ± SD</th>
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<tr>
<td><strong>Clinical Appointments</strong></td>
<td>56</td>
<td>11/8 ± 0</td>
<td>52</td>
<td>11/8 ± 0</td>
<td>40</td>
<td>11/8 ± 0</td>
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<td><strong>Necessary Dislocations to the Unit</strong></td>
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<td>0.17 ± 0</td>
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<tr>
<td><strong>Non-Presential Appointments</strong></td>
<td>0.164 ± 0.09</td>
<td>0.15 ± 0</td>
<td>0.15 ± 0</td>
<td>0.15 ± 0</td>
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</tr>
<tr>
<td><strong>Hospital Admission</strong></td>
<td>0.004 ± 0.29</td>
<td>0.00 ± 0</td>
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<tr>
<td><strong>Peritonitis</strong></td>
<td>0.05 ± 0.17</td>
<td>0.00 ± 0</td>
<td>0.00 ± 0</td>
<td>0.00 ± 0</td>
<td>0.00 ± 0</td>
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<tr>
<td><strong>Exit-Site infection (ESI)</strong></td>
<td>0.06 ± 0.24</td>
<td>0.00 ± 0</td>
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<tr>
<td><strong>Peritoneal Equilibration Test (PET)</strong></td>
<td>0.24 ± 0.43</td>
<td>0.75 ± 0</td>
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<tr>
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<tr>
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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 cojoined target genes of COVID-19, CKD and AKI; (E) Underlying significant target genes of 8 active compounds.

Exploration on Renal Protective Compounds and COVID-19-Induced Renal Injuries Based on Network Pharmacology and Molecular Docking
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Background: The fullscreen of COVID-19 is getting revealed as some of the infected patients had developed severe renal complications. Natural compounds may have protective effects against COVID-19-induced renal injuries. The aim of this study is to explore the interactions and underlying mechanisms between active compounds and COVID-19-induced renal injuries.

Methods: The interaction network of 8 collected natural compounds (Hederagenin, β-sitosterol, Luteolin, Quercetin, Kaempferol, Jaranol, Formononetin and Calycosin) and COVID-19-related target proteins was established by using the pharmacological database. GO and KEGG pathways were also analyzed. Molecular docking was run by AutoDockTools and Discovery Studio.

Results: 259 target genes are potentially related to COVID-19, AKI and CKD. Active compounds may improve COVID-19-induced renal injuries by alleviating the inflammatory response, vascular abnormal changes, cell apoptosis and necrosis in kidneys. The docking results had indicated that 8 compounds may show great possibilities to interact with SARS-CoV-2 main protease 3CL and ACE2 by showing significant binding energy.

Conclusions: Our study may provide molecular evidence and support on compounds from herbal medicines or dietary supplements may serve as potential perspective drugs to protect kidneys from COVID-19-induced renal injuries.

Funding: Government Support - Non-U.S.
Two doses of Tocilizumab (IL-6 inhibitor) were given. Patient improved significantly and PCR on four subsequent tests. She developed progressive hypoxia. Oxygen requirements removal because of pulmonary vascular congestion. She was positive for SARS COV-2 and bacterial infection. Maintenance hemodialysis was resumed with challenging fluid prominence; underlying pneumonia could not be excluded. Patient was admitted to and urine cultures showed no growth. Imaging showed prominent interstitial vascular 15.06, ferritin 2532, She was positive for both influenza and SARS COV-2 PCR. Blood chloride 96, bicarbonate 24, blood urea nitrogen 71, creatinine 13.5, C-reactive protein the exam was within normal limits. Laboratory results showed sodium 138, potassium 5.7, 102, RR 18, oxygen saturation of 99% on 2liters of oxygen. Examination revealed normal.

**Case Description:**

**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 fatigue, 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 2liters 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 COVID-19 isolation unit and empirically started on oseltamivir, Hydroxychloroquine, Zinc sulfate, vancomycin and, piperacillin-tazobactum for influenza, possible COVID and bacterial infection. Maintenance hemodialysis was resumed with challenging fluid removal because of pulmonary vascular congestion. She was positive for SARS COV-2 PCR on four subsequent tests. She developed progressive hypoxia. Oxygen requirements increased to 15 liters tolerant oxygen consistent with acute respiratory distress syndrome. Two doses of Tocilizumab (IL-6 inhibitor) were given. Patient improved significantly and discharged home with two SARS CoV-2 PCR negative results.

**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.

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

**Underlines represent presenting author.**
developed myalgia. There was no family history of myopathies, or binge alcohol intake beforehand. On physical examination, patient was hypertensive, euvolemic, and afebrile, with normal oxygenation. Chest x-ray showed subtle increased interstitial reticulosis in the perihilar regions and COVID-19 rapid test returned positive. Laboratory data showed very high creatinine kinase (CK) (208,456 U/L). Urinalysis 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. The patient received 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.

**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.

**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%), 32(82%) Hypertensives, 23(59%)diabetics. Outcome: 8(20%) expired, 18(46%) discharged, 12(31%) in hospital and 1 at home. Mean Hb (77%): 9.81 ± 1.71 g%, Adequacy (74%): 1.30 ± 0.44, Vascular access (72%): 75% permanent access, 7% temporary catheter, 18% tunneled catheter, Albumin (64%): 3.69 ± 0.31.

**Conclusions:** Maintenance HD patients have increased mortality as compared 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**

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**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 - 100.4°F, 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 ketonemia. 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.
Kidney Transplantation in the United States During the Coronavirus Disease 2019 Pandemic: An Interrupted Time Series Analysis
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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±3 vs 318±119 cases/week, mean differenceSEM 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 (IRR) of new KT during pre- and post-COVID-19 periods were 727±58 and 511±176 cases/FWC-week, respectively (Figure 1). 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, 2.60, 2.63). 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 COVID19 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-yr-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 anuric 24 hrs post-intubation. Case 3 was a 72-yr-old female with hypothyroidism 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+ prealbumin, and 2+ 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 thereafter for case 2. Glomerulonephritis specific work-ups 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.

Conclusions: 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 artery stenosis, hypertension), drugs, 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 Infection in Renal Transplant Patients

Background: The SARS CoV-2 pandemic has disproportionately affected vulnerable patient populations including kidney transplant recipients (KTR).

We present 3 cases of AKI in COVID19 patients 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. When COVID-19 was confirmed or suspected, anti-protiferative 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 20th March and 31st 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 28 days (range 14 – 41) without adverse events. 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 ethnicitly 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
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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) shifts became the designated unit to provide maintenance HD for all COV positive (+) pts in our region 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 ERSD. 3 initiated HD in the last 2 months. 8 pts were on HD ≤ 1 yr. 11 were hospitalized, 3 were intubated and 2 died. 78% had DM. Compared to 2 months prior to COV + testing, pts lost a mean wt of 8 ± (± 1.8) kg in the first month in our COV + unit (p = 0.0002). Albumin decreased from 3.75 ± (± 0.60) to 3.33 ± (± 0.54) (p = 0.0005) and ferritin rose from 753 ± (± 512) to 1526 ± (± 1147) (p = 0.0019). Potassium and Phos did not change. COV - pts lost no wt. Ferritin was higher in COV + pts (1526 vs 993, p = 0.026). Mean time to first neg COV test was 26 days (range 13 - 55). Importantly, no MWF pts or any staff became COV + during the 2 months of caring for COV+ TTS pts.
Conclusions: While respiratory symptoms of COV are often stressed we noted few symptoms of other diseases. The severity of proteinuria and renal injury observed in this clinically asymptomatic patient highlight an unusual infection-driven mechanism.

AKI in Hospitalized Patients with COVID-19: A Mexican Population

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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 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. 42.2%, p=0.043) and older (55.68 years vs. 48.89 years, 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 (2.4%).

AKI Lingering in a Patient with Novel Coronavirus

Marc Saad, Brandon Kirshner, 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 hematuria 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 CKDI-II b with baseline eGFR of 50 ml/min/1.73m2 (creatinine of 1.5 mg/L) 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 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, 10-10 WBC with a protein/creatinine ratio of 12.8 mg/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 immunofluorescence with free kappa/lambda 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 rate. The levels of AKI, proteinuria and hematuria suggested 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.

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.

AKI Patients with COVID-19 and Kidney Disease: Who Fared Best?

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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 Oxygenation). 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=20; mean age 68y) – 20 prevalent adult HD patients tested positive for COVID-19. 10 recovered and discontinued HD. 10 died. Kidney Transplant Recipients (KTR) (n=4; mean age 59y) – 3 were managed as outpatients and have recovered with functioning grafts. 1 died.

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 KTRs (total cohort of 352) contracted COVID-19. The introduction of virtual transplant clinics, minimisation of face-to-face contact and efforts on shielding may have influenced this. These data aim to reinforce the international collaborative against this global pandemic.

COVID-19: Angiotensin Receptor Blocker to the Rescue?

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Background: An unusual suspect has been incriminated in the Coronavirus outbreak, Renin-angiotensin-aldosterone system (RAAS). RAAS is an intriguing system that holds many mysteries that are still waiting to be unraveled and explored.

Methods: Angiotensin-II (Ang II) is well known for its proliferative and vasoconstrictive effects and the important role of ACE2 in controlling Ang II formation and angiotensin receptor blockers (ARB) for inhibition of Ang II receptor binding. Angiotensin-1-7 (Ang 1-7) along with ACE2, in the other hand, known to have vasodilatory, antiproliferative and overall protective effects. Given the beneficial effects of ACE2 and Ang 1-7, it would make sense to potentiate this pathway for our sake, especially in the setting of lung injury.

Results: In the recent years, it’s been shown that Coronavirus is not only using the ACE2 to enter the cell, but also decreasing ACE2 expression at the same time. This is detrimental. ACE2 expression seems to be decreased in elderly and elevated in obese. It is very interesting to see that COVID severity varied among these individuals, likely due to the precarious balance between the amount of viral entry and activity of ACE2/ Ang-1-7. If we can upregulate the expression of ACE2 by some mechanism, this would in turn increase the production of beneficial Ang 1-7. But with upregulated ACE2, one must make sure that there is a competitive substrate for ACE2, in order to make the Coronavirus binding of ACE2 difficult. A suitable candidate for that substrate, is Ang II, ARB, as opposed to ACE1, would seem to increase the levels of Ang II, while upregulating the expression of ACE2. Theoretically, we could reap the benefits of enhanced ACE2 expression while competitively inhibiting Coronavirus binding to ACE2, by the increased levels of Ang II. Titrating up ARB dosing as tolerated by the patient, will be necessary for the above mechanism to work effectively.

Conclusions: Increasing ACE2 and Ang 1-7 receptor binding, will determine the degree of benefit of ARBs in diminishing Coronavirus infectivity and severity. Tolerability to ARBs, will also be a limiting factor when treating the patients. Studying ACE2 levels, Ang 1-7/Mas receptor activity in different patient populations and the correlation between Coronavirus infection and severity, would be of value in the forthcoming months in the world of RAAS.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
COVID-19 Financial Ramifications on the Pediatric Nephrology Workforce
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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=997) 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 to assume 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 a Patients Are Dying from Broncho-Pneumonia:
Most Might Be Dying from Cerebro-Neurologic-Vascular Diseases and Cardiovascular Complications
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Introduction: Acute bronchopneumonia is not sufficient to explain deaths. Lungs, brain-nerves - heart- cardiovascular system might be playing 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 heart 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-zig-zig system or reverse neurotransmission system is occurring as zig-zig-zig system to destroy body. If it is so this strange system can be called from now on in "SAGLIKER'S REVERSE NEUROLOGICAL WORKING SYSTEM."

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

A Case of Novel Coronavirus Disease 19 in a Chronic Hemodialysis Patient with Severe Cardiovascular Disease
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Introduction: Patients on maintenance hemodialysis (MHD) are vulnerable to COVID-19. MHD individuals are usually old with chronic comorbidities while these features are all risk factors of poor prognosis.

Case Description: Our patient was a 79-year-old female with ESRD and had been on MHD for 12 years in Wuhan. She had a history of severe coronary heart disease. The patient firstly reported fever, chest tightness and cough. One week later, she developed diarrhea and the chest CT indicated “viral pneumonia”. Her COVID-19 testing was reported positive, and she was admitted to the hospital with SpO2 of 92% and high level of hs-CRP, cardiac troponin I (TNI) and creatine kinase MB isoenzyme. She was prescribed oxygen therapy, methylprednisolone, intravenous immunoglobulin, prophylactic anticoagulation and CRRT therapy. Her respiratory condition improved gradually and COVID-19 testing showed negative. However, on admission day 19, the patient presented psychiatric symptom, and was considered as secondary higher-level cognitive impairment since she received regular CRRT therapy without using drugs which could cause mental disorders. Two days later, her chest X-ray showed lung infection advanced with increased hs-CRP and PCT indicating bacterial infection. We prescribed meropenem and vancomycin. Meanwhile, there was an increasing trend of TNI, and electrocardiogram indicated acute coronary syndrome (ACS). Clopidogrel, aspirin and atorvastatin were prescribed immediately. Unfortunately, on admission day 22, the patient suffered cardiac arrest and was declared dead after active rescue. The cause of death was considered as cardiogenic shock and ACS.

Discussion: To our experience, personalized immunomodulation therapies against “cytokine storm” including steroid, intravenous immunoglobulin and CRRT might play...
Pink Urine in a Patient with COVID-19

Mengqin Ma, Sir Run Run Hospital, Nanjing Medical University, Nanjing, China.

Introduction: 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 to 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 crystals, 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.
Table 2: Clinical course of the three patients with COVID-19 who were managed via telemedicine

<table>
<thead>
<tr>
<th>Hospital Day</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>White blood cells</td>
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<td>4.7X</td>
<td>4.5X</td>
<td>3.8X</td>
<td>3.8X</td>
<td>4.5X</td>
</tr>
<tr>
<td>Absolute lymphocyte count</td>
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<td>0.3</td>
<td>0.4</td>
<td>0.2</td>
<td>0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>Hemoglobin</td>
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<td>11.6</td>
<td>12.3</td>
<td>11.6</td>
<td>11.4</td>
<td>12.0</td>
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<tr>
<td>Platelets</td>
<td>318</td>
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<td>310</td>
<td>279</td>
<td>311</td>
<td>402</td>
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<tr>
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<td>Serum potassium</td>
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<td>Serum creatinine</td>
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<td>0.8</td>
<td>0.7</td>
<td>0.8</td>
<td>0.8</td>
<td>0.8</td>
</tr>
<tr>
<td>Serum bicarbonate</td>
<td>20</td>
<td>20</td>
<td>21</td>
<td>20</td>
<td>20</td>
<td>24</td>
</tr>
<tr>
<td>Serum uric acid</td>
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<td>1.4</td>
<td>1.0</td>
<td>0.9</td>
<td>0.9</td>
<td>0.9</td>
</tr>
<tr>
<td>Urea nitrogen (concentrate)</td>
<td>19</td>
<td>15</td>
<td>18</td>
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<td>Alanine aminotransferase</td>
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<td>Alkaline phosphatase</td>
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<td>7.0X</td>
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</tbody>
</table>

Table 1: Patients 1 and 2 laboratory test results during hospitalization. Patient 3 was not hospitalized.

**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 to 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 hemodialysis (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 hemodialysis, and 2 subsequently died (14.2%).

**Conclusions:** The urinary sediment is a cheap, available tool for the prognosis of need for hemodialysis 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 centers and ambulatory locations. In April, observed 1,811 COVID-19 patients admitted within; B) a granular cast with several isomorphic erythrocytes.

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 hemodialysis 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 hemodialysis we observed zero positive COVID-19 dialysis staff
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 (% of total population)</th>
<th>COVID Cases (% of cases)</th>
<th>COVID Deaths (% of deaths)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black</td>
<td>21.0% (348)</td>
<td>30.0% (64)</td>
<td>35.7 (5)</td>
</tr>
<tr>
<td>Asian</td>
<td>27.5 (457)</td>
<td>31.8 (65)</td>
<td>30.5 (9)</td>
</tr>
<tr>
<td>White</td>
<td>21.9 (369)</td>
<td>23.2 (48)</td>
<td>27.8 (8)</td>
</tr>
<tr>
<td>Other</td>
<td>21.0 (358)</td>
<td>18.4 (37)</td>
<td>25.5 (8)</td>
</tr>
</tbody>
</table>

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.
Effect of COVID-19 Infection in Three Patients Treated with Rituximab

Anushya Jevabalan, Reza Zonoozi, Jillian Rosenthal, Karen A. Laliberte, John Niles. Massachusetts General Hospital, Boston, MA.

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

*PR3-Anti Neutrophil Antibody (ANCA): Patient with eye, ENT, lung and kidney involvement
†MP0-ANCA: Patient with ENT, lung and joint involvement
HCQ: Hydroxychloroquine
FSGS: Focal segmental glomerulosclerosis
C: Caucasian, H: Hispanic

AKI Following Hemolysis Related to Hydroxychloroquine Treatment for COVID-19 in a G6PD-Deficient Patient


Introduction: COVID-19 is associated with significant morbidity and mortality. As a potential treatment, Hydroxychloroquine (HCQ) is actually widely used. Concern has arisen about side effects of HCQ. Here, we describe severe AKI following HCQ administration for COVID-19.

Case Description: A 65-year-old patient has been admitted for fatigue. His treatment was glimepiride, lercanidipine for T2DM and arterial hypertension. Initial evaluation has aroused about side effects of HCQ. Here, we describe severe AKI following HCQ administration for COVID-19.

Case Description: A 65-year-old patient has been admitted for fatigue. His treatment was glimepiride, lercanidipine for T2DM and arterial hypertension. Initial evaluation has aroused about side effects of HCQ. Here, we describe severe AKI following HCQ administration for COVID-19.

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 at-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 in life. 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

Rachana Marathi, Paul W. Davis, Franco H. Cabeza Rivera, Wisit Cheungsapattison, Swetha Rani Kanduri, Karthik Kovvuru, Pradeep Vaitla. University of Mississippi Medical Center, Jackson, MS.

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.


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 3 weeks and was positive for IgM and 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.
from transplant 3.5 yrs (1.5-11 yrs). All patients have HTN (8/8), half the patients have Diabetes 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 resolution of fever and cough. 6/8 patients required supplemental oxygen. 2/6 patients required ICU stay and 1/6 required mechanical ventilation and renal replacement therapy. 3/6 hospitalized patients received hydroxychloroquine/ Azithromycin 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. Reduction of immunosuppression appears to be helpful, however, no control group available. COVID-19 affected population is predominantly predominantly Caucasian patients (7/8) and older recipients with age > 50 yrs (7/8).

Cases of COVID-19 Reported in a Predominantly White Rural Hemodialysis Cohort
Ravi K. Thimmisetty. Nephrology Associates, Cape Girardeau, MO.

Background: COVID-19 is a novel coronavirus disease causes by the severe acute respiratory syndrome coronavirus 2. Because of its high infectivity rate, WHO described the disease as a Pandemic on March 11th 2020. Severe infections were reported in adults with underlying comorbid conditions, therefore hemodialysis patients are not an exception. We are reporting COVID-19 cases in a rural hemodialysis center predominantly Caucasian patients.

Methods: We reviewed the cases of confirmed and suspected COVID-19 infections in our dialysis center. Precautions were taken promptly after COVID-19 infection become Pandemic. All patients were taken temperature check at the entrance door, surgical face mask was provided, sanitizers were provided, social distancing was followed. All physicians and dialysis staff followed the same guidelines. All suspected and confirmed cases should get two negative SARS CoV-2 PCR tests for acceptance at our dialysis center.

Results: Out of 71 dialysis patients, men and women were 56% and 43%. 73.2% of them were Caucasians and 23.9% were African Americans. There were one confirmed COVID-19 disease who was hospitalized for about a month. She acquired from a community spread. She improved and resumed schedule after two negative SARS CoV-2 PCR results. Four people were sent to hospital for having cough, fever, dyspnea, all of them were negative for COVID-19 infection. In our dialysis unit, 55.7% of patients have diabetes, 83% have hypertension, 47.8% of them have both diabetes and hypertension. Patient with confirmed COVID-19 fall into age group of 65-79 yrs. 35.2% of the patients fall into age group of 65-79 yrs. 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 given1 liter IVF 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 donepezil. At our ER, the patient was awake, alert, oriented to self and year. T 98.3, BP 119/71, P 119, RR 18, SpO2 95% on RA. PE was unremarkable. Bladder scan: 150 ml. Lab: WBC 10.9, Hb 13.3, Plt 207, Na 130, K 4.0, Cr 79, 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. Three of six patients 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 lingered. He was treated with IV fluid to optimize his hemodynamics. Over the next 5 days patient’s serum Cr decreased to 4.9.

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 both, mechanically induced AKI- possibly secondary to sepsis, and direct viral (SARS-CoV-2) cytotoxicity. 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.

De-Differentiation of Human Urine-Derived Stem Cells to SIX2+/CITED1+ Cells by 3D Tubuloid Culture
Julie Bejoy, Richard C. Welch, Lauren E. Woodard. Woodard Lab Vanderbilt University Medical Center, Nashville, TN.

Background: In contrast to pluripotent stem cell-derived organs which take nearly one month to derive for kidney, adult stem cell (ASC) derived organs can be derived within 7 days of culture without exogenous factors. As any epithelium is formed from direct ectodermal epithelial development. Protocols have been generated to derive organs or spheroids of intestine, liver, prostate, pancreas, stomach, salivary gland, breast, colon and taste buds from ASCs. These 3D cultures have been used for disease modeling and personalized medicine approaches. Recent work from the Hans Clevers lab showed that cells derived from the urine of a patient with cystic fibrosis could be made into kidney epithelial tubular organoid structures termed “tubuloids.”

Methods: These tubuloids cultures developed quickly and exhibited many of the hallmark features of an intact tubular epithelium. The tubuloid culture media includes Wnt signaling enhancers, EMT inhibitors, and fibroblast growth factors which are all reported to be essential for kidney development. We applied this tubuloid 3D culture protocol [MOU1] to our cultures of human urine-derived stem cells (USCs). USCs were isolated from the epithelial cells lining the glomeruli that are shed into the urine. The USCs from healthy adult donors were grown on 96 well U-bottom suspension culture plates in tubuloid media for 10 days. The 3D tubuloid-like structures harvested at Day 10 were stained for both early nephron progenitor markers and tubulic precursor markers. 

Results: Tubuloid-like spheres derived from USCs expressed both nephron progenitor markers SIX2 and CITED1 as well as tubulic cellar precursors Pax2 and Pax8.
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

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**PUB077**

Comparative Evaluation of Orthostatic Hypotension in Patients with Diabetic Nephropathy

Gamze Aydin, Rumeyza Kazancioglu, Omer C. Elcioglu, Meltem Gursu, Serra Aran, Aysegul Yabaci. Bezmialem Vakfi Universitesi Tip Fakultesi, Istanbul, Turkey.

**Background:** Orthostatic Hypotension (OH) affects 5-20% of our population. Our study investigates the prevalence 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 analyzes were performed with IBM SPSS22.0 program.**

**Results:** 112(51F,61M, mean age:62,56a±9,35 years) DNP and 94(40F,54M, mean age:62,23a±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 16,63±9,03mmHg in diastolic BP. In CKDP mean change in systolic BP was 22,1±13,90mmHg and it was 5,96±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% of 74.7% M patients had OH (p=0,026). 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.

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**Blood Pressure Results**

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**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; 2UCHicago 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 and responses were de-identified and aggregated prior to analyses. Initial data collection occurred from February 26, 2020, to April 20, 2020.

**Results:** To date, 193 nephrologists completed the full assessment. Physicians demonstrated gaps in the following areas. When asked how satisfied nephrologists were with current treatment approaches for managing CKD in patients with T2D, 10% selected very satisfied, 74% selected moderately-mostly satisfied, and 16% slightly-not satisfied.

**Conclusions:** This educational research on assessment of physicians’ clinical practices yielded important insights into clinical gaps related to identification, screening, diagnosis, and management of CKD in patients with T2D. Further studies are planned to assess the effect of medical education on decreasing these clinical practice gaps.

**Funding:** Commercial Support - Bayer Global

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**PUB079**

Practice Patterns of SGLT2 Inhibitor and GLP-1 Agonist Treatment in Eligible Type 2 Diabetes Patients Before and After the Publication of the 2018 ADA/EASD Position Statement

Bijn Thajudeen, Wei Xiang Wong, Saeed Bidar, Sevag C. Boyadjian, Wina Youssman, 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 SGLT2 inhibitors (SGLTI1) 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 SGLT2 and GLP1A.

**Methods:** This study had two phases, a retrospective phase and prospective phase to determine utilization of SGLT2/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 SGLT2/GLP1A, Hba1c, eGFR, new CVD events and adverse effects of SGLT2/GLP1A therapy. Primary outcomes measured was the change in percentage of eligible patients treated with an SGLT2/GLP1A.

**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 retrospective phase, percentage of patients on SGLT2/GLP1A at the end of prospective phase remained the same. Utilization of SGLT2/GAPA 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.

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**PUB080**

A Study on an Early Marker of Renal Damage in Known Diabetics Living in an Urban Slum of Hyderabad, India

Rahay K. Ranga,1 Mahesh Kumar Mummid,2 Rhonda Dzakpasu.1 1Georgetown University, Washington, DC; 2National Institute of Nutrition, Hyderabad, India.

**Background:** India is the nation with the second largest prevalence of type 2 diabetes mellitus in the world, with an estimated 69.2 million people having the condition as of 2015. In the surrounding as a whole, 78.3 million people live with type 2 diabetes, out of which 52.1% are undiagnosed. 44% of all cases of nephropathy are caused by type 2 diabetes mellitus.

**Methods:** There are two goals for this cross-sectional study: i) to measure the prevalence of microalbuminuria and albuminuria in type 2 diabetic patients and ii) to determine associated factors that elevate a diabetic’s risk for kidney disease. The study was done with 100 type 2 diabetics from Adda Gatta, Hyderabad, India. We performed urinalyses to measure urinary albumin, and gave a modified WHO STEPS questionnaire to assess lifestyle risks.

**Results:** 42 of the 100 patients surveyed were normoalbuminuric, 46 were microalbuminuric, and 12 were albuminuric. Significant risk factors were: being older than 44, having type 2 diabetes for longer than 6 years, drinking alcohol, and smoking.

**Conclusions:** The prevalence of microalbuminuria in type 2 diabetic people is quite a bit higher than it was in previous studies. Primary prevention needs to be emphasized in this population so that future generations don’t get type 2 diabetes mellitus. If patients get their serum creatinine checked, then should nephropathy arise, then it will be detected earlier, and treatment could start earlier. Future studies could ask questions regarding stress on the questionnaires, as well as check the patients’ serum creatinine, blood pressure, and lipid profiles.

**Funding:** Private Foundation Support, Government Support - Non-U.S.
Table 1. Summary of the status of the patients’ kidneys. Patients, based on the ACR, were classified into three groups: normalalbuminuric, microalbuminuric, and macroalbuminuric (n=100)

<table>
<thead>
<tr>
<th>Group</th>
<th>Normalalbuminuric</th>
<th>Microalbuminuric</th>
<th>Macroalbuminuric</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium Excretion</td>
<td>62</td>
<td>46</td>
<td>12</td>
</tr>
</tbody>
</table>

PUB081

**The Miraculous Shrinking Kidney**


**Introduction:** Glomerular hyperfiltration is common in conditions such as diabetes and obesity and can result in glomerular hypertrophy and organ growth as well as corresponding GFR increase. When hyperfiltration results in proteinuria this is a poor prognostic sign for CKD progression and needs to be managed appropriately. With this case report, we document dynamic progressive reduction in sizes of almost 18 and 16 cm kidneys, associated with resolution in proteinuria, after weight loss.

**Case Description:** A 70-year-old man with type II diabetes mellitus with retinopathy, hypertension, and morbid obesity was referred to nephrology for very enlarged kidneys and proteinuria. Of note, two weeks prior he had undergone a gastric bypass surgery. Prior to gastric surgery his BMI had been as high as 41.6 kg/m2. Kidneys measured 17.7 cm on the right and 15.9 cm on the left. His spot protein to creatinine ratio pre-gastric bypass was 2,388 mg/dL. Due to the significant growth of the kidneys, concern was initially for an infiltrative process and kidney biopsy was considered. However, the patient had just had gastric bypass surgery for weight loss, so the decision was made to serially monitor kidney sizes as hyperfiltration was high on the differential. With weight loss surgery and dietary changes, within six months, the patient had lost sixty pounds and decreased his BMI to 32.5 kg/m2. His A1C had decreased from 8.1 to 6.9. He was able to stop insulin and was maintained on metformin 1000mg bid and sitagliptin 100mg. His urine protein to creatinine ratio dramatically reduced from around 2388 mg/dL to normal level of 78 mg/g.

**Discussion:** This case illustrates dynamic change in kidney size by imaging with large weight loss as well as successful remission of sub-nephrotic range proteinuria following gastric sleeve surgery, extensive weight loss and glucose control.

PUB082

**Multiple Targets on Sodium Excretion with SGLT2 Inhibitors, Furosemide, and Spirolonactone Improves Diuretic Resistance in Patients with Diabetic Nephropathy on CKD Stage 3-4: A Pilot Study**

Wei T. Liang, Renmin Hospital of Wuhan University, Wuhan, China.

**Background:** At stage 3-4 of chronic renal disease, patients with diabetic-induced renal dysfunction are not sensitive to the conventional diuretic therapy based on loop diuretics and thiazide diuretics, leading to the earlier renal replacement at stage CKD 3-4. The lower sodium excretion could contribute to the development of diuretic resistance. The protective effects of SGLT2 inhibitors on cardiovascular is contributed by metabolic regulation and osmotic diuretic effect of glucose due to extra excretion of Glucose. The present study aims to investigate the efficacy and safety of SGLT2 inhibitors on the diuretic resistance of diabetic nephropathy at CKD 3-4 stage.

**Methods:** Patients with Diabetic nephropathy at CKD3-4 stage were administrated with furosemide + hydrochlorothiazide for 3 days with urine volume <1000ml, sodium urinary excretion >90mmol followed by Dapagliflozin/Canagliflozin once a day for 7 days.

**Results:** 3 male and 7 female patients with diabetic nephropathy were included, aged 51-80 years, with eGFR 60-4.6 ml/min, and 3 patients presented with cardiac insufficiency. Urine volume was 800±300/24 hours before treatment and 2000±500/24 hours after treatment. Sodium excretion in urine was 80±20mmol/24 hours before treatment and 150±50mmol/24 hours after treatment. The average net weight change was -3.5±2.2 kg. The Scr increased by 30%±5% before and after treatment, and the renal function in 2 patients increased by >30% after 7 days of treatment, and returned to the level of Scr before treatment after 7 days of treatment with Dapagliflozin/Canagliflozin. Electrolyte levels were comparable before and after treatment.

**Conclusions:** The diuretic regimen based on SGLT2 could significantly improve the resistance of diabetic nephropathy patients to loop 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 SGLT2 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:**


**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 electrolysates, 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 86-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, tamulosin, and pravastatin. His dietary history was significant for poor nutritional intake. Laboratory findings showed Hb 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 follic acid level of 11.4 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 organ 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**

Muhammad T. Shakoor, Jie Tang. Warren Alpert Medical School of Brown University, Providence, RI.

**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, osmolal gap 57, along with stage 2 AKI. His whole blood lactate was >171 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 eculizumab, an expensive HD prescription. We calculated HD prescription based on a simple 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 weight and EG clearance (ClEG) which we have been using reliably to calculate HD duration and post HD EG level. His weight and EG clearance (ClEG) for the F200 filter under Qb400 ml/min and Qd 800 ml/min is 147 ml/min. We decided to dialyze him for 4 hours. His post HD EG level was estimated to be: KG of EG = 240 min (HD time) * 147 ml/min (ClEG) + ClEG, for the F200 filter under Qb400 ml/min and Qd 800 ml/min is 147 ml/min. We decided to dialyze him for 4 hours. His post HD EG level was estimated to be: KG of EG = 240 min (HD time) * 147 ml/min (ClEG) + ClEG .

**Discussion:** Generally, the diagnosis 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 without waiting 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.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
The Estimation Formula of Phosphorous, Potassium, and Salt Amounts Excreted into Urine in Hemodialysis Patients

Momoko Fukazawa,1 Shunichiro Urabe,1 Motoko Kato,1 Yukie Kitajima,2 Akihito C. Yamashita,1 Toru Hyodo.1 Ejin Clinic, Hiritakura, Japan; 2Tokyo University of Technology School of Health Sciences, Shinagawa, Japan; 1Hosei University, Koganei, Japan.

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 hour urine from 22 hemodialysis patients (mean age: 73±12.1 years old, dialysis history: 31±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 urinary volume was 862±421 mL/day. The mean phosphorous amount in the urine was 114±55.9 mg/day, potassium 418±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 amount (r=0.759, p<0.001), urine volume vs potassium amounts (r=0.662, p<0.001). (Phosphorous amounts in the urine=101× [24 hours urine(L)/28] (Potassium amounts in the urine=334× [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=5.7× [24 hours urine(L)] -0.2).

Conclusions: As for phosphorous and potassium, if 24 hour 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 Calcino sis in Maintenance Hemodialysis Patients

Guibao Ke, Fengxia Zhang, Xueqin Chen, Hong Zhang, Shuai C. Dou, Zhiwen Liu, Shi Wei, Xining Liang, Shuangxin Liu. Department of Nephrology, Guangdong Provincial People’s Hospital, Guangdong Academy of Medical Sciences, Guangzhou, China.

Background: Uremic tumoral calcinosi s (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. During Haemodialysis

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 calcinosis tissue.

Funding: Government Support - Non-U.S.
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 dialysate flow rates of up to 500ml/min.

**Funding:** Commercial Support - Quanta Dialysis Technologies

**PUB089**

Clinical Performance of the Optiflux® F160NR Dialyzer

Jill M. Meyer,1 Dylan Steer,2 Lisa A. Weber,3 Mayuri Thakuria,4 Chiang-Hong Ho,4 Claudy Mullon,5 Robert J. Kossmann.4 California Institute of Renal Research, Chula Vista, CA; 4California Institute of Renal Research, San Diego, CA; 4Research Management Inc./ Kansas Nephrology Research, Wichita, KS; 3Freensius Medical Care North America, Walhalla, MI.

**Background:** Subjects in the clinical trial (NCT# 0356663), An Open-Label Clinical Study to Assess the Performance of the Dialyzer with Endexo® 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, spk/U, serum albumin and a-2-microglobulin levels with removal rates measured pre and post HD, complement activation, and Adverse Events (AEs).

**Results:** Sixteen subjects were screened. Twenty-three subjects were enrolled in the study (median age 64 years, females 73.91% and white 73.91%) and completed 288 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 parameters 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) reported for enrolled subjects were: 80.5% (4.5) for URR, 1.9 (0.3) for spk/U, 47.1% (7.4) for corrected a-2-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 spk/U were high with the Optiflux® F160NR dialyzer. Serum albumin levels increased post HD. Complements showed no overt activation.

**Funding:** Commercial Support - Freensius Medical Care North America

Table 1. Delivered HD for completed subjects (n=19, 228 HD sessions)

<table>
<thead>
<tr>
<th>URR</th>
<th>spk/U</th>
<th>Albumin</th>
<th>C3a</th>
<th>C5a</th>
<th>sC5b-9</th>
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<tbody>
<tr>
<td>1.9</td>
<td>0.3</td>
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**PUB090**

Dialysis Disequilibrium Syndrome: Severe Irreversible Brain Injury Following Hemodialysis

Fatima Ballout, Pravir V. Baxi, Roger A. Rodby. Rush University Medical Center, Chicago, IL.

**Introduction:** Dialysis 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, hypothermia, 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 osmoles 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.

**Results:** HD treatments were well tolerated and URR and spk/U were high with the Optiflux® F160NR dialyzer. Serum albumin levels increased post HD. Complements showed no overt activation.

**Funding:** Commercial Support - Freensius Medical Care North America

Table 1. Delivered HD for completed subjects (n=19, 228 HD sessions)

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**PUB091**

Sustained High-Dose Chronic CRRT Fails to Attenuate Severe Lactic Acidosis in an Immuno-therapy-Resistant Case of Malignant Melanoma with Liver Visceral Crisis

Mabel S. Tan, Han K. Tan. Singapore General Hospital, Department of Renal Medicine, Singapore, Singapore.

**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 65-year-old Chinese 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 dialysis fluid multiBic 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 demised 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 hypoperfusion (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 tuning is less likely to affect outcome.

**PUB092**

Primary Caregiver Burden in a Hemodialysis Clinic in Mexico: Prevalence and Caregiver-Related Risk Factors

Eduar Solis, Joselyn Rivera, Juan M. Ardanuy Izurte. Medica Santa Carmen, San Miguel de Allende, Mexico.

**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 responders 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 take 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
Masuko Iwasaki,1 Hitoshi Suzuki,1,2 Aiko Wakahayama,2 Maiko Akira,1 Yusuke Suzuki,2 1Juntendo University Urayasu Hospital, Urayasu, Japan; 2Juntendo University Faculty of Medicine, Tokyo, Japan.

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 cervicotoracic posterior longitudinal ligament ossification. After the operation, maximum 3.5 mg/kg/hr of propofol was used for sedation treatment of severe pneumonia under the mechanical ventilator. Catecholamines was also used to support hemodynamics. However, unidentified hemorrhage and impaired blood pressure were prolonged, then administration of propofol was discontinued on POD6. Acute kidney injuries (sCr2.3mg/dl), metabolic acidosis and high serum CK (79300U/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 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
Vladimir Rigoson,1 Yue Jiao,1 Lori Viennet,1 Joanna Willetts,1 Sheetal Chaudhuri,2 John W. Larkin,1 Len A. Usvyat,2 Jeffrey L. Hymes,2 Robert J. Kossman,2 Franklin W. Maddux,2 Kurt Mussina.1 1Fresenius Renal Research, Waltham, MA; 2Fresenius Medical Care, General Medical Office, Waltham, MA; 3Fresenius Medical Care North America, Waltham, MA; 4Fresenius Medical Care AG & Co. KGaA, General Medical Office, Bad Homburg, Germany.

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 clinical quality target achievement in dialysis facilities conducting trials versus matched facilities with similar attributes that were not involved in research activities.

Methods: We used data from adult (age ≤18 years) hemodialysis patients treated at a network 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 metrics in dialysis facilities that conducted trials versus matched facilities not involved in research (Figure 1).

Conclusions: 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).

Funding: Commercial Support - Fresenius Medical Care
Impact of Major Surgical Operations on Clinical Outcome in Dialysis Patients


Background: We aimed to study the impact of major surgical operations on clinical outcome in patients with haemodialysis (HD) or peritoneal dialysis (PD).

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 each major surgical operation performed was 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 cardiovascular in 14 patients, orthopaedic in 11, gastrointestinal in 6, parathyroidectomy in 5 and brain, pulmonary and breast in 1 patient each. 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 (57 to 49 months), while it was 49 months (46 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 1.033, 95% CI 1.010-1.057, p=0.005), diabetes (RR 2.581, 95% CI 1.474-4.521, p=0.001), preoperative C-reactive protein level (RR 1.005, 95% CI 1.002-1.007, p=0.001) and having a major surgical operation (RR 1.868, 95% CI 1.068-3.268, p=0.028) were the 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.

Outcomes of Ceftolozane/Tazobactam Recommended Doses in Treating Multidrug-Resistant Bacteria in Critically Ill Patients Using Renal Replacement Therapy

Wasim El Nekidy,1,2 Leen Oyoun Alsaoud,3 Nizar M. Attallah,1 Laila Riekib,4 Fadi A. Hijjazi,5 Ahmad R. Nusair,3 Jihad Mallat,4 Islam Ghazi.1 1Cleveland Clinic Abu Dhabi, Abu Dhabi, United Arab Emirates; 2Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, OH, 3University of the Sciences in Philadelphia, Philadelphia, PA; 4Trillium Health Partners, Mississauga, ON, Canada.

Background: Ceftolozane/tazobactam (CEF/TAZ) is a new broad spectrum cephalosporin effective against Multi-drug Resistant (MDR) bacteria. The clinical outcomes of the recommended dose of CEF/TAZ in patients utilizing renal replacement therapies are lacking. The purpose of this study was to evaluate the clinical and microbiological efficacy of CEF/TAZ in treating MDR in patients utilizing continuous venovenous hemofiltration (CVVH) and intermittent hemodialysis (IHD).

Methods: A retrospective cohort study was conducted at our quaternary care hospital between May 2015 and December 2019. We reviewed all hospitalized adults who had MDR Pseudomonas aeruginosa or MDR enterobacteriaceae treated with CEF/TAZ while utilizing CVVH or IHD.

Results: We identified 11 patients who met the inclusion criteria with a mean age of 63.0 ±17.8 years and a mean weight of 63.8 ±15.7 kg. All patients were critically ill, needed mechanical ventilation, and used vasoressors. All 11 patients had pneumonia, one of them developed secondary bacteremia and two had decubitus ulcer. Nine patients had MDR pseudomonas aeruginosa while two had MDR E. coli and Klebsiella pneumonia. Six patients were on IHD, while the remaining 5 patients were on CVVH. The most commonly used dose for CVVH was 450 or 750 mg intravenous (IV) every 8 hours (only one received 1500 mg at the same frequency). For IHD, the common dose was 450 mg IV every 8 hours. Of the 7 patients who had repeated cultures, three had microbiological cure and four had clinical cure. Two patients expired within 30 days and 3 more expired within 90 days. Two of the patients who had clinical cure, had recurrence within 4 weeks.

Conclusions: The efficacy of the recommended CEF/TAZ dose in patients utilizing RRT is uncertain. Pharmacokinetics and pharmacodynamics studies are urgently needed to determine the adequacy of CEF/AEI dosing in this population.

Does Dialyzer Surface Area Alone Adjusted to Body Surface Area Have Any Clinical Impact on Adequacy: A Single-Center Observation Study in Saudi Arabia

Najlaa Almalki, Ahmad S. Ghanem, Azharuddin Mohammed. Armed Forces Hospitals Administration in Taif Region, Taif, Saudi Arabia.

Background: Dialysis adequacy using sp Kt/V is a standard KPI in HD units, determined by dialyzer clearance(K), Volume of distribution urea(V) and treatment time(t). Increase in larger dialyzer size (t, V being constant) is a norm to improve Kt/V during HD as the patients gradually lose residual kidney function. However initial and subsequent dialyzer prescription using Body Surface Area(BSA) instead of Weight(V) is less well studied. We looked into effect of BSA and DSA on Kt/V.

Methods: 163(n=) patients receiving in-center HD on Gambio dialyzers (Polyflux, Revecache) studied. Demographic and clinical data collected. Patients were stratified into 4 groups based on their dialyzer surface area (DSA) as 1.4, 1.7, 1.8 and 2.1 m². For each group, we then calculated BSA(Bois Bois method), HD vintage, treatment time(hours), Access type, sp Kt/V (Dougirdas) and % pts with inadequate sp Kt/V , <1.2. Hemoglobin during HD as the patients gradually lose residual kidney function. However initial and subsequent dialyzer prescription using Body Surface Area(BSA) instead of Weight(V) is less well studied. We looked into effect of BSA and DSA on Kt/V.

Results: Our patients were representative of any HD center in terms of demographics; age 57.8 ±18.3, 50.9%Males, 28.2% DM, vintage 59.3±51.2, BMI 25.1±6, BSA 1.7±0.3 and Kt/V 1.7±0.4. The use of dialyzer with DSA’s 1.4, 1.7, 1.8 and 2.1 were 63.2%, 55.5%, 8.6% and 22.1 %. Among 4 groups, there was no significant difference in terms of age, treatment time, vascular access and hemoglobin, Image 1. But when DSA and BSA were stratified for adequacy, there was a modest linear trend of decreasing Kt/V with increasing BSA among 4 increasing DSA groups. Although all met the minimum sp Kt/V of 1.2, the proportion of patients with inadequate Kt/V were increasing despite their increasing dialyzer sizes. Factors. For equilibrated Kt/V, adequacy could just be borderline for larger patients.

Conclusions: Dialyzer size change in itself may not be effective in achieving target Kt/V as BSA increases; attention must be paid to increasing dialysis time. Dialyzer prescription, adjusting for BSA may be more appropriate, particularly in large patients.
**PUB101**

**High Ultrafiltration Rate: Is It Bad? A Case Report of a Patient on Hemodialysis for 29 Years with High Ultrafiltration Rate**

Aziz U. Seedy, Diaverum, Riyadh, Saudi Arabia.

*Introduction:* High ultrafiltration on Hemodialysis stresses cardiovascular and could have negative effect on survival. This is the notion of many studies done in line with High ultrafiltration. However, dismissing the other side of coin, cumulated effect of fluid removals,.Cardiovascular overload on cardiovascular system.

*Case Description:* We present a case 60 year male develop proteinuria lost follow up, presented with CKD 5, started on hemodialysis which he is on for 29 years now. He was hypertensive to start with later became normotensive. His intradialytic weight gain is 4.5 to 5.5 liters, which he tolerates well without any episode of intradialytic hypotension. We report a case of successful emergent PD with high bicarb dialysate in an actively dying patient not tolerating standard renal replacement therapies.

*Discussion:* Except Carpal, tunnel Syndrome for which he had surgery, clinically stable, normal biochemical parameters and acceptable cardiovascular status with this entire very remarkable journey.

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**PUB102**

**The Influence of Different Hemodialysis Frequency on Maintenance Hemodialysis Patients**

Hou Li. the first affiliated hospital of Xi’an Jiaotong University, Xi’an, China.

*Background:* To investigate the effects of different dialysis frequencies on anemia, nutritional status, calcium and phosphorus metabolism, renal function indicators in patients.

*Methods:* The general data of MHD patients in our center from 2017 to 2019 and annual laboratory monitoring indicators (including HGB, SF, Bun, Scr, Ca, P, iPTH, ALP, ALB, ABG, urine volume and eGFR, were used to compare in patients with different hemodialysis frequency groups (Group A: 2 times/week; B: 3 times/2 weeks; C: 3 times/ week).

*Results:* There were 269 patients (163 males, 106 females), with an average age of 52.65±14.982 years. There were statistical differences among HGB, Ca and ALB, but no statistical differences among SF, P, iPTH, ALB, Bun and Scr. The three-year overall compliance rate evaluation found that the overall compliance rate of HBG and Ca significantly increased. It was found that the compliance rates of HGB and Ca at the dialysis frequency of 2 times a week were significantly lower than those of the other two groups, but there is no difference for P, iPTH and ALB.

*Conclusions:* Different from western countries or developed areas, the frequency less than 3 times is more twice in the western region in China. In this study, the average of HGB and Ca in patients with dialysis 3 times a week is significantly higher than other groups with low-frequency, and the compliance rate of HGB and Ca in group with the dialysis 3 times a week increased significantly. The results suggested that the higher frequency group was better in anemia and calcium correction.

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**PUB103**

**Achromobacter Xylosoxidans, Subspecies Denitrificans, Exit Site Infection, and Aeromonas Hydrophlia Peritonitis: Rare Infections in Peritoneal Dialysis Patients**


*Background:* Achromobacter xylosoxidans, species 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 gramm 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 hydrophila 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.

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**PUB104**

**Bicarbonate-Rich Peritoneal Dialysis as Salvage Therapy for Metabolic Acidosis**

Elise L. Stephenson, Ryan A. Carver, Jessica R. Burgess, Thomas R. McCune. Eastern Virginia Medical School, Norfolk, VA.

*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 declining oxygenation 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 goodies 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 mLq 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 vaspressor requirements decreased. After four exchanges, CRRT was initiated. His acidosis resolved within 24 hours and he was vaspressor 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.

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**PUB105**

**Myoclonic Seizures and Altered Mental Status in a Patient on Peritoneal Dialysis Treated with Piperazine**

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1Universidad de los Andes, Bogota, Colombia; 2Hospital Universitario Fundación Santa Fe de Bogotá, Bogotá, Colombia; 3Healthy Medical Center, Zipaquira, Colombia.

*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, an anthelmintic. 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 neuropathy that lead to ESRD. He was started on RRT 1 year before presentation; initially hemodialysis but later APD. He had no history of seizures or any other neurological disease. Physical examination on admission revealed a dehydrated, ill-looking patient. He was unresponsive to verbal commands. Myoclonus predominantly in his left arm was noticed. Initially we
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 dialyzability 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. A75% 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**

Aireen Kate M. Kuan, Shamir Hasan, Yuriy 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, celecoxib and plaquenil). ESKD on peritoneal dialysis (PD), subclinical hypothyroidism, anemia and hypertension was admitted for her lesions of 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, CI 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 Dislodgment 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 dislodgment 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 the 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 dislodgment 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.

**Funding:** Commercial Support - AcuSense Biomedical Technology Corp.
Catheter Malposition: Unacceptable Reason for Access Dysfunction

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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 IJV non-tunneled CVC placed for continuous 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 IJV. Case 2: 30 y/o male with a pre-existing right port cath was attempted several episodes of non-sustained ventricular tachycardia, 2 days after a newly placed left dialysis CVC. Chest XR showed port cath had disconnected and migrated to the right ventricle. Removal of the dislodged port cath 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 replacement with a longer CVC. Case 4: 65 y/o female with left IJV tunneled 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 cloting of the continuous dialysis circuit soon after initiation with a left IJV 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 IPA. Most of these mechanical complications are preventable with proper training and utilizing imaging tools during the procedure.

Percutaneous Transluminal Angioplasty in Arteriovenous Fistula Dysfunction Secondary to Vascular Stenosis

Mohammed Sheeb Ahmed Khan, Vinod Kumar. Aster Medcity Aster Medcity, Kochi, India.

Background: Arterio-venous fistula (AVF) is the lifeline of a hemodialysis patient and the number of vascular accesses in a hybrid in a patient. Vascular stenosis necessitates vascular intervention or creation of a “de novo” AVF. In this study we aimed to evaluate the outcome of percutaneous transluminal angioplasty (PTA) in arterio-venous fistula due to vascular stenosis.

Methods: This is a prospective study of two years (02.05.17 to 02.05.19). Records of patients admitted to our hospital were obtained from hospital archives and images from the hospital radiology imaging system. Demographic characteristics, duration of dialysis, stenosis or occlusion level, patency rates of AVF were evaluated. All procedures were performed by interventional radiologists in a hybrid in a patient. Antegrade, retrograde, or both antegrade and retrograde punctures were used, depending on the site of the stenosis as deemed on preoperative ultrasound. A complete angiogram from the proximal arteriovenous anastomosis to the central venous outflow was performed in all cases. A successful percutaneous balloon angioplasty was defined when there was no more than 30% residual stenosis (KDQI). AVF patency rates were assessed at six months and one year.

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 (31.25%) and central vein stenosis (18.75%). Successful PTA was done in 12 patients. There were no complications; hemodialysis was resumed with native AVF after the procedure. The AVF 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 ± 6.79 months. None underwent a repeat PTA.

Conclusions: Percutaneous transluminal angioplasty is effective for salvaging arterio-venous fistula in majority of hemodialysis patients.

A Tale of Two Accesses: The “Less is More”

Sherif Metwalli, Anilk. Agrawal, 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 resumption of HD. His vascular access was through 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 supervised 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 followed the patient to optimize dialysis through their existing ‘malfuctioning’ access and avoided further interventions that could result in worse complications, proving the adage ‘Less is More’ still true for dialysis access.

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 any 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 (76%) Most preferred for 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 activities: content description (60%) and learning objectives (56%) The most important factors in selecting which symposia to attend at a scientific congress were content (60%), learning objective (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%) Successful 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.
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 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 therapeutics 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 therapeutics 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

Optimizing On-the-Go Learning Utilizing Short Modules on Topics Related to Nephrology

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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: Wolconx 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, 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 Osmolar 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 (HAGM). Neurological and gastrointestinal symptoms predominate early while renal failure and death occur if not diagnosed and treated promptly. The diagnosis is usually suggested by HAGM 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, restless and elevated creatinine of 1.4 mg/dl (baseline 1.2mg/dl). History was difficult to obtain. Vital signs were normal and the physical exam was remarkable only for altered mental status. CT scan of the head did not reveal any acute abnormality. Laboratory workup revealed HAGMA (anion gap = 21 mEq/L, arterial blood pH = 7.62, serum bicarbonate = 9.3 mmol/L, lactic acid = 2.2 mmol/L) with a near-normal serum osmolal gap (12 mOsm/kg). Urinalysis, urine drug screen, blood ethanol, beta-hydroxybutyrate, acetaminophen and salicylate levels were normal. Given a high clinical suspicion for toxic alcohol ingestion, the patient was treated with IV fluids and fomepizole. Over the next few days, his mental status improved, and repeat laboratory workup demonstrated correction of the anion 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 was normal.

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.

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

Compensatory Rules for Simple Acid-Base Disorders
Mohammad Amin Fallahzadeh,1 Mohammad Kazem Fallahzadeh Abarghouei,2 Michael Emmett.1 1Department of Internal Medicine, Baylor University Medical Center, Dallas, TX; 2Division of Nephrology, University of California San Francisco, San Francisco, CA.

Background: Most acid-base compensatory equations are based on limited numbers of human observations. We searched the literature for all studies addressing the issue of acid-base disorder compensation. We then utilized all the available data to create an acid-base compensation diagram and generate more accurate compensatory equations.

Methods: We used 84 published articles that evaluated the acid-base blood gas parameters of patients with simple acid-base disorders. We extracted the measured bicarbonate and PCO2, and the authors were requested to send us the full text of articles to calculate the most accurate compensatory formulas for simple acid-base disorders.

Results: Our database was comprised of 3806 observations with simple acid-base disorders. Our results generally agreed with the Goldberg acid-base nomogram except for hyperkalemia which was better described with severe metabolic alkalosis (Figure 1). The best proposed formula in the literature for simple acid-base disorders and the compensatory formulas generated by our data are illustrated in Table 1.

Conclusions: Although the formulas described in the literature perform relatively well in predicting the appropriate compensatory response to simple acid-base disorders, more accurate predictive formulas were developed.

Table 1. The best proposed equations in the literature and most accurate formulas for simple acid-base disorders

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<tr>
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Figure 1. Comparison our data points (a) with acid-base map proposed by Goldberg et al. (b)

Hypernatremia Three Ways
Jordan R. Evans,1 Shweta Bansal.2 1US Army Brooke Army Medical Center, Fort Sam Houston, TX; 2University 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 urinary 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 D5W 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 mmol/L, creatinine returned to baseline, and the D5W 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 was 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 2 hours after desmopressin 2 mcg SQ, confirming the suspicion. His serum sodium and urine volume remained in

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

Underline represents presenting author.

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normal limits on scheduled desmopressin doses over next week; however, on day 15 family requested withdrawal of care due to ongoing seizures and futility of care.

Discussion: Our patient developed 3 episodes of hyponatremia during same admission, all due to different etiologies. This case highlights the importance of careful ongoing assessment of history and lab parameters since the best treatment strategy may change for the same diagnosis during the same admission.

Nephrotoxicity is induced after amphotericin B inserts into tubular cell depletes intracellular glutathione resulting in increased levels of 5-oxopropyl. Patients, like the one reported here, with malnutrition, female gender, sepsis, and kidney dysfunction are especially susceptible as they have lower glutathione levels leading to faster 5-oxopropyl accumulation despite standard dosing of amphotericin. Prompt recognition is essential for treatment with acetaminophen cessation and bicarbonate supplementation. Use of acetaminophen as an analgesic alternative to opioids is recognized is essential for treatment with acetaminophen cessation and bicarbonate supplementation. Clinical awareness of predisposing conditions and close monitoring of patient’s acid-base and kidney status can help us mitigate this underrecognized complication of acetaminophen use.


Introduction: Amphotericin B is the drug of choice for most life-threatening fungal infections. Nephrotoxicity is a common adverse reaction of this medication and its lipid complex formulation is an alternative to ameliorate this risk. Renal Tubular Acidosis (RTA) is an uncommon but major complication that can occur, and close monitoring should be performed for rapid identification and management. We hereby present the case of a patient who developed distal RTA secondary to amphotericin B lipid complex.

Case Description: A 59-year-old male patient without known medical history was admitted to Hematology-Oncology Ward with acute Myeloid Leukemia. Chemotherapy with cytarabine and idarubicin was initiated. The patient developed pancytopenia secondary to chemotherapy nadir and septic shock dependent of vasopressors. In addition, the patient suffered an intractable sinus congestion that lead to a biopsy in which invasive fungal sinusitis secondary to Aspergillus was revealed. Amphotericin B lipid complex was started and resulted in improvement of the infectious process. However, the patient developed a stage three acute kidney injury with associated hypokalemia of 2.9 mmol/L, hypophosphatemia of 129 mmol/L, and mixed high and normal anion gap metabolic acidosis of 21.4 mmol/L. Noted findings were consistent with distal RTA and high anion gap component due to renal failure. Amphotericin B was changed to another anti fungal and potassium and bicarbonate were replaced. Treatment led to resolution of azotemia, electrolyte, and acid-base disturbances.

Discussion: Nephrotoxicity is induced after amphotericin B inserts into tubular cell membranes and creates pores that increase permeability, leading to kaliuresis and back diffusion of secreted hydrogen ions. Although this effect is less common with liposomal amphotericin, it has been described in the literature. In addition, the risk increases in diffusion of secreted hydrogen ions. Although this effect is less common with liposomal

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) >5.0mmol/L, from 2015.1.1 to 2017.12.31 were included. The diagnosis rate was defined as the proportion of HK episodes that have diagnoses records. Treatment rate was defined as a 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 record(s) within 1 day.

Results: A total of 36,615 ED patients with S-K ≥5.0mmol/L each 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 45.3%, 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, were used only in 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 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 (22.4-30.6%).

Conclusions: In China, the diagnosis and retesting 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.
therapy is of utmost importance in patients with clinical suspicion of a hematologic malignancy, and hypoxia. A 56 year old woman presented with right knee pain due to septic arthritis. Her admission labs were notable for a sodium of 124 mEq/L, Cr 4.76 mg/dL. Her anion gap was -3 and her serum osmolality was measured as 316 mOsm/kg, with a 50 mOsm/kg osmol gap. Her total protein was noted to be 12.6 g/dL, albumin 2.1 g/dL, with a total bilirubin of 11.1 mg/dL, and glucose 69 mg/dL. Her bicarbonate was 137 mEq/L consistent with pseudohyponatremia. UAC and UPC were 187 mg/w and 780 mg/g respectively. SiEP and UEIP ultimately demonstrated monoclonal IgG kappa. Her total protein increased to 13.7 g/dL, she subsequently became lethargic and developed epistaxis. Further labs revealed a hyperviscosity syndrome with a serum viscosity of 9.2 cP. Her WBC was 140 K/mm3. She underwent 3 sessions of plasmaspheresis and her pseudohyponatremia resolved (Na 139 mEq/L) and total protein improved to 8.9 g/dL. SAG increased to 7. Her mental status and epistaxis improved. Subsequent bone marrow biopsy confirmed 65% plasma cells. She underwent 3 sessions of plasmaspheresis and her pseudohyponatremia resolved (Na 139 mEq/L) and total protein improved to 8.9 g/dL. SAG increased to 7. Her mental status and epistaxis improved. Subsequent bone marrow biopsy confirmed 65% plasma cells. She underwent 3 sessions of plasmaspheresis and her pseudohyponatremia resolved (Na 139 mEq/L) and total protein improved to 8.9 g/dL. SAG increased to 7. Her mental status and epistaxis improved. Subsequent bone marrow biopsy confirmed 65% plasma cells. She underwent 3 sessions of plasmaspheresis and her pseudohyponatremia resolved (Na 139 mEq/L) and total protein improved to 8.9 g/dL. SAG increased to 7. Her mental status and epistaxis improved. Subsequent bone marrow biopsy confirmed 65% plasma cells.
was started on IV hydration, dexamethasone, rasburicase, and allopurinol. On the fifth hospital day, the patient was stable, 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 8.3 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 65 μM2. Consequently, hemodialysis was performed with good tolerance and response to treatment.

Discussion: The criteria for hemodialysis in this case of a non-oliguric euvoletic 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.

Rising from Death: A Case of Life-Threatening Hyperkalemia

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

Introduction: Hyperkalemia affects the cardiac conduction and can result in fatal consequences. We describe a rare case of life threatening hyperkalemia presenting in setting of hyperglycemia, sepsis and shock and manifesting as new ST elevation in anterior leads, which resolved with correction of hyperglycemia.

Case Description: A 63-year-old male with intellectual disability and diabetes presented in state of shock after refusing his medications for last 5 days. His vitals on arrival were pertinent for hypothermia (T 29.1°C) and hypotension (56/30 mm Hg). He had cold and clammy extremities and Glasgow Coma Scale of 5. Cardiovascular and bicarbonate levels improved with conservative management without need for renal replacement therapy. Subsequent transthoracic echocardiogram was negative for acute ischemic changes and repeat EKG showed sinus rhythm and resolution of ST changes. The creatine kinase (CK) levels were normal but troponin T high sensitivity were elevated.

Discussion: Severe hyperkalemia is dangerous and can result in cardiac arrest. Our patient presented with very high potassium levels, however hypertensive state might have reduced cardiac output and prevented immediate cardiac arrest. Hyperkalemia in setting of uncontrolled hyperglycemia usually responds to medical management if the patient is not anuric. Moreover, pseudo infarction as seen in this case is a rare manifestation of hyperkalemia. With the recent emphasis on reducing door-to-balloon times in acute myocardial infarction, it is important to be aware of its association with hyperkalemia as it usually resolves with reduction of the serum potassium levels.
An Unusual Cause of Rhabdomyolysis

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Introduction: Rhabdomyolysis results from muscle cell injury and often leads to AKI. Common causes include trauma, medications, electrolyte abnormalities, and metabolic myopathies. The clinical presentation includes muscle pain, dark urine, and possible oliguria. Here, we present an unusual etiology of rhabdomyolysis resulting from sustained hyperosmolarity due to severe hyperglycemia and hypernatremia.

Case Description: 23-year-old male with no significant medical history presented with fatigue, shortness of breath, nausea, vomiting, and severe muscle pain, diarrhea. Despite drinking large amounts of fluids, he felt thirsty, with frequent urination. Family history: diabetes. Social history: no alcohol, smoking or drug use. No prescription/OTC medicines, or herbal supplements. Vital signs were notable for a heart rate of 110-120 beats/min. He appeared lethargic. Physical exam showed dry mucous membranes and tachycardia, otherwise unremarkable. Initial laboratory values showed blood glucose of 1132 mg/dL, Cr 3.5 mg/dL, Na 147 mEq/L (see table). Urine showed glucosuria and ketones, sediment was bland. He was started on an insulin drip. Corrected Na was 172 with a free water deficit 10L. Initially given 3L NS bolus followed by 1/2NS maint. Blood was drawn to look for rhabdomyolysis in HHS. It is unclear why our patient showed such a severe response to HHS. In up to 50% of HHS cases, this is an extreme case and highlights the importance of looking for rhabdomyolysis in HHS.

The clinical presentation includes muscle pain, dark urine, and metabolic acidosis (CO2 16 [22-30 mmol/L]). Ionized calcium (iCa) was low at 3.34 [4.60 - 5.30 mg/dL] and metabolic acidosis (CO2 16 [22-30 mmol/L]). Ionized calcium (iCa) was low at 3.34 [4.60 - 5.30 mg/dL] and phosphorus 4.6mg/dL [2.2 - 4.6 mg/dL]. His intact parathyroid hormone (PTH) was elevated at 121 [14.0 - 72.0 pg/mL], however, his PTH went back up to his previous baseline at 220 pg/mL. He was discharged from the hospital with close outpatient follow up.

Discussion: Hyperparathyroidism and hypocalcemia (6.3 mg/dL [8.6 - 10.5 mg/dL]), hypomagnesemia (0.6 mg/dL [0.6-2.6mg/dL]) and metabolic acidosis (CO2 16 [22-30 mmol/L]). Ionized calcium (iCa) was low at 3.34 [4.60 - 5.30 mg/dL] and phosphorus 4.6mg/dL [2.2 - 4.6 mg/dL]. His intact parathyroid hormone (PTH) was elevated at 121 [14.0 - 72.0 pg/mL]; however, this was relatively lower than his baseline of 200-250 pg/mL. After adequate magnesium repletion and discontinuation of patiromer, his Calcium improved to 8.4 mg/dL, iCa improved to 4.20mg/dL, and his PTH went back up to his previous baseline at 220 pg/mL. His AKI improved following placement of a ureteral stent.

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 did not 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 IM 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 involvement. 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.
**PUB138**

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 father and three unaffected family members had not found this variant. This mutation was results into frameshift followed by formation of a truncated protein, which is responsible for translated protein rather than complete deficiency seen in autosomal recessive disorders. Our results provide a signal of more complicated genetic inheritance in type IV collagen, approximately 80% of which is caused by X-linked mutations in the COL4A5 gene, which were significant for screening and genetic diagnosis for Alport syndrome.

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

**PUB139**

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 females, 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=3) 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/1.73 m², 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.
Findings of Whole-Exome Sequencing in a Tunisian Man with Congenital Anomalies of Kidney and Ureteral Tract and Dilated Cardiomyopathy
Sabra Aloui,1 Majdi Nagara,2 Salima Ltaief,1 Ahmed Letaief,1 Manel Ben salah,1 Mouna Hamouda,1 Meriem Ben salem,1 Habib Shkiri,1 Ridha Mrad,2 Sonia Abdeljuk,1 1Department of Nephrology, Monastir University, Monastir, Tunisia; 2Department of Human Genetics, Charles Nicolle Hospital, Tunis, Tunisia; 3Laboratory of Biomedical Genomics and Oncogenetics, Institut Pasteur de Tunis, Tunis, Tunisia.

Background: Congenital Anomalies of Kidney and Ureteral Tract (CAKUT) is a paediatric concern but can be diagnosed in adults adding challenges in the identification of CAKUT’s etiology. To date, there are more than 50 single-gene disorders known to underlie CAKUT. Furthermore, a substantial number of CAKUT causes are extremely rare in the general population. Whole exome sequencing (WES) has been proposed as the solution in some cases.

Methods: Whole exome sequencing and case study of an adult with CAKUT, cardiomyopathy, factor7 and other anomalies

Results: It is about a 30-years-old Tunisian man. He was referred to our unit for renal failure. His parents are second degree consanguine. He was hospitalized at age 2 years for dehydration. He had a brother with Parkinson disease started early at age of 20 years. He was hospitalised at age 29 in cardiology unit for heart failure. Explorations revealed dilated cardiomyopathy (DCM) and an elevated plasmatic creatinine. Physical examination showed a peculiar facies with crying facial expression when laughing, dental anomalies, mild mental retardation, strabismus, large prominent earlobes, brachydactylia, right cryptorchidism and normal blood pressure. Laboratory exams confirmed kidney failure: creatinine at 900μmol/L without proteinuria or haematuria. Prothrombin level was low to 50%, the exploration revealed a factor VII deficiency. Ultrasound scans showed a single right kidney of reduced size. We concluded at chronic renal failure due to tubulointerstitial nephritis associated with urofacial syndrome, DCM and factorVII deficiency. The diagnosis of a CAKUT with OCHOA syndrome was suspected but heart failure and factor VII deficiency were not explained. A whole sequencing exome was performed. It reversed the Osha syndrome and revealed two other possible genetic etiologies of CAKUT: a Kabuki syndrome and a Sensenbrenner syndrome. It also revealed a mutation of TTN, the gene encoding the sarcomere protein titin, explaining the DCM.

Conclusions: Exome Sequencing have a dual role as a discovery and diagnostic Tool. It’s clinical utility will be discussed especially in in countries with strong consanguinity and low-income as in North Africa

ANCA-Negative Pauci-Immune Crescentic Glomerulonephritis: A Positively Rare Cause of RPGN
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Introduction: Pauci-immune crescentic necrotizing glomerulonephritis (PICGN) is the most common subset of RPGN. Most cases of PICGN are antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides; however, about 10-30% of patients are ANCA negative. Several studies have suggested that ANCA-negative PICGN has a lower incidence of extra-renal involvement, a poorer prognosis, and often dialysis dependent. Unfortunately given our limited understanding of the pathophysiology of ANCA-negative PICGN, current therapy is similar to ANCA-positive despite its worse prognosis.

Case Description: 60-year-old female presented for hypertension emergency. She had an elevated creatinine (Cr) of 1.48; baseline was 1.29 two weeks ago. Her Cr worsened to 2.05. Renal biopsy was consulted. Initial differential included acute drop in BP from restarting medications. UA showed 2+ protein, quantified 2 grams/gCr and RBC > 100. Findings of ANCA testing negative. Several studies have suggested that ANCA-negative PICGN has a lower incidence of extra-renal involvement, a poorer prognosis, and often dialysis dependent. Unfortunately given our limited understanding of the pathophysiology of ANCA-negative PICGN, current therapy is similar to ANCA-positive despite its worse prognosis.

Discussion: Since patients with ANCA-negative PICGN have few extra-renal manifestations, they are often dialysis dependent and have a worse prognosis, early recognition is crucial. The diagnosis primarily relies on performing a kidney biopsy rather than serological testing, otherwise the diagnosis may be missed. Early initiation of empiric therapy is appropriate to minimize the degree of irreversible injury and delay dialysis initiation. The use of deferasirox in non-renal fibrotic lesions in renal biopsy may predict treatment response. ANCA negative PICGN is a rare diagnosis; this case highlights why it is important to keep this diagnosis in the differential and why novel treatment options are needed.
Case Description: A 32-year-old female with prior history of gestational hypertension presented to our hospital 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 kidney protection 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 the 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

Background: Robert J. Turner, Stefan Gola, Carina Wollnik, Nils Burkhardt, Ina Sternberger, Uwe Andag, Hauke Cornils 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 (AAN), is rare disease associated with variable outcomes. These patients often do not have typical presentation of either anti-GBM disease or AAN, 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, HCV, 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 variable 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: The purpomycin aminonucleoside nephropathy (PAN) model is associated with proteinuria and matrix accumulation. We tested the hypothesis that renal COL1A1 and COL3A1 are differentially expressed genes in PAN nephropathy.

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, antimetabolites, 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 hemodialysis-requiring acute renal failure. He received a single dose of ecclizulam empirically due to concern for atypical HUS, but platelet counts improved too rapidly.

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to be consistent with eculizumab benefit. Kidney biopsy revealed acute tubular injury with 70% of GOM did not have detectable monoclonal serum protein. Like other reported cases, he responded well to a bortezomib based regimen.

PUB51B
A Challenging Case of Renal-Limited Vasculitis
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Introduction: Anti-neutrophil cytoplasmatic 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. Uramyc 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, HbsAg, 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, titers 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 waxing and waning renal function. Atypical features of AAV should raise concern for drug-induced etiology.

PUB512
Collapsing Focal and Segmental Glomerulosclerosis with Thrombotic Microangiopathy Found on Renal Biopsy in a Patient Receiving Intravitreal Aflibercept for Age-Related Macular Degeneration
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Introduction: Intravitreal Vascular Endothelial Growth Factor (VEGF) Receptor blockade medications are used for a variety of retinal diseases. 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 (TMs) are also being increasingly reported. One variant of TMs that has been described is collapsing focal and segmental glomerulosclerosis (cFSGS). cFSGS has been postulated to occur due to VEGF-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 aflibercept for age-related macular degeneration. The patient presented with bilateral visual loss. On examination, he responded well to a bortezomib based regimen.

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A Case of IgA Vasculitis in Liver Cirrhosis
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**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 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, leukocytes, 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 pervaicular neutrophil 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 taper along with monthly IV cyclophosphamide infusions. Petechial lesions improved markedly but renal function was unchanged at 4-month follow-up. Unfortunately, the patient died 5 months after initial presentation due to complications of underlying liver disease and secondary infection.

**Discussion:** IgA vasculitis, more commonly observed among children than adults, manifests clinically as palpable, blanching purpura, arthritis, urticaria, palpable and non-pruritic petechial lesions, and kidney injury. Adults commonly develop ESRD in one of three circumstances. Similar to crescentic IgA nephropathy, a combination of IV followed by oral steroids and IV cyclophosphamide is recommended in patients with rapidly progressive renal failure with more than 50% crescents on renal histology. In our case, the patient had an underlying liver disease which is an independent risk factor associated with glomerular IgA deposition due to inadequate clearance. The degree of contribution to the pathogenesis of IgA vasculitis remains unknown.

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A Remission Case with Obsolescent IgA Nephropathy in Aspirin Plus Eicosapentaenoic Acid
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**Introduction:** In case of evading immunosuppression therapy to IgA nephropathy, ACEI, ARB, or both has statistically improved renal prognosis evaluated in urine protein(UP)

**Case Description:** A 68-year-old woman was referred to nephrologist with complaint of bilateral leg edema accompanied with proteinuria and microscopic hematuria to acute nephritic syndrome, with oliguria, edema, hypertension, and acute kidney injury (AKI). It most often 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 dyspea and swelling in her lower extremities. On presentation, BP was 252/120, CXR showed cardiomegaly and pulmonary edema. Labs revealed a creatinine of 2.72 (baseline 1.4). She was started on IV diuretics, BIPAP, and nortriptyline drip with improved BP control. She remained oliguric.

Nephropathy was consulted due to no improvement in urine output despite bunetamide and thiazide diuretic challenge. Renal ultrasound was unremarkable. The patient 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 patients aged 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 is 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 differential diagnosis in elderly patients with severe AKI. Treatment is mainly supportive, and patients, like ours, might require HD.
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Our patient, it is an intriguing question based on new evidence. Certainly, her underlying mechanism connecting these conditions remains poorly understood. Here we present a patient with profound hypothyroidism and idiopathic membranoproliferative changes consistent with class IV/V lupus nephritis. Eculizumab was discontinued and she was started on cyclophosphamide and pulse dose steroids. Her kidney function continued to decline and she eventually required hemodialysis. Serial echocardiograms revealed improvement in cardiac function and she was discharged from the hospital on dialysis.

Discussion: TMA can occur with autoimmune diseases. Although the mechanism remains unclear, there is evidence of complement activation leading to injury. For these cases, there is no evidence that treating TMA itself changes outcomes. It is important for clinicians to discuss diet changes and received blood pressure medications. Some patients also received steroids and immunosuppressants. Frequency of monitoring kidney function varied and created anxiety for both patients and caregivers. Understanding the patient journey, Perceptions, and Burden Associated with Immunoglobulin A Nephropathy (IgAN): A Qualitative Study

Patient Journey, Perceptions, and Burden Associated with Immunoglobulin A Nephropathy (IgAN): A Qualitative Study

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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 diet changes and received blood pressure medications. Some patients also received steroids and immunosuppressants. Frequency of monitoring kidney function varied and created anxiety for both patients and caregivers. Understanding the patient journey, Perceptions, and Burden Associated with Immunoglobulin A Nephropathy (IgAN): A Qualitative Study

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RETINAL DRUSEN IN AUTOIMMUNE-MEDIATED AND PAUCI-IMMUNE GLOMERULONEPHRITIS

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Background: Membranous nephropathy (MN) is the most common type of primary glomerular disease. It is characterized by subepithelial immune complexes, located in the mesangial region of the Bowman’s capsule. The pathogenesis of MN is not fully understood, but several factors have been implicated, including genetic susceptibility, infections, and environmental factors. Retinal 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 membranoproliferative glomerulonephritis to determine how often drusen are observed in individuals with antibody-mediated or pauci-immune glomerulonephritis to determine how often drusen occur in each group.

Methods: This was a cross-sectional observational case-series of individuals with antibody-mediated (n=15, membranous n=9, anti-glomerular basement membrane (GBM) 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 hospital in 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 a 10% were considered abnormal.

Results: Four (27%) individuals with antibody-mediated disease (membranous n=2, anti-glomerular basement membrane (GBM) n=2) but only 4% (1/25) with pauci-immune disease. Gender, mean age and disease duration were not different between the two groups. Conclusions: These results suggest that retinal disease occurs together with glomerulonephritis 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.
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.

A retrospective analysis of 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±2.0), 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 partial remission (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.

Association Between Anti-GBM Titers and Kidney Inflammation with a New Activity Score


Background: Anti-glomerular basement membrane (anti-GBM) disease is a rare glomerulopathy 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, diagnosis, change, 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 2 in 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.

Antisynthetase Syndrome and Nephrotic Syndrome

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Introduction: The presence of anti-synthase syndrome and IgA nephropathy is unusual. Symptoms similar to other diseases that affect the connective tissue: Lupus, Rheumatologic and Dermatologic.

Case Description: A 39-year-old female with acute renal failure due to a one day history of shortness of breath. Her admission was complicated by polymicrobial sepsis, severe hypotension, acute renal failure, worsening of proteinuria and dysphagia to solids then to liquids. The diagnostic approach for the cases of rheumatological diseases is addressed, with negative ANA, positive ANCA 1:10 (MPO (-) and PR3 (-), Low C3 complement and positive Anti J01 and Anti R0 52 ++. Electromyography was performed reporting normal sensory neuroconduction as well as motor conduction. Muscle biopsy showed the presence of perimysial infiltrate. Renal biopsy showed mesangial proliferation and immunofluorescence with IgA. Symptoms progress to type 2 respiratory insufficiency, severe hypercapnia, starting with methylprednisolone 3 doses with slight improvement, adding immunoglobulin at dose of 2 g / kg, recovering muscle strength, respiratory parameters and decreasing CPK.

Discussion: IgA nephropathy is an atypical manifestation in patients with antisynthetase syndrome, only 3 cases have been reported, the pathophysiological origin is unknown, the most accepted hypothesis is humoral activation.
Case Description: A 46-year-old male with a history of Intravenous (IV) drug use and hepatitis C presented with shortness of breath and chest pain. Patient was found to have Methylcellulose Resistant Staphylococcal 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 1.0 mg/dl). Urine analysis revealed proteinuria and hematuria, and the sediment was consistent with isomorphic WBCs and RBCs with many granular casts. Renal US revealed right kidney 11.6 cm and left kidney 13.5 cm in maximum dimension with no hydronephrosis. All serology tests were negative except for a low C3 and positive cryoglobulins. The percutaneous renal biopsy showed proliferative GN (diffuse proliferative GN) with focal MPGN pattern in two glomeruli and rare crescent (in one glomerulus), full house immunofluorescence (IF) with IgA co-dominance and both capillary wall and mesangial staining (IgA 3+, IgG1 2+, IgM 2+, C3 3+, C1q 1+) and small subepithelial (hump-like) and both small and large subendothelial deposits on ultrasonography. Final biopsy diagnosis was given as IgA-cadominant staphylolococcal infection-associated glomerulonephritis (SAGN). Patient was treated with eight weeks of IV antibiotics and underwent supportive hemodialysis during hospitalization. He was discharged home off hemodialysis and followed up in outpatient clinic for Chronic Kidney Disease stage IV.

Discussion: The presence of nephrotic syndrome in this patient presents a challenging scenario and MPGN secondary to hepatitis C may be considered a differential here although SAGN is a stronger contender based on clinical and biopsy findings and protein-range proteinuria, though not common, has been described in SAGN and endocarditis-associated GN cases in variable percentages, ranging from 6-48%.

PUB168

Unmasking of Pancreatobiliary Carcinoma in a Patient with Fibrillary Glomerulonephritis

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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/day and hematuria. She had a past medical history of smoking (>20 years) and hypertension. Serologic workup and urology evaluation were unrevealing. Kidney biopsy reported FGN with minimal interstitial 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 medical therapy. Introduction of ACE-I 1.25 mg oral in proteinuria to 0.6 g/day. Unfortunately, she had decline in creatinine from 0.6 to 1.0 mg/dl, and worsening of proteinuria to 1.3 g/day 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 resolve. During the second hospitalization, a month later, HIDA scan and EGD performed with un reveling 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 lesions demonstrated poorly differentiated PBC. Palliative chemotherotherapy 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

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Introduction: Proliferative glomerulonephritis with monoclonal immunoglobulin deposits (PGNMID) is relatively a new entity. It is a form of monoclonal gammapathy with renal significance. Our patient was 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 IIIIB, 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 ciprofloxacin after 1 week due to concern for pneumonia. In the emergency room, she was hypertensive otherwise hemodynamically stable. Her physical exam was significant for right-sided costovertebral angle tenderness. BMP showed creatinine at 2.7 mg/dl which was 1.33 mg/dl at baseline. She was diagnosed with acute kidney injury and started on IV fluid resuscitation. Her urinalysis revealed 58/HFP red blood cells and 7/HFP white blood cells. The kidney ultrasound was normal. CT abdomen and pelvis did not show any evidence of

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urotheliosis or hydronephrosis. Urine albumin/creatinine ratio was 470.8 mg/g in a spot urine sample which was 104 mg/g before admission. Serum C3 level was normal at 134 mg/dL (reference: 88-201). Anti-streptolysin O antibody (ab), c-ANCA (antineutrophil ab), p-ANCA, anti-glomerular basement membrane ab were negative. Her immunoglobulin G level elevated to 1,740 mg/dL (reference 649-1618), kappa level elevated to 1,470 mg/dL (reference 750-1276), and lambda level elevated to 774 mg/dL (reference 269-638). Serum electrophoresis did not show M-spike and serum immunofixation test was negative for monoclonal gammopathy. Kidney biopsy was recommended by nephrology which revealed endocapillary-proliferative glomerulonephritis with linear glomerular capillary wall staining for IgG-kappa. She did not receive any immunosuppressive treatment as her kidney function returned to baseline without intervention.

Discussion: PGNMID is a rare form of glomerulonephritis which can mimic immune-complex glomerulonephritis especially in a patient with an infection. Therefore, considering renal biopsy with light-chain and IgG staining is crucial for proper diagnosis.

PUB170 Dual Positive Myeloperoxidase and Proteinase 3 Antibodies and Class V Lupus Nephritis in an Elderly Female with Cocaine Use Aniruddh R. Gons1, Molly Fisher2, Daniel Schwartz2, Mary J. Dominguez2, James M. Pullman1,2.1, Montefiore Medical Center, Jack D Weiler Hospital, Bronx, NY; 2Montefiore Medical Center, Bronx, NY.

Introduction: Cocaine contaminated with levamisole is a reported cause of dual positive ANCA vasculitis and rarely has been associated with lupus nephritis. We present a case of an elderly female who presented with unexplained acute kidney injury (AKI) and chronic cocaine use and was found to have dual positive ANCA and Class V lupus nephritis.

Case Description: A 70-year-old female with a history of hypertension, coronary artery disease, atrial fibrillation on warfarin, pre-diabetes, history of breast cancer status post lumpectomy, baseline serum creatinine (SCR) 0.8 mg/dL was sent to the emergency room after being found to have a SCr 6.0 mg/dL on outpatient labs. Urinalysis was significant for proteinuria and microscopic hematuria. Urine protein-creatinine ratio was 2.7 g/g. Workup revealed positive anti-nuclear antibody titer of >1:320, double-stranded DNA antibody titer 270 IU, myeloperoxidase (MPO) antibody of 5.1 Al and proteinase 3 (PR3) antibody of 1 Al. Serum complement 3 was 149 mg/dL and complement 4 was 31 mg/dL. She had no clinical symptoms of systemic erythematosus lupus (SLE) or systemic vasculitis. Urine toxicology was positive for cocaine. She was pulsed with steroids due to concern for a rapidly progressing glomerulonephritis and then underwent kidney biopsy, which demonstrated full house immunofluorescence with IgG predominant subepithelial deposits, few mesangial deposits and mild acute tubular injury. No proliferative glomerular lesions or crescents were observed. She was initiated on mycophenolate molifit with improvement in SCr to 3.88mg/dL and proteinuria to 1.2g/g.

Discussion: Dual positive (MPO and PR3) ANCs have been reported in patients with lupus nephritis, but rarely in the setting of class V lupus nephritis. Although our patient’s history of cocaine use may explain positive MPO and PR3 antibodies, she did not have the pauci-immune crescentic glomerulonephritis often seen with ANCA, but rather an immune complex, non-inflammatory glomerulopathy. Given her unusual 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 ISN/RPS class IV, seven patients belonged to class III, and four patients belonged to class V. Conclusion: 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.


Introduction: Collapsing glomerulopathy (cFSGS) is most commonly seen in association with Human Immunodeficiency Virus infection (HIVAN) and can also occur in association with viral and non-viral infections, autoimmune diseases, malignancy and drug exposure. Patients typically present with rapidly worsening renal function and nephrotic syndrome. We report a case of cFSGS due to Hemophagocytic lymphohistiocytosis (HLH).

Case Description: A 41-year-old man with acute myeloid leukemia and allogenic cancer status post lumpectomy, baseline serum creatinine (SCr) 0.8 mg/dL was sent to the emergency room after being found to have a SCr 6.0 mg/dL on outpatient labs. Urinalysis was significant for proteinuria and microscopic hematuria. Urine protein-creatinine ratio was 2.7 g/g. Workup revealed positive anti-nuclear antibody titer of >1:320, double-stranded DNA antibody titer 270 IU, myeloperoxidase (MPO) antibody of 5.1 Al and proteinase 3 (PR3) antibody of 1 Al. Serum complement 3 was 149 mg/dL and complement 4 was 31 mg/dL. She had no clinical symptoms of systemic erythematosus lupus (SLE) or systemic vasculitis. Urine toxicology was positive for cocaine. She was pulsed with steroids due to concern for a rapidly progressing glomerulonephritis and then underwent kidney biopsy, which demonstrated full house immunofluorescence with IgG predominant subepithelial deposits, few mesangial deposits and mild acute tubular injury. No proliferative glomerular lesions or crescents were observed. She was initiated on mycophenolate molifit with improvement in SCr to 3.88mg/dL and proteinuria to 1.2g/g.

Discussion: Dual positive (MPO and PR3) ANCs have been reported in patients with lupus nephritis, but rarely in the setting of class V lupus nephritis. Although our patient’s history of cocaine use may explain positive MPO and PR3 antibodies, she did not have the pauci-immune crescentic glomerulonephritis often seen with ANCA, but rather an immune complex, non-inflammatory glomerulopathy. Given her unusual manifestation of late-onset lupus nephritis, we hypothesized that chronic cocaine use may have led to an altered immune response and autoimmune disease, as rarely described for SLE in young men with chronic cocaine use.

PUB172 Epidemiology of Glomerular Diseases in Minia Governorate: A 5-Year Single-Center Experience Waleed Hassan1, Hisham Mostafa2.1 The University of Tennessee Health Science Center College of Medicine, Memphis, TN; 2Minia Nephrology and Urology University Hospital, Minia, Egypt.

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 ISN/RPS 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.
A for Amyloidosis
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Introduction: We present a case of osteomyelitis related amyloidosis presenting as acute injury (AKI) with nephrotic range proteinuria.

Case Description: A 62 years old male 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 osteomyelitis. 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 osteomyelitis. 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 cephalaxin. 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 basement 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 IgA was 95%, C3 15-20 cm) and lymphadenopathy (negative BM and lymph node biopsy). ADAMTS13 level was 50 and plasmaspheresis was stopped. Further infections and autoimmune workup was negative. Renal biopsy showed a TMA process and C5b-9 staining was positive in the glomerular and arteriolar vessels. Serum C5b-9 level was elevated (343). A genetics panel showed no variant associated with AHUS nor predisposition to poor response to eculizumab. He was discharged with eculizumab maintenance and dialysis. Recently, his labs improved with a Cr of 1.5 and platelets of 163.

Discussion: Here, typical features of hemolysis were missing, and diagnosis was made on renal biopsy with findings of TMA and C5b-9 stain. Ongoing understanding of causes for AHUS include hereditary (complement and DGKE gene mutations) and acquired (infection, autoantibodies to complement, drug toxicity and autoimmune). Although genetic panel was negative, it cannot be ruled out as genetic mutations are only identified in 50-70% of cases. Shiga-toxin and pneumococcal-HUS are causes, but here we found rare C.difficile-induced cause. Patient was successfully treated with eculizumab. Thus, AHUS is elusive and clinically challenging in diagnosis.

Factors Related to Clinical Efficacy of Corticosterone Combined with Tonsillectomy for IgA Nephropathy
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Background: IgA nephropathy (IgAN) is the most frequent primary glomerulonephritis in Japan. Treatment combining tonsillectomy with intermittent intravenous methyl prednisolone (PSL) and alternate-day oral PSL (TSP therapy) may be sometimes chosen, and results from multiple prospective multicentered studies have been reported for its clinical usefulness. However, the treatment selection criterion 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 therapy in our hospital from April 2012 to July 2019. Intravenous methyl PSL 500 mg/day was administered for 3 days in the first 2 weeks after tonsillectomy, followed by oral PSL 30 mg every other day. The protocol was repeated 3-times every 2 months, then PSL was tapered off. Treatment evaluation was performed 6 months after initiation of the therapy. When urinary protein was 0.5 g/gCr or less or decreased by 50% or more, and the urine red blood cell count was less than 20 per microscopic field, the treatment was considered to be effective.

Results: The mean age of enrolled patients was 36.2 ± 13.5 year, eGFR 75.2 ± 23.6 mL/min, urine protein 0.92 ± 0.81 g/gCr, and serum IgA 332. 9 ± 141.2 mg/dL. Thirty-two patients were effective and 31 patients were non-effective at 6 months after the start of the therapy. Clinical parameters showing significant difference between the two groups were age (33.2 ± 13.5 in responder vs 39.4 ± 10.9 in non-responder, p<0.02), diastolic blood pressure (71.2 ± 10.1 in responder vs 78.5 ± 13.2 in non-responder, p=0.017) and serum IgA (368.3 ± 174.3 in responder vs 296.2 ± 84.0 in non-responder, p=0.024). Logistic-regression showed a significant association with respect to efficacy only for serum-IgA (OR=1.010, 95% CI 1.00-1.02, p=0.047). Cut-off level of serum IgA to the efficacy of TSP therapy by ROC-analysis was 291 mg/dL (AUC=0.675, sensitivity=0.842, specificity=0.571).

Conclusions: Serum IgA levels may be a reference for predicting the efficacy of TSP therapy for IgAN.

Funding: Government Support - Non-U.S.

An Elusive Case of Renal Failure in a Patient with Atypical Hemolytic Uremic Syndrome
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Introduction: AHUS is microangiopathic hemolysis, thrombocytopenia, and AKI with normal ADAMTS13 and absence of STEC. It involves activation of complement via alternative pathway causing TMA with end-organ involvement. Causes can be complement regulation deficits, infections, and drugs. Here is a rare case of AHUS after a Cdifficile infection, requiring dialysis.

Case Description: 19-year-old man with OSA, ADHD, and obesity had a 3-week course of diarrhea and fever. Cr was 2.15, platelet 143, and tested + for C.diff and was on po vanco then flagyl. Given worsening symptoms, he went to the ER and Hb was 13.9, platelets 24, WBC14.8, BUN 130 and Cr 8.4. He had low complements (C4=7.9, C3 46.2), few schistocytes on peripheral smear, mildly elevated LDH and high-normal haptoglobin. He began dialysis, plasmaspheresis and had a renal biopsy. Imaging showed splenomegaly (15-20 cm) and lymphadenopathy (negative BM and lymph node biopsy). ADAM13 level was 90 and plasmaspheresis was stopped. Further infections and autoimmune workup was negative. Renal biopsy showed a TMA process and C5b-9 staining was positive in the glomerular and arteriolar vessels. Serum C5b-9 level was elevated (343). A genetics panel showed no variant associated with AHUS nor predisposition to poor response to eculizumab. He was discharged with eculizumab maintenance and dialysis. Recently, his labs improved with a Cr of 1.5 and platelets of 163.

Discussion: Here, typical features of hemolysis were missing, and diagnosis was made on renal biopsy with findings of TMA and C5b-9 stain. Ongoing understanding of causes for AHUS include hereditary (complement and DGKE gene mutations) and acquired (infection, autoantibodies to complement, drug toxicity and autoimmune). Although genetic panel was negative, it cannot be ruled out as genetic mutations are only identified in 50-70% of cases. Shiga-toxin and pneumococcal-HUS are causes, but here we found rare C.difficile-induced cause. Patient was successfully treated with eculizumab. Thus, AHUS is elusive and clinically challenging in diagnosis.

IgA Nephropathy in a Patient with Beta-Thalassemia Minor: A Case Report
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Introduction: IgA nephropathy (IgAN) is the most prevalent type of primary glomerulonephritis worldwide. There are few reports on IgAN development in thalassemia, especially among beta-thalassemia trait (minor) carriers.

Case Description: A 52-year-old male Mexican patient was evaluated for hypertension, hematuria, proteinuria, and rising serum creatinine levels. His history included an ischemic cerebrovascular accident and beta-thalassemia minor (trait). He was treated initially, by another provider, with hydrochlorothiazide/irbesartan and carvedilol for hypertensive nephropathy. Despite treatment, he continued with rising creatinine levels. Then, he was switched to irbesartan only. During this period, the patient developed metabolic acidosis treated with NaHCO3. When referred to our care, we began our approach by completing biochemical and immunodiagnostics assessments (IF), ultrasound imaging (USG), and pathology for glomerulonephritis. On biopsy, we observed IgA nephropathy with advanced nodular glomerulosclerosis and grade II interstitial fibrosis. On IF, IgA, C3, lambda, and kappa chains (mild) were positive. IgG, IgM, C3q were negative. On USG, we documented renal replacement lipomatosis. The patient had microcytic hypochromic anemia, but GBM, C3, C4, ANA antibodies were negative. We managed successfully with irbesartan, amiodipine, NaHCO3 then furosemide.

Discussion: To our knowledge, there are only three additional cases of IgA nephropathy among beta-thalassemia minor. All, including ours, shared as chief complaint rising serum creatinine, hypertension, and persistent microscopic hematuria. However, one report noted bilateral sensorineural hearing loss and prior psychosis under treatment, which may be a syndromic disease presentation. A common feature also is negative antinuclear, anti-DNA, anti-neutrophil cytoplasmic, anti-glomerular basement membrane antibody, HBV, HIV, serum complements antibodies. Significantly, at the time of biopsy, all cases had fibrosis in various degrees ranging from partial to global sclerosis with fibrous crescents. Notably, prior cases occurred in Asian ethnicities, were IgAN is prevalent; our case is the first Hispanic affected patient.
Sudden Explosive Onset of Collapsing FSGS in the Setting of Influenza: An Unusual Presentation

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Introduction: Collapsing FSGS (Focal Segmental Glomerulosclerosis) is often seen in the setting of HIV, pannoniculate use, parvovirus infections. Here we present a case that was explosive in onset and was associated with influenza.

Case Description: Elderly African American male in his 60s presents with flu-like symptoms. His influenza swab was positive. His past medical history was significant for occasional cocaine use, hypertension, parathyroid adenoma, hypercalcemia, prostate cancer. His vitals revealed BP 107/64 | Pulse 61 | Temp 97.2 °F (36.2 °C) | Resp 16 | SpO2 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 UJV stone with hydronephrosis. 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 sensipar 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. He also had lower extremity edema indicative of nephrotic syndrome. Of note, he did not have proteinuria a week before his hospital admission. At this point, a renal biopsy was undertaken and was noted to have collapsing glomerulopathy with 80-90 percent effacement of foot processes. 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 including infection, acute kidney injury due to other etiologies, genetic risk factors such as APOL1. Recent cases of COVID-19 related AKI point towards the possibility of collapsing FSGS as the etiologic mechanism, especially with APOL1 association. Though it is traditionally described in the setting of infections like parvovirus and HIV, there could underlying common mechanisms for infections that may not be exclusive to these and may expand to other infectious etiologies like influenza, COVID.

Hypoaalbuminemia Out of Proportion to Proteinuria in a Patient with Nephrotic Syndrome

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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 man 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 allogeneic 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 24-hour urine protein of 3.5 g/day. A lipid panel showed a cholesterol of 391 and a LDL of 292. Serologies for hepatitis and lupus were negative. Complement levels were normal and no monoclonal protein was seen on serum/urine electrophoresis. A serum PL2-R was negative. He underwent a kidney biopsy that demonstrated subepithelial glomerular, mesangial, and tubular basement membrane deposits consistent with secondary membranous nephropathy. Staining for PLA2-R was positive. He was started on Rituximab 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 diarrhea 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.

Renal Response and Its Predictive Factors of Lupus Nephritis: A Two-Year Cohort of 77 Hospital-Based Patients

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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 visits, 53(68.8%) patients completed the whole 2-year follow-up. CR was achieved in 38(71.7%) and 59(49.4%) 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 decrease 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.

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AKI After Eculizumab Interruption in a Case of C3 Glomerulopathy
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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 proteinuria 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

Pathological Features and Clinical Course of IgA Nephropathy Patients with Isolated Hematuria
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Background: Microscopic hematuria is the most common manifestation of IgA nephropathy (IgAN). There are a few studies identifying the remission rate of microscopic hematuria as an important clinical predictor of deterioration of renal function. Microscopic hematuria caused by glomerular microvasculitis may have clinical significance. Renal biopsy was performed rarely in case with isolated hematuria. Renal pathological features and the renal prognosis of IgAN patients with isolated hematuria are unclear. Thus, there are no established treatments guides. In present study, we evaluated the pathological features and clinical course in IgAN patients with isolated hematuria in our cohort.

Methods: We retrospectively recruited 47 biopsy proven patients with IgA nephropathy who showed isolated hematuria at real biopsy from 2012 to 2017. We evaluated renal pathological findings in those patients. Moreover, we analyzed clinical course during 24 months from the diagnosis. Thirty of these patients were treated with steroid pulse therapy combined with tonsillectomy (TSP group) and the others were conservatively treated (CT group). In CT group, only three patients were treated with renin-angiotensin system inhibitor. We analyzed clinical parameters, such as, levels of urinary red blood cells, onset of proteinuria, eGFR and serum IgA.

Results: Although age, sex and degree of hematuria at the time of renal biopsy were not significantly different between the TSP and CT group, baseline eGFR was significantly lower in TSP group (88.7 versus 105.9 mL/min/1.73 m²). Of note, 51% of patients showed crescent or endocapillary proliferation. At the end of observation period,
remission rate of hematuria in TSP group (100%) was much higher than that in CT group (66.7%). 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 crescent 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

IgG4-Related Disease Presenting with Membranous Nephropathy

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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 declining 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 creatinine to protein. A renal ultrasound showed structurally sound kidneys. Common infectious causes of renal disease were excluded.

C3 and C4 were normal and MPO-PR3-ELISA were negative. C4d in serum and renal biopsy was negative. C4 was normal and C4d were not seen to be 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

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Introduction: Immunoglobulin G4-related disease (IgG4-RD) is a condition, affecting multiple organs. Retropitoneal 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 with renal biopsies and diagnosed as PGNMID between January 2016 and December 2017.

Case Description: Method

In 73 years old Caucasian female with a history of arterial hypertension, diabetes, skin patchy hyperpigmentation, asthma and nasal polypsymptoms manifested in 2016 with the weight loss and skin rash. 9 months later, at admission, she was undernourished, with multiple skin scratchs, 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% - 2.6-10^9/L). Her blood chemistry tests, serum and urine immunocommunity, p and c ANCA, anti-GBM and anti-CEP-RA were within normal range. Kidney biopsy showed MN with IgG3, C3, kappa and lambda fine granular deposits on the capillary loops periphery. Her anti-PLAR2 antibodies titer was <1:10; kidneys, abdomen, neck and pelvis ultrasound, chest CT, gastroscopy and colonoscopy were unremarkable. Tests for parasitic infections and mycoid hypersyrnthetic syndrome markers (FP1/L1- PDGF-Rα and ETV6-PDGFβR) 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 she achieved partial 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 hypersyrnthetic syndrome causes was negative, and only IgG4 testing gave a clue to the diagnosis. Steroids allowed controlling hypersyrnthetic symptoms, but no kidney biopsy was performed.

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

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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±12.12 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 intertime 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. Hiperkalanemia was managed in 8 patients (100%). After one year, 75% of the patients had renal recovery (cre±5mg/dl±12.12 vs cre±2-6mg/dl±16.1, p=0.06) and 67% of the patients who required 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

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Introduction: Background 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/body, 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 of the first month of the treatment had partial remission (KIDIGO 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. Hematuria 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 hematuria 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.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only
Underline represents presenting author.
AA Amyloidosis and CKD in a Patient with Coexisting Hepatitis C Infection and Crohn Disease
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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 35% 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.

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Atypical Presentation of Microscopic Polyangiitis

Introduction: MPA is an uncommon disease, more common in men, in white and Asian populations and whose incidence increases with age. We describe an atypical presentation of MPA

Case Description: 48-year-old female patient, no relevant past medical history, who came to the ER with a 2-week history of bradypnea, gait disturbances, arthralgia, lower limb pain. On PE non-blanching red-purple papules were noted. A lab panel showed increased creatinine at 5.79 mg/dl (baseline Cr was 1.09), microscopic hematuria and sub-nephrotic proteinuria. Kidney ultrasound was normal, urinary sediment showed dysmorphic RBC with RBC casts. She was placed an acute catheter for HD prior biopsy. Immunological panel showed positive ANCA, specificity for PR3 antigen; C3 and C4 levels were normal; the rest of the panel and HIV, HBB and HCV serologies were negative. CT showed maxillary sinusitis, lungs were normal Skin biopsy showed a leukocytoclastic vasculitis and kidney biopsy showed a pauci-immune necrotizing glomerulonephritis, with diffuse extra-capillary proliferative lesions, mild interstitial fibrosis; no granulomas. Patient was diagnosed with a MPA, and treatment was started with IV GC and RTX. Patient was discharged to continue treatment in the out-patient clinic and currently has received a second dose of rituximab, with no need for hemodialysis and a creatinine of 2.5 mg/dl. (7 days after starting treatment)

Discussion: MPA is a rare disease with unknown frequency in Mexico. Our case was atypical since it presented in a Hispanic female younger patient, with a histopathological phenotype of MPA but positive to PR3, with no respiratory involvement and no upper airway destructive lesions

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Kidney Changes: 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. Fortunately, 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, diltiazem, propranolol, insulin, presented to an outside hospital with 10 days of weakness, decreased appetite & leg swelling. On exam BP 191/79, T97°F & anasarca was present. Labs showed Na128, K5.3, Cl100, bic19, BUN79, creatinine (Cr) 2.8, increased to 4.18 by admission day 10, Ca 7.6, phos 4.7, WBC 8.8, Hb 9.4 & PLT 214. CT abdomen showed renal cysts, mild ascites & no hydropneumonia. Renal biopsy showed nonspecific glomerulitis associated with positive pANCA, MPO, ANA, DS-DNA, Rf & low Cr. He received IV methylprednisolone for 3 days, followed by prednisone 60mg od, transferred to our hospital, then started on cyclophosphamide 15mg/kg q2 weeks with plasmapheresis. There was suspicion for DAV secondary to diltiazem. Anthisthine Ab(ANA) was sent & diltiazem stopped. Electron microscopy showed subendothelial deposits & intracellular macromages suggestive of SLE. Ab(ANA) was positive with negative cryoglobulin. Diagnosis of drug induced SLE from diltiazem with p-ANCA positive RPGN was made. He was discharged on prednisone 60mg daily with slow taper & Rituximab. Cr at discharge was 1.6.

Discussion: DAV is an elusive diagnosis due to limited epidemiological data & identical features to primary ANCA associated vasculitis (PAAV). Although there is no clear definition, CHCC2012 describes it as “Vasculitis associated with probable specific etiology”. Pathophysiology of drug induced ANCA formation & DAV is poorly understood. Possible mechanisms include reversal of epigenetic silencing & increased MPO & PR3 autoantigen expression in neutrophils, if in hyalurondase, or formation of reactive intermediate species by PTU that act as MPO substrates. Regardless DAV must be differentiated from PAAV. It may present with lower Cr, urinary protein & CRP levels, tendon xanthomas, ANA & Ab. Treatment involves drug cessation of the offending agent & immunosuppression, with improved prognosis compared to PAAV.

C3 Glomerulonephritis: Can Therapy Be Individualized?

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Introduction: C3 is a rare form of glomerulonephritis with variable clinical course. Therapeutics traditionally include corticosteroids, MMF and plasma exchange. Complement directed therapies remain under investigation. We report a case of C3Nef and C5Nef positive C3GN treated with ecuclizumab.

Case Description: A 31 year old female was diagnosed with membranoproliferative glomerulonephritis (MPGN) in 2006 at age 19. She was treated with high dose prednisone for 6 months with no response. Conservative therapy was instituted. She was referred for tumour centre for evaluation in 2018. At this time she was nephrotic with proteinuria 12g/day, serum albumin 21 g/L, serum creatinine 101 μmol/L and low C3 was 0.15 (0.8-1.9) and normal C4 at 0.13 (0.13-0.4). Repeat kidney biopsy revealed C5Nef positive C3Nef and C5Nef positive podocyte effacement consistent with MPGN. As complement functional testing suggested targeted terminal complement pathway defect and of C5Nef treated with ecuclizumab. We have demonstrated a case of C3Nef with positive C3 adn C5Nef with cell surface activation of complement, classical and terminal complement pathway involvement. This highlights the importance of complement function studies to help aid the localization of complement pathway defect, and to individualize therapy.

A Rare Case of NSAID-Induced Minimal Change Disease

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Introduction: Nonsteroidal anti-inflammatory drugs (NSAIDs) can cause acute tubular necrosis (ATN) via inhibition of prostaglandin synthesis, and vasorestriction. Drug-induced minimal change disease (MCD) is postulated to be due to a reduction in renal perfusion and glomerular filtration rate. We present a case of NSAID induced acute renal failure (ARF) due to ATN and MCD in a 37-year-old adult.

Case Description: A 37-year-old male with no medical history came to the ED with 1 week of vomiting, abdominal pain, and reduced urine output. He attributed his symptoms to food poisoning but sought evaluation after no improvement. Over the last 2 weeks, he had no upper respiratory infection and dental pain for which he took 1g of ibuprofen daily. Labs yielded a BUN of 104mg/dL, creatinine (Cr) of 16.9mg/dL, and urine protein to creatinine ratio of 5.85. Renal ultrasound showed no hydropneumonia. 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 olugria 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, MDRD5c, 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 sCr 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 slightly higher eGFR and was the most advanced CKD according to sCr levels. There was no obvious trend for age-related change in the 3-year mean rate of eGFR change when compared across age groups. For subjects aged over 70 years, the MDRD and MDRD5c 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 eGFR 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(cm) were collected at weeks 0(baseline), 6, and 12 following the conclusion of the intervention. Statistical analysis was performed using SPSSv.24. 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±0.31 kg, p<0.05), body mass index (p=0.03), 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 staff’s 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 the elderly. Even small increases in prevalence of frailty in the elderly population are of concern. In this study, the prevalence of frailty was assessed in the staff in the hemodialysis clinic.

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 (6 in the experimental group, 5 in the control group). The experimental group received

Results: Of the 623 patients visiting each institution, 300 were enrolled in this study. The mean age was 61.9 (0.36) years, with mean duration of HD 30.7 (0.39) months. 116 patients (38%) were female and 112 (44%) had diabetes or renal 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, DM, SARS, SD. 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 HD patients. MHD patients had both anxiety and depression generally 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 (ZN-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 a148 years old who were dispensed SPS, patiromer, and/or ZN-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 RAASIs. 28 respondents had used SPS, 6 had used patiromer, and 1 had used ZN-9. 18% of respondents treated with SPS vs. 0% treated with patiromer reported side effects. 1 reported discontinuing 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/Air Force, the Department of Defense, nor the US Government.
**Method**: A face-to-face survey was conducted in a random convenience sample of pts in CKD and FM clinics. Patients chose answers from 5 Likert style questions about PBE assessing their beliefs regarding difficulty in finding foods in restaurants, affordability, ability to get proteins and vitamins, and ability to find good tasting recipes. A mean score was calculated with lower score indicating more difficulty (PBE-score). Diet adherence was based on 24hr recall and analyzed using ASA-24 software. Comparisons are by t-test unless noted.

**Results**: Mean age was 54.3±2.5 yrs. There were 16 (36%) males and 29 (64%) females with 40 black (89%), 36 (80%) had not completed college. 23 (51%) had an -18% HD interval. 20 (43%) had diabetes and 36 (80%) had hypertension. 30.4±1.6 with 41% >30. There were no differences in these variables between clinics. CKD pts had a higher creatinine (2.0±0.3 vs 0.8±0.5) more positive attitude towards PBE (PBE-score 2.5±0.7 vs 1.1±0.3, p<0.05) and more ate cholesterol (411±2.6 vs 287±1.9, p=0.034), fatty acid (14±154 vs 17±181, p=0.054) and dietary sodium (5±5.27 vs 0.42±0.16, p=0.048) and drank more fluid (249.0±33.5 vs 136.7±16.7, 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 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 seafood. 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.
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 serum sodium level in 4.

Conclusions: The current evidence on the prognostic prognostic value of hypochloremia for adverse outcomes in HF is keeping with distinct physiologic mechanisms relating it to rennin 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 Jianfeng Lin, Hua Zheng, Peng Xia, Limeng Chen. Peking Union Medical College Hospital, Dongcheng-qu, China.

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, CPCHC). A questionnaire, physical examination, and biochemical tests were performed. The PM2.5 data used were derived from aerial optical depth with the GWR model and GFS/Chem 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 CPCHC study was 33.4 (14.0-53.4) μg/m3. Multivariate linear regression showed that each 10μg/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 SBP (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 Wentao Hu, Xin Liu, Shaomin Li. the Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China.

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 prognostics 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 date 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) is the best prediction model of cardiovascular events (P=0.088*1.93584*APoB + 0.00356*pre-albumin + 0.00679*HGB + 1.11488*heart failure - 0.22131*K - 0.10215*CKD progression) is 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 of it. And we establish the best prediction model (P=0.088*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 Muntazir Ali Sayed,1 Navneet K. Guri,1 Adil A. Akbani,1 Ali Hamza,1 Sadiq Ali Sayed,2 Farhin N. Sayed,2 Sayed Mohd Tahir Rizvi,3 Desi Doctors Aricenna Medical College, Lahore, Pakistan; 4National Pirogov Memorial Medical University, Vinnytsya, Ukraine; 5Rajiv Gandhi Chhatrapati Shahu Maharaj Government Medical College and CPR Hospital, Kolhapur, India; 6Government Medical College, Patiala, India; 7KI Somiya College of Engineering, Mumbai, India.

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), dyslipidemia (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 Amjad E. El Agroudy. Arabian Gulf University, Manama, Bahrain.

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 gathered 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 20.4±1.9 years. Normotensives 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.
Higher body mass index was associated with significantly high prevalence of hypertension (47.3%), overweight (33.2%), 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 (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. The findings are consistent with previous studies associated with high prevalence 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/Valsartan and Evolocumab on Chronic Heart Failure in an ERSD Patient

Hun M. Aung,1,2 Aye M. Thida,1,2 Myat E. Mon,3 Phyo Wai Khine,1 May T. Zin,2 Banya M. Win,2 Kyaw Hla,2 Alexander M. Swan,2,* Interfaith Medical Center, Brooklyn, NY; *Nephrology Hypertension Renal Transplant & Renal Therapy, LLC, Avenel, NJ;1 Woodland Medical and Mental Health Center, Brooklyn, NY; Rutgers New Jersey Medical School, Newark, NJ.

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/valsartan 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 enalapril, metoprolol, clopidogrel, glipizide, repaglinide, allopurinol, and folinic acid. He was on maintenance hemodialysis for 15 years. His creatinine was 10.4 mg/dL on admission.

On presentation, he had AKI, hypokalemia, metabolic acidosis, and electrolyte abnormalities. His 24-hour urine sodium was 245 mEq/day. He had high renin activity with low aldosterone levels. His urine sodium/potassium ratio was 15. The patient was started on enalapril and furosemide.

The patient presented with anasarca, peripheral edema, hypotension, tachycardia, and increased heart rate. His blood pressure was 90/45 mm Hg. He was started on intravenous fluid resuscitation, as well as cytochrome c repleting fluid. His urine output was 30 mL/h, and his creatinine clearance was 7 mL/min. His hemoglobin was 9.8 g/dL. Given these findings, a diagnosis of PLA2R associated membranous nephropathy was made. Bumetanide was started for management of fluid overload with good effect. Given proteinuria improved significantly after stopping therapy, sunitinib may have contributed to worsening of the underlying nephrotic syndrome. Ultimately, a decision was made to restart sunitinib with a plan to treat the membranous nephropathy with rituximab.

Discussion: Our patient developed hypertension and nephrotic syndrome, ultimately found to be PLA2R associated membranous nephropathy, in the setting of sunitinib use. It is possible that in our patient, sunitinib contributed to worsening of the nephrotic syndrome, as evidenced by the fact that proteinuria improved with stopping the TKI. While TKIs have been implicated in the development of proteinuria and nephrotic syndrome, it is important to rule out other possible causes to allow for continuation of oncological therapy if deemed necessary.

Table 1. Trend of laboratory testing

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Conclusions: We present a case of a patient presenting in stage III acute renal failure with Lamba light chains measured at a level almost 9 fold greater at 3684 mg/dL. While TKIs have been implicated in the development of proteinuria and nephrotic syndrome, it is important to rule out other possible causes to allow for continuation of oncological therapy if deemed necessary.

**PUB209**

Fanconi Syndrome and Acute Interstitial Nephritis: A Toxic Combination Associated with Ifosfamide

Hafsa, Nissreen El Fadawy, Miroslav Sekulic, Arshad Rashidi. University Hospitals, Cleveland, OH.

Introduction: Ifosfamide is an alkylating chemotherapeutic agent used in the treatment of various soft tissue tumors. Nephrotoxicity associated with ifosfamide is less frequently reported in adults. We describe a patient with Ewing sarcoma, who presented with AKI, nephrotic syndrome, and proteinuria. Given this is a rare presentation, we sought to present our case in the literature.

Case Description: A 17-year-old female with a history of Ewing sarcoma treated with ifosfamide (3000 mg/m2) and doxorubicin. On presentation, she had AKI, hypokalemia, metabolic acidosis, and electrolyte abnormalities. Her 24-hour urine sodium was 245 mEq/day. She was started on intravenous fluid resuscitation, as well as cytochrome c repleting fluid. Her urine output was 30 mL/h, and her creatinine clearance was 7 mL/min. Her hemoglobin was 9.8 g/dL. Given these findings, a diagnosis of PLA2R associated membranous nephropathy was made. Bumetanide was started for management of fluid overload with good effect. Given proteinuria improved significantly after stopping therapy, sunitinib may have contributed to worsening of the underlying nephrotic syndrome. Ultimately, a decision was made to restart sunitinib with a plan to treat the membranous nephropathy with rituximab.

Discussion: Our patient developed hypertension and nephrotic syndrome, ultimately found to be PLA2R associated membranous nephropathy, in the setting of sunitinib use. It is possible that in our patient, sunitinib contributed to worsening of the nephrotic syndrome, as evidenced by the fact that proteinuria improved with stopping the TKI. While TKIs have been implicated in the development of proteinuria and nephrotic syndrome, it is important to rule out other possible causes to allow for continuation of oncological therapy if deemed necessary.

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Conclusions: We present a case of a patient presenting in stage III acute renal failure with Lamba light chains measured at a level almost 9 fold greater at 3684 mg/dL. While TKIs have been implicated in the development of proteinuria and nephrotic syndrome, it is important to rule out other possible causes to allow for continuation of oncological therapy if deemed necessary.
AKI Associated with Immune-Checkpoint Inhibitors: Management Challenges and Dilemmas Without Renal Biopsy

Hui Zhan Tan, Jason Choo Chon Jun. Singapore General Hospital, Singapore, Singapore.

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 tubulointerstitial nephritis is the most common, with glomerulonephritis (GN) being increasingly recognized.

Case Description: A 61 Chinese male presented with generalized arthralgia and AKI with nephritic-nephrotic syndrome on a background of Stage IV metastatic clear cell RCC and left radical nephrectomy. At presentation, he was on treatment with pembrolizumab (PD-(L)1 inhibitor) and axitinib (VEGF receptor TKI). Investigations revealed 24hr 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 226 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 virus 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.

Amitraterone-Induced Rhabdomyolysis as an Unusual Cause of AKI Requiring Hemodialysis

Juan Carlos Garcia Yanez,1,2 Hospital Aranda de la Parra, Leon, Mexico; Universidad de Guanajuato - Campus Leon, Leon de los Aldama, Mexico.

Introduction: A 86-year-old male diagnosed with metastatic, castration-resistant prostate cancer (mCRPC) treated with abiraterone (Zytiga) for 3 months was admitted to the emergency department due to hypoxia, 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 diaytic emergency: serum creatinine of 6.1mg/dL, urea 295 mg/dL, BUN 139mg/dL and potassium of 7.3mEq/L. The patient refused renal replacement therapy. Aggressive hydration and treatment with calcium gluconate, IV insulin and beta-agonist administration was initiated. Subsequently he developed anasarca, hypotension, metabolic acidosis, hyperkalemia and respiratory distress. He was intubated and treated with haemofiltration. Subsequently he developed ARDS, IHD and multiple organ failure. In view of concurrent rheumatological IRAE, we postulated that his AKI was related to abiraterone 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.

Bilateral Renal Burkitt Lymphoma Presenting with Persistent Lactic Acidosis in an HIV-Negative Patient

Oscar A. Garcia Valencia,1,2 Juan D. Salcedo Betancourt,1,2 Victor G. Becerra-Gonzalez,1,2 Karla G. Carias martinez,1,2 Marco A. LadinoAvellaneda,1,2 1Jackson Memorial Hospital, Miami, FL; 2University of Coral Gables, FL; 3Miami VA Healthcare System, Miami, FL.

Introduction: Burkitt lymphoma is an uncommon and aggressive B-Cell lymphoma accounting for <1% of adult Non-Hodgkin Lymphomas. The ileocecal 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 hematoma 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 92rpm, RR 20rpm and SO2 96% on RA somnolent but arousable, pale, no abdominal, spinal 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 potassium of 7.3mEq/L. The patient refused renal replacement therapy. Aggressive hydration and treatment with calcium gluconate, IV insulin and beta-agonist administration was initiated. Subsequently he developed anasarca, hypotension, metabolic acidosis, hyperkalemia and respiratory distress. He was intubated and treated with haemofiltration. Subsequently he developed ARDS, IHD and multiple organ failure. In view of concurrent rheumatological IRAE, we postulated that his AKI was related to abiraterone 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.
Clinicians need to be aware of this potential adverse effect related to oxaliplatin therapy, extent carboplatin have been known to cause electrolyte disturbances, in particular hypomagnesemia. 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 (ICIs) are increasing in frequency. We report a case of sarcoid involvement in both the kidney and heart 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 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 ipilimumab and nivolumab. In March 2020 he was admitted with acute kidney injury, with high index of suspicion to diagnose GiTMA early in the course of the disease. Mainstay of management is withdrawal of the offending drug and supportive care. In all reported cases, patients presented with lymph node, skin, or lung involvement. We present the first case of sarcoid lesions in the heart in a patient being treated with immune checkpoint therapy.

**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 performed may be a side effect from 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 lesions in the heart in a patient being treated with immune checkpoint therapy.

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

**Underline represents presenting author.**
Prevalence is around 10% of all membranous nephropathy (MN) cases. Anti M-type dose >90–120 g/m² are risk factors for AKI. Management is mainly supportive such as notable given lower cumulative dose (11.25 g) resulting in nephrotoxicity. Case reports 10 g/mg creat. Urine sediment exam showed granular casts. He had proximal RTA and proteinuria and 3+ glycosuria and protein creatinine ratio was 4.69 and on repeat, it was associated hypokalemia and hypophosphatemia. Urine pH was 8 and patient had 2+ developed a non-anion gap hyperchloremic metabolic acidosis around that time. There chemotherapy with ifosfamide, carboplatin, etoposide (carboplatin and etoposide – day 1 tract symptoms. No NSAID use. No IV contrast exposure. No hypotension. Patient got throat and non-productive cough. Patient did not have any vomiting or diarrhea or fever in past who was admitted for ICE chemotherapy. Patient reported fatigue and chills, sore Urinothorax: A Rare Cause of Pleural Effusion Anusha Ananda,2 Abigayle Kallapur,2,1 Juan Gables, FL; 2Jackson Memorial Hospital, Miami, FL

Introduction: Hypertrophy of the prostate (BPH) is a common cause of obstructive prostatitis in old men. Here we present a case of a 62-year-old Hispanic man with BPH who was found to have an additional rare cause of hypocomplementemia, namely 10-19% membranous nephropathy (RMC). The patient had a long history of intermittent dysuria and acute retention of urine. Laboratory data were remarkable for serum creatinine of 2.7 mg/dl. Urinalysis showed 2+ proteinuria and 3+ glucose and protein creatinine ratio was 4.69 and on repeat, it was 10 g/mg creat. Urine sediment exam showed granular casts. He had proximal RTA and Fanconi syndrome due to ifosfamide nephrotoxicity. He was managed with supportive treatment with repletion of potassium and phosphate and bicarbonate drip. This was notable given lower cumulative dose (11.25g) resulting in nephrotoxicity. Case reports mention nephrotoxicity mostly in children with 60-120 g cumulative dose. Discussion: Ifosfamide induced AKI is reversible but can be permanent. Biopsy shows tubular injury/necrosis with swollen mitochondria. Ifosfamide enters proximal tubule cells via OCT 2. Chlordecone aldehyde is the toxic metabolite produced by ifosfamide that causes kidney injury. Usually,CKD, previous cisplatin exposure and cumulative dose >90–120 g/m² are risk factors for AKI. Management is mainly supportive such as repletion of deficient electrolytes and renal replacement therapy if indicated. 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.

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that gemfibrozil may affect the active site of both KAT I and KAT II. Results of the molecular docking suggested that gemfibrozil at 50 μM, 500 μM and 1 mM decreased KYNA production in vitro to 47% (\(P<0.001\)) and 26% (\(P<0.001\)) of control value, respectively. At 100 μM, 500 μM and 1 mM concentration decreased KYNA activity in vitro to 66% (\(P<0.001\)), 56% (\(P<0.001\)) and 52% (\(P<0.001\)) of control value, respectively. Moreover, gemfibrozil at 500 μM and 1 mM concentration decreased of control value, respectively. Results of the molecular docking suggested that gemfibrozil may affect the active site of both KAT I and KAT II. Publicly available microarray data suggested that the expression of KAT-coding genes does not change after gemfibrozil administration.

Conclusions: Gemfibrozil decreases KYNA 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.

MRI lower extremity: Diffuse fatty replacement of all of the muscles of the bilateral thighs, with no loss of overall muscle bulk. This could be due to muscular dystrophy or end-stage myositis.

Successful Treatment of the Pediatric Case with Anti-MDA5 Antibody-Positive Interstitial Lung Disease by Plasma Exchange Therapy

Christina Yonezawa,1 Shinya Kitajima,1 Hisayuki Ogura,1 Koichi Sato,1 Taro Miyagawa,1 Tadashi Toyama,1 Akinori Hara,1 Yasunori Iwata,1 Noriko Sakai,1 Miho Shimizu,1 Taizu Wada,1 Takashi Wada,1 Kanazawa University Hospital Department of Nephrology, Kanazawa, Japan; 2Kanazawa University Hospital Department of Pediatrics, Kanazawa, Japan.

Introduction: Anti-melanoma differentiation-associated gene 5 (MDA5) antibodies are a type of myositis-specific autoantibodies. They are strongly related to rapid progressive lethal interstitial lung disease (ILD) with dermatomyositis. We experienced the 2 years old pediatric case with refractory anti-MDA5 antibody positive ILD and successfully treated with plasma exchange (PE).

Case Description: Two years old girl with normal development showed acute lower extremity weakness, dysphagia and face erythema three months before admission. She developed non-productive cough and fever. She visited nearby hospital one month before admission and was diagnosed as bilateral pneumonia with high KL-6 titer (2500 U/mL). Antibiotics had no effect and she admitted to another hospital. Additional examination revealed the high titer of anti-MDA5 antibody (1270 index) and normal creatinine (0.3 mg/dL). She also exhibited Heliotrope rash and Gottron’s sign. She was diagnosed as anti-MDA5 antibody positive juvenile dermatomyositis with ILD. Methylprednisolone pulse therapy (mPSL) and intravenous cyclophosphamide therapy were started but ILD was sustained. She transferred to our hospital for additional therapies. On the second hospital day, intravenous immunoglobulin was given and intravenous rituximab therapy was added on day 7 and 16. In spite of eradication of CD20-positive cells, her symptom was not improved. Therefore, we carried on PE with albumin-based replacement solution. After three courses of PE, the titer of anti-MDA5 antibody decreased to 83 index from 980 index on admission and her respiratory status was significantly improved.

Discussion: The mortality of anti-MDA5 antibody-positive ILD was reported as 20-30% regardless of intensive immunosuppressive therapy. Previous studies reported that anti-MDA5 antibody-positive ILD patients had high level of serum inflammatory cytokines and cytokine levels were related to the disease activity of ILD. Lowering them may have a crucial therapeutic effect for anti-MDA5 antibody-positive ILD. Plasmapheresis therapy might be one of options to treat anti-MDA5 antibody positive patients with dermatomyositis complicated ILD.

Use of Lisinopril in an Adolescent with “Extreme Dipper” Autonomic Hypertension Profile

Siddharth A. Shah,1 University of Louisville, Louisville, KY.

Introduction: The interaction between renin angiotensin aldosterone system and autonomic nervous system for blood pressure (BP) control is described. Angiotensin type-1 receptor activation in hypothyroidism increases activity of parasympathetic pre-synaptic neurons as well as increases permeability of blood brain barrier to angiotensin. ADHD stimulant medication may be associated with cardiac autonomic dysfunction in children. Standard deviation (SD) of systolic BP (SBP) may be a better measure to study autonomic BP pattern particularly with nighttime extreme dipper hypertensive profile.

Case Description: A 16-year-old non obese male presents with hypertensive urgency; BP of 168/102 mm Hg and symptoms of headache and vomiting. He was maintained on stimulant medication for ADHD that was stopped at initial presentation. The evaluation of secondary causes of hypertension was negative. He was started on Ca channel blocker. Four months after initial presentation, the 24-hour ambulatory BP monitoring (ABPM) study was done that showed hypertensive profile with extreme nighttime dipping. SD of SBP was 24.29 suggesting significant BP fluctuations (Figure-1). He was started on Lisinopril at the dose of 20 mg daily. ABPM study was repeated 3 months latter (Figure-2). There was marked improvement in daytime BP fluctuations (daytime SD of SBP-8.48) without worsening nighttime BP dipping. Dizziness on changing posture was not reported.

Discussion: ACE inhibitors may be considered as an option for treatment of autonomic hypertension in adolescents with extreme nighttime dipping BP profile.
**PUB230**

**Influence of Biopsy Prognosis on Graft Survival**

Cristina Andrades Gómez, Jorge Calvillo-Arbiizu, 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.

**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 f/u. At routine 3 yr f/u, Cr of 4.4mg/dL, BUN of 70 mg/dL, and Ca of 12.6mg/dL were noted. Kidney biopsy showed ATI, 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)D: 70 ng/ml, angiotensin converting enzyme level: 42 (9-47 U/L), serum urine protein electrophoresis: negative, PTHrp: < 2 pmol/L, Vit A: 76.82 (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-

**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 KTxs. 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.
Outcomes in Kidney Transplantation from Increased-Risk Donor Organs: A Single-Center Experience

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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. 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 1. Donor and recipient characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Donor (41 patients)</th>
<th>Recipient (41 patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at death (years)</td>
<td>55 (17-79)</td>
<td>50 (18-74)</td>
</tr>
<tr>
<td>Creatinine at death (mg/dL)</td>
<td>2.0 (1.0-5.0)</td>
<td>1.5 (0.8-2.5)</td>
</tr>
<tr>
<td>Donor gender</td>
<td>Male 22, Female 19</td>
<td>Male 22, Female 19</td>
</tr>
<tr>
<td>Dialysis status</td>
<td>Dialysis 23, Nondialysis 18</td>
<td></td>
</tr>
<tr>
<td>Cause of death</td>
<td>Anoxia 24, Other 17</td>
<td></td>
</tr>
<tr>
<td>Methylprednisolone concentration</td>
<td>25 mg (10-50 mg)</td>
<td>25 mg (10-50 mg)</td>
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<tr>
<td>Mycophenolate dosage</td>
<td>2.0 (1.0-4.0)</td>
<td>2.0 (1.0-4.0)</td>
</tr>
<tr>
<td>Vincristine dosage</td>
<td>1.0 (0.5-2.0)</td>
<td>1.0 (0.5-2.0)</td>
</tr>
<tr>
<td>Recipient age (years)</td>
<td>51 (21-73)</td>
<td>51 (21-73)</td>
</tr>
<tr>
<td>Recipient sex</td>
<td>Male 22, Female 19</td>
<td>Male 22, Female 19</td>
</tr>
<tr>
<td>Diabetes status</td>
<td>Type 1 1, Type 2 40</td>
<td></td>
</tr>
<tr>
<td>HCV status</td>
<td>Positive 17, Negative 24</td>
<td></td>
</tr>
<tr>
<td>HLA match</td>
<td>HLA A, B, DR matched 21</td>
<td></td>
</tr>
<tr>
<td>Number of rejections</td>
<td>1 (0-3)</td>
<td>1 (0-3)</td>
</tr>
<tr>
<td>Induction therapy</td>
<td>Thymoglobulin 20, ATG 21</td>
<td></td>
</tr>
<tr>
<td>CyA toxicity</td>
<td>CyA 1.0 (0.5-2.0)</td>
<td>CyA 1.0 (0.5-2.0)</td>
</tr>
<tr>
<td>Protec信仰 at one year (mg/dL)</td>
<td>2.7 (1.0-4.0)</td>
<td>2.7 (1.0-4.0)</td>
</tr>
</tbody>
</table>

sd = standard deviation

Increased-risk Criteria

Increased-risk Criteria

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

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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%) they were transplanted by a living donor, cold ischemia an average of 127 min, days in hospital an average of 5.3, serum phosphorus prior kidney transplant an average 5.7(2.3) mg/dl, in the ANOVA analysis a mean serum creatinine (Group A=0.9, B=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=-1121/3913, creatinine at discharge P=0.1 IC=-2.6/0.2, GFR discharge P=0.03 IC=-1.9/1.7, A vs C urea P=0.07 IC=256/3527, creatinine at discharge P=0.01 IC=-4.2/0.4, GFR at discharge P=0.01 IC=-8.5/9.7, AUC of 0.9, with a cutoff value of 3.6 mg/dl have a TFG >60 ml/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 an ABMR, in the 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 9177 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. ADMATS-13, anti neutrophilic antibodies H, I, B, C3, C4, and stool panel tests 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 4.5 mg/dl at month 10-11. Plasmapheresis (PP) and IVIG were initiated for suspected non-HLA antibody mediated rejection (AMR) with CYC.

Discussion: The constellation of TMA, CMV viremia, tubulitis, microvascular inflammation and myelosuppression, poses dilemmas in balancing management as FK506, CYC and AMR may all be contributory, in isolation or combination to TMA. We elected to maintain a calcineurin inhibitor and mycophenolic regime in the face of TMA and CMV due to the risk of florid rejection, and initiated PP with IVIG.

PUB239
Hypofibrinogenemia as a Risk Factor of Bleeding After Plasmapheresis with Centrifuge in Renal Transplantations with Active Humoral Rejection
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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 the presence of low figures during the platelet count of the session, for confirmation 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 TPEA 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 397 mg/dl, after the 1st session a reduction of 33% was observed, with an average value of 133 mg/dl. The lowest level was 43 mg/dl, the most important bleeding event was documented 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 79 mg/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<50 mg/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, 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.

PUB237
De Novo Thrombotic Microangiopathy Associated with Cytomegalovirus Infection and Alloreticivity: A Fork in the Road of Immunomodulation
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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 nephrotic nephropathy received a deceased donor kidney transplant (KDPI 73%) complicated by progressive allograft dysfunction after 6 months. Anti-thymocyte globulin was used for induction, steroids, mycophenolate and pre-emptive maintenance of immunosuppression. With step-wise rise in serum creatinine (baseline 1.7 mg/dL) to 2.5, 3 and 4 mg/dL at months 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 with 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 (plated 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 9177 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. ADMATS-13, anti neutrophilic antibodies H, I, B, C3, C4, and stool panel tests 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 4.5 mg/dl at month 10-11. Plasmapheresis (PP) and IVIG were initiated for suspected non-HLA antibody mediated rejection (AMR) with CYC.

Discussion: The constellation of TMA, CMV viremia, tubulitis, microvascular inflammation and myelosuppression, poses dilemmas in balancing management as FK506, CYC and AMR may all be contributory, in isolation or combination to TMA. We elected to maintain a calcineurin inhibitor and mycophenolic regime in the face of TMA and CMV due to the risk of florid rejection, and initiated PP with IVIG.

PUB238
Kidney Transplant Recipients Suffer Fewer Complications After Adrenergic Surgery
Ankur P. Chouhey,1 Darren Abbas,1 Jonathan Demeter,1 Afshin Parsiakia,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 paucity of data regarding the incidence and effects of adrenergic tumors after renal transplant. We aim to evaluate the differences in short-term outcomes between renal allograft recipients and the general population undergoing adrenergic 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 undergoing adrenergic surgery. ICD-9 codes were used to identify the procedures. Sample mean with standard deviations, and Student’s t tests were calculated for categorical variables. Odds ratios were computed using weighted data. Multivariable linear regressions were utilized to compare outcomes at transplant and non-transplant centers.

Key: TH - Thursday; FR - Friday; SA - Saturday; SU - Sunday; OR - Oral; PO - Poster; PUB - Publication Only Underline represents presenting author.
Granulomatous Tubulointerstitial Nephritis in a Kidney Transplant Recipient
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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 included nonsteroidal anti-inflammatory drugs, riluzole, carvedilol, insulin, and tacrolimus. Serum labs showed: creatinine (Cr) 2.65 mg/dL (baseline Cr 1.3 mg/dL), corrected calcium 13.2 mg/dL, and tacrolimus trough level 7.6 mg/mL. Urine sediment examination and kidney ultrasound were unremarkable. Further workup for hypercalcemia revealed: parathormone (PTH) 7 pg/mL, 1,25-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. Despite negative T-cell 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.

Kidney Transplants from Deceased Donor After 11 Days of Hemodialysis
Ankur P. Chouhey, Obi Ekwenwa, Michael Rees, Jorge Ortiz. The University of Toledo Medical Center, Toledo, OH.

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 transplant from a donor after 11 days of hemodialysis.

Case Description: Donor was a healthy 41-year-old male with severe injuries from a car accident. He suffered severe AKI from rhabdomyolysis requiring 11 days of hemodialysis. Peak and terminal creatinine (Cr) were 4.55 and 3.23, creatine kinase was 10,582 U/L, and KDPI was 37%. Biopsy showed no vessel or interstitial injury, or global glomerulosclerosis. No casts were seen on urinalysis. Recipient was a 60-year-old female from a matched donor with ESRD from IgA nephropathy, on dialysis for 2 years with EPTS of 41%. Cold ischemia time (CIT) and pump time were 32 and 103.5 hours. Post-operative DGF required two dialysis sessions. Recipient 2 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 24 hours. Profuse bleeding from graft biopsy site and pseudoaneurysm formation required treatment with transfusions, and dialysis for DGF. He was readmitted with hyponatremia and carbapenem resistant enterobacteriaceae sepsis, requiring nephrostomy tube and antibiotics.

Discussion: 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 mofetil, 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 Aways 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.
Rapid Renal Allograft Failure Following Recurrence of Lupus Nephritis 12 Years After Renal Transplant

Sreedevi koppisetti Jenigiri, Jayesh B. Patel, Prerna Kumar, Christie P. Thomas, Sarat C. Kuppachi. University of Iowa, Iowa City, IA.

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 34-year-old developed LN and her kidney biopsy (KB) demonstrated global sclerosis with immune complex glomerulonephritis with positive serum antinuclear (ANA) and antinuclear 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 remained free of treatment and attained a baseline creatinine (Cr) measuring 1.2 to 1.3 mg/dL. She 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.

Rapid Renal Allograft Failure Following Recurrence of Lupus Nephritis 12 Years After Renal Transplant

Vatsalya Korus, Imran Y. Gani, Azem A. Mohammed, Rajan Kapoor, Sandeep A. Padala. Augusta University, Augusta, GA.

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 treatment: 3 were submitted to radiotherapy (RT), 1 to chemotherapy (CT) and 2 had both RT and CT. Pegylated liposomal doxorubicin 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 KT diagnosis, and one by chronic graft dysfunction after 19y of KT, 14y after KT). Three patients have already died (with graft function) one directly to the 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 main presentation.

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. However, thorough surveillance in higher-risk groups, as HIV patients, should not be forgotten.
Late-Onset Recurrent Granulomatous Interstitial Nephritis in Transplanted Kidney with Successful Treatment: A Case Report
Fatmah Yamani,1 Miroslav Sekulic,1,2 Arksarapuk Jittirat,1,2 1Case Western Reserve University, Cleveland, OH; 2University Hospitals Cleveland Medical Center, Cleveland, OH.

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(MMP) 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.

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.
Native Kidney Cytomegalovirus Nephritis

Sandra 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, and hepatitis. However, active CMV nephritis is rare, reported in less than 1% of renal biopsies. We present a case of CMV nephritis in a high-risk kidney transplant recipient who completed six months of CMV prophylaxis four weeks prior to presentation.

Case Description: A 66-year-old man with a 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 cryptogenic cirrhosis and hepato-renal syndrome. Immunotherapy consisted of tacrolimus (target 8-10 ng/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 herpetic simplex virus-1, and Clostridium difficile 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. Urine culture grew >10^5 cfu/mL of Pseudomonas aeruginosa species. 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 and transplanted 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.

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: A 70-year-old man with a history of chronic renal failure on hemodialysis, diabetes, hypertension, and chronic lung disease presented to our hospital after being diagnosed with a left atrial myxoma at another institution. 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). His last biopsy was unremarkable. He recently received intravitreal injections of fluocinonide and ranibizumab. A nasolacrimaloryngoscopy showed unilateral paralysis of the left vocal cord with saliva aspiration. Computed tomography scan of cranium, neck and thorax excluded expansive lesions. Blood polymerease 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 cranial 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.

Incidence and Risk Factors in Mexican Patients with Diarrhea After Kidney Transplantation


Results: 92 patients were evaluated. Thirty two diarrhea episodes were recorded in 28 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 was 58.7% and was performed in at-risk patients with no history of diarrhea. The cumulative incidence was calculated for the evaluation of risk factors. Survival analysis made by Kaplan-Meier curves.

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 calculation was performed. The incidence regression was used for the evaluation of risk factors. Survival analysis made by Kaplan-Meier curves.

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.

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Use of Donor-Derived Cell-Free DNA to Identify Allograft at Risk by Late Surveillance

Amna Agha,1,3 Anna Iha,1,2 Diana Mahbod,1 Rama Nadella,1 Irfan Agha.1,3 1Dallas Renal Group, Dallas, TX; 2Methodist Dallas Medical Center, Dallas, TX; 3Medical City Dallas Hospital, Dallas, TX.

Introduction: Monitoring allograft function remains inadequate. Many allografts sustain subacute injury not detected in time resulting in poor long-term outcomes. Traditional tools utilized (creatinine, proteinuria and DSA) are insensitive and imprecise. The gold standard, allograft biopsy, is invasive and expensive. DD CF DNA has emerged as a sensitive and specific marker of allograft injury. This test is valuable in the early detection of allograft injury.

Case Description: A 66-year-old man 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 g/dl. Approximately five weeks following transplantation, the patient was found to have profound anaemia with haemoglobin level falling to 57 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, temporal relation of withdrawal of tacrolimus with improvement of anaemia suggests an etiological role of tacrolimus. The close inverse relationship between viral DNA PCR titre and erythropoietic activity reflected by the improvement of refractory anaemia shows the close relationship between early renal allograft injury and parvoviruses. Parvovirus B19 infects erythroblasts and is believed to be the cause of the persistent renal failure, a renal biopsy was performed. The incidence regression was used for the evaluation of risk factors. Survival analysis made by Kaplan-Meier curves.

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Ab positive by EIA with a level > 40 units/ml. Treated for Acute active ABMR due to ATG with plasmapheresis and IVIG for four sessions. Creatinine stable at 0.9 mg/dL. All 10 patients were alive and treatment at 1.5 years.

Discussion: Monitoring allograft function, especially late after transplant, can be difficult given lack of sensitivity and precision of traditional markers. DD CF DNA Allosure down to 1% after treatment.

Conclusions: The percentage of recipients in the low DD CF DNA group had significantly lower risk of acute cellular rejection compared to recipients in the high DD CF DNA group. These results suggest that monitoring DD CF DNA levels could be a useful adjunct in detecting early acute cellular rejection.

PUB258

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 has dropped to < 1% in the first year following transplant. However, acute rejection remains a major cause of early graft dysfunction. The incidence of acute rejection in the first year following transplant is 1-2% lower in living donor kidney transplants (LDKT) 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 Rituximab 1g. He achieved diuresis 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 antigens (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 KDGE 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 presence of HLA mismatches and the long-term allograft outcomes following acute rejection.

PUB259

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 pregnancy complications compared to women 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 to 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 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 an overall 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 0.69). 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.

Conclusions: 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

Harshitha Kota,1 Xuerong Wen,2 Chao Chen,3 Jie Tang.1,4 Brown University, Providence, RI; 2University of Rhode Island, Kingston, RI; 3University of Florida, Gainesville, FL; 4University Medicine Foundation Inc, Providence, RI.

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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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 30–500 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 and placebo, respectively (hazard ratio [HR]=0.82; 95% confidence interval (CI) 0.73–0.93; 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). Finerenone significantly reduced kidney and CV outcomes in patients with T2D and advanced CKD and was well tolerated. While the primary adverse event (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 (2.3% and 0.9%, respectively). Finerenone significantly reduced kidney and CV outcomes in patients with T2D and advanced CKD and was well tolerated. While the primary adverse event (2.3% and 0.9%, respectively).

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 regimn 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 progression after a 6-month observation period were assigned to receive a 6-month 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 membranous 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 15pts (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 similar in both groups.

Conclusions: Treatment with corticosteroid-cyclophosphamide induced remission in a significantly greater number of patients with PMN than tacrolimus-rituximab.

Acknowledgement: Supported by 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 supported by a prespecified composite renal outcome (defined as a profound sustained decrease 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 HFHF, 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.

Acknowledgement: Supported by Sanofi and Regeneron.
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-untrained NDD-CKD trial, NCT02668347) 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-untreated 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, 1752 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 - Glynn L. Weintraub, Dialysis Clinic Inc, Nashville, TN.

Oral Intradialytic Nutritional Supplements and Mortality in Hemodialysis Patients: A Cluster-Randomized, Pragmatic Clinical Trial

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Background: Dialysis is a catabolic state 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 (REdUCING)

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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, 19-70h] in the regional citrate and 26h [IQR, 2-51h] 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%]; adjusted HR, 0.79 [95% CI, 0.63 to 1.00]; unadjusted P=0.05; unadjusted AD, -2.4% [95% CI, -10.5% to 5.8%]; unadjusted HR, 0.91 [95% CI, 0.72 to 1.13]; unadjusted P=0.38). Compared with systemic heparin anticoagulation, the regional citrate anticoagulation group had significantly fewer bleeding complications (15/300 [5.1%] vs. 49/296 [16.9%]; AD, -11.8% [95% CI, -16.8% to 6.8%]; P=0.001) and significantly more new infections (24/300 [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 etiology of kidney disease in this study.

Methods: 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.

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.

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 build 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
PO0262

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 ≥11.5 g/dL. 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 12 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.

PO0264

Continuous Low-Dose Iron Sucrose or Periodic High-Dose Ferric Carboxymaltose Therapy in Hemodialysis Patients (COPEFER): A Randomized Controlled Noninferiority Trial

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Background: Intravenous iron is a cornerstone in the treatment of anemia in chronic hemodialysis patients. However, optimal dosing and frequency of administration is unknown and varies widely between centers. We compared the impact of equal cumulative doses of ferric carboxymaltose (FCM), which is not yet approved for use in hemodialysis patients, and iron sucrose (IS) administered as either a high dose bolus or low dose maintenance iron dosing strategy on hemoglobin concentration, iron balance, use of erythropoiesis stimulating agents (ESA), and adverse events in prevalent chronic hemodialysis patients.

Methods: We performed an open-label randomized controlled non-inferiority trial in 245 patients on hemodialysis since 1994. A total of 480 iron atoms/m² were administered. The IS arm received 100 mg every two weeks, the FCM arm 500 mg every 10 weeks. Hemoglobin, iron markers, ESA use, C-reactive protein (CRP), phosphate, and liver enzymes were assessed. Primary end-point was the difference in hemoglobin at week 40 from baseline. A non-inferiority margin of 0.8 g/dL between both groups was pre-specified. Secondary end-points were differences in ferritin, transferrin saturation (TSAT), and ESA use.

Results: 108 patients completed the study. By 40 weeks non-inferiority criterion was not met (Hb increased by 0.47 g/dL (95% CI 0.35 to 0.59) in the FCM compared to the IS arm. In intention-to-treat analysis hemoglobin was significantly lower in the FCM arm compared to the IS arm (p = 0.046 g/dL (95% CI -0.92 to -0.01). At week 40, ferritin was 29.7% (95% CI 6.6 to 46.1) and TSAT was 27.7% (95% CI 16.3 to 38.6) lower in the FCM compared to the IS arm. ESA dosing, CRP, phosphate, and liver function parameters did not differ between groups. Adverse events that caused intermittent drug discontinuations and infections occurred more often in the IS arm.

Conclusions: IS administered more frequently at lower doses maintained hemoglobin and iron stores more effectively than FCM administered less frequently but at higher doses. However, FCM appeared safe in dialysis patients where we observed less infections compared to the IS group.

Funding: Commercial Support - Vifor
**PO2627**

**Abstract Withdrawn**

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**PO2628**

**A Prospective, Double-Blind, Randomized, Placebo-Controlled Intervventional Study to Evaluate the Safety and Efficacy of Enzobiotics in Pre-Dialysis CKD Patients**

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**Background:** Synbiotics and proteolytic enzymes supplemented in CKD prevent formation of uremic toxins (UT) generated by undigested protein. Aim: Affect of Enzobiotics in reducing generation of P-Cresols and Indoxylsulfate and quality of life in pre dialysis patients.

**Methods:** Double blind, randomized, placebo controlled multicentric clinical trial CTRI/2019/01/017070 conducted over 90 Days. Eighty CKD stages 3-5 ND subjects from 5 centers divided into two groups of 40 each: group A received 1 Enzobiotic capsule TID, Group B 1 placebo capsules TID, for three months 5 minutes before food. Blood samples taken on visits 1 and 4 to measure serum creatinine, p cresols, indoxyl sulphate (IS), platelet count (PC) hsCRP etc.

**Results:** Placebo increased p-cresol by 21% while drug reduced by 23%. Enzobiotic reduced indoxyl sulfate by 500 µg/ml (from 17200 to below 16700) with reduction in creatinine. The potential patients above p-cresol level of 20 mg/l between drug and placebo after 90 days were found to be 55% for placebo against 33% for drug. If testing is not available, Indoxyl sulfate and p-Cresol can be predicted by 2 equations (applied for patency) SF36 standard questionnaire revealed improvement in quality of life of treatment group. Adversity ratio reduced significantly from 0.3362 to 0.1736 P-Value for patency) SF36 standard questionnaire revealed improvement in quality of life of treatment group. A
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dversity ratio reduced significantly from 0.3362 to 0.1736 P-Value for patency) SF36 standard questionnaire revealed improvement in quality of life of treatment group. A

**Conclusions:** Enzobiotics improve make gut microbiome favourable, can delay dialysis in CKD patients by reducing uremic toxins, CRP, thrombocytopenia and improve cardiac performance, lipid profile, and quality of life.

**Funding:** Commercial Support - Mylin Biotech India Private Limited

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**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 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.

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PO2630

Canagliflozin Across the Spectrum of Kidney Function and Albuminuria: Integrated Data from CANVAS and CREDENCE

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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% 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.

Funding: 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 (AUC0-t). 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 AUC0-t 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.
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 placement, respectively (Figure 1). At median follow-up of 321.0 days, primary AV access failure was noted in 31% in each group. Successful cannulation occurred in 8% and 44%, and surgical re-interventions in 23% and 25% (Table 1). AV access infection was seen in 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%, ≥2-microglobulin, compared to a high-flux dialyzer (Elisio-17H) in the US (Weiner 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).

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 κ and β free light chains, complement factor D, TNF-α, and β2-microglobulin, compared to a high-flux dialyzer (Elisio-17H) in the US (Weiner et al. 2020).

Background: The Theranova 400 was an expanded HD via the Theranova 400 medium cut-off dialyzer had superior reduction ratios of large and middle molecules uremic toxins such as κ and β free light chains, complement factor D, TNF-α, and β2-microglobulin, compared to a high-flux dialyzer (Elisio-17H) in the US (Weiner 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).

Results: There were 86 patients (389 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 patient hospitalization events.

PO2644

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 AVG placement and maturation with size expectations and effectiveness.

Methods: This 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.

B7
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 effects 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) but not significant. FA3M : 3-Month Vein diameter (AP), with cuff, at 1 cm above elbow UA : Enrollment-Vein diameter (AP), with cuff, at 1 cm above elbow UA : Enrollment-Vein diameter (AP), with cuff, at 1 cm from radial bone UA3M : 3-Month Vein diameter (AP), with cuff, at 1 cm above elbow UA : Enrollment-Vein diameter (AP), with cuff, at 1 cm from radial bone Difference between mean of (FA3M-FA) : t = 1.72, p-value = 0.03 for Clinical Effectiveness: FA: 18%± 2.5 mm and 33% reached 2.0 mm or greater UA: 44% ± 2.5mm 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.

Funding: National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) Support

Table 1

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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.

Methods: 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 in South Korea Participants: 178 patients aged 18-80 years with symptoms and blood-corrected serum sodium (sNa) ≤125 mmol/L were included. Interventions Either RIB or SCI of 3% hypertonic saline for 24-48 hours stratified by the severity of clinical symptoms. Main outcome and Measures The primary outcome was overcorrection as follows: increase in the sNa level by >12/18 mmol/L within 24/48 hours. Secondary outcomes included efficacy and safety of the treatment approaches. SNa concentrations were measured at every 6 hours for 2 days.

Results: Patients (mean age 73.1 years, 45% male, mean sNa concentrations 128±3 mmol/L) were randomly assigned to RIB (n=87) or SCI (n=91). Overcorrection occurred in 17.2% and 24.2% in RIB and SCI groups, respectively (absolute risk difference, -6.9% [95% CI -18.8% to 4.9%]). RIB group showed lower incidence of re-lowering treatment than SCI group (41.4% vs 57.1%; absolute risk difference, -15.8% [95% CI -30.3% to -1.3%]; number needed to treat [NNT]=6.3). Groups did not differ in terms of efficacy in increasing sNa concentrations or improving symptoms but RIB showed better efficacy in achieving target correction rate within 1 hour (32.2% vs 17.6%, absolute risk difference 14.6% [95% CI 2% to 27.2%]; NNT=6.8).

Conclusion: Both RIB and SCI therapies of hypertonic saline for treating hyponatremic encephalopathy were effective and safe, with no difference in the overcorrection risk. However, RIB had a lower incidence of therapeutic re-lowering treatment and tended to have a better efficacy in achieving sNa within 1 hour than SCI. RIB could be suggested as the preferred treatment of symptomatic hyponatremia, consistent with the current consensus guidelines.

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PO2638
Rituximab vs. Cyclophosphamide in the Treatment of Membranous Nephropathy: The RI-CYCLO Trial
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7 Azienda Ospedale Policlinico, Bari, Italy.

**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 two weeks apart) or CYC. Complete remission (CR) was defined as proteinuria ≤0.3 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 2/37 pts (5%) 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 protocol” PP 0.28, 95% CI 0.08-0.95). 23/37 (62%) in the RTX arm and 27/37 (73%) in the CYC arm had CR+PR (OR ITT analysis 0.61, 95% CI 0.23-1.63, OR PP 0.11, 95% CI 0.42-2.98). Probabilities of CR and CR+PR at 24 months were 0.42 (CI 0.26-0.62) and 0.83 (CI 0.65-0.95) in the RTX arm and 0.43 (0.28-0.61) and 0.82 (0.66-0.93) in the CYC arm. Serious adverse events occurred in 7 and 5 pts, in the RTX and CYC arm, respectively.

**Conclusions:** Although the probability of CR was lower in the RTX arm at 12 months, the probability of CR at 24 months and of CR+PR at 12 and 24 months was similar in the two groups. 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.

PO2639
The Immunoglobulin G Degrading Enzyme Imilidase 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. Imilidase 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 imilidase (non-proprietary name for Idex® – 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 imilidase 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 imilidase (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:** Imilidase 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.

**Funding:** Commercial Support - Hansa Biopharma, Private Foundation Support

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, this may contribute to podocyte dysfunction and proteinuria. We showed in nephrotic 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 nephrotic 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.

**Funding:** NIDDK Support, Other NIH Support - NIHGRI Support

Underline represents presenting author/disclosure.