Kidney News

Less Than Perfect Kidneys May Help Expand Transplant Access

By Bridget M. Kuehn

Kidneys from donors with acute kidney injury (AKI) are often discarded, but a recent study suggests that transplant patients who receive donor kidneys with AKI do as well as those who receive comparable kidneys without AKI.

The findings are the latest in a growing body of evidence that suggests using more donor kidneys that are less than perfect may help increase access to transplantation. Transplantation is considered the best treatment option for most patients with kidney disease because it can improve their quality of life and help them live longer, according to the National Kidney Foundation. But with about 100,000 patients on the waiting list for transplantation and only about 20,000 kidney transplants completed each year, many patients end up waiting years for a kidney. Currently, about one-third of donor kidneys with AKI are discarded, noted Chirag Parikh, MBBS, PhD, Director of the Division of Nephrology at Johns Hopkins Medicine in Baltimore. Other studies have suggested that donor kidneys that are seropositive for hepatitis C virus (HCV) or kidneys from older donors might also be underutilized options.

“We and other groups are looking at opportunities where there are kidneys in the discard pool that can potentially work well and can benefit more people who are on the waiting list,” Parikh said.

Currently, many deceased donor kidneys with AKI are discarded because patients and nephrologists fear they may not last as long, explained Parikh. But some evidence suggests that these fears may be misplaced. With their recent study, Parikh and his colleagues strengthened the case for using donor kidneys with AKI.

In the study, they analyzed data from DonorNet on transplant outcomes in 12,810 patients who received deceased donor kidneys with AKI and 12,513 patients who received kidneys without AKI from donors with similar characteristics. They found that there wasn’t a significant difference in all-cause graft failure or death-censored graft failure in the two groups. Although more patients who received AKI kidneys experience delayed graft function (29% vs. 22%), Parikh said the rigorous design of the study and the fact that it included all kidneys transplanted between Jan. 1, 2010, and Dec. 31, 2013, bolster the evidence base.

Based on the evidence, Parikh said he thinks between 500 and 700 deceased donor kidneys with AKI could be used.

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Does Fistula Creation for Dialysis Access Have its Own Benefits?

Because patients often resist surgery to create recommended arteriovenous fistulas for dialysis, some researchers have hoped to find advantages

By Eric Seaborg

An arteriovenous fistula (AVF) is the guideline-recommended vascular access for hemodialysis, yet a large majority of patients in the US and Canada begin dialysis using catheter access, despite its higher rates of complications. Because patients resist having the AVF surgical procedure, many nephrologists have looked to the results of observational studies that led to the hypothesis that AVF creation could affect kidney function—and even lead to benefits that could postpone the need for dialysis.

Definitive evidence for such a benefit remains elusive, however, with two new studies contributing to the discussion.

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Public awareness campaign launches during National Kidney Month to urge early detection and management of kidney disease

Bloodstream Infections in Dialysis
New tools and insights into preventing bloodstream infections in hemodialysis patients

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A trio of articles about education, including the science of learning, a plea for nephrology fellows to embrace teaching, and a viral international website
Less Than Perfect Kidneys

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added to the donor pool each year. This could be beneficial for both patients and society, he said, noting the huge costs of maintaining patients on dialysis. "Taking these people off dialysis and giving them a meaningful life back makes a huge difference," he said.

Another potentially underutilized pool of deceased donor kidneys are HCV-positive organs. Until recently, HCV-positive donor kidneys could not be used for transplant because peginterferon plus ribavirin, the gold standard treatment, could cause rejection, said Xingxing Cheng, MD, a transplant nephrologist and clinical assistant professor at Stanford University in California. But the emergence of direct-acting antiviral drugs that have been shown to eliminate the HCV virus in up to 100% of patients after transplant has changed the landscape. The number of HCV seropositive donors has also increased from 181 to 661 per year between 2000 and 2016 as opioid overdose deaths have increased, a recent study co-authored by Cheng showed. The study showed the number of HCV-positive donor kidneys transplanted increased from 165.4 to 334.7. Most are transplanted into HCV-positive patients, but some centers are also transplanting them into patients without HCV. Cheng noted. Both groups of patients are treated with direct-acting antivirals after transplant.

But the use of HCV-positive donor kidneys has lagged behind the use of HCV-positive donor livers, the study found. Cheng said there are several likely explanations for this: Kidney patients can stay on dialysis while they wait for a kidney, while liver transplant patients don’t have such an option. Hepatologists also may be more experienced and comfortable using direct-acting antivirals than their nephrologist counterparts. Another potential concern is whether patients have access to direct-acting antiviral medications, which can cost as much as $94,000 per treatment. Cheng said she and her colleagues seek preapproval for coverage of direct-acting antivirals for prospective kidney transplant patients who are already HCV-positive. "I think there is a great role for [HCV positive donor kidneys]," she said. The biggest thing that needs to be overcome is the financial hurdle of financing the treatments, so that we don’t create two classes of kidney transplant recipients, one who have good insurance that can afford the treatment, and one who can’t.

Another group of kidneys that may be underutilized are those from older donors, as studies have found that older recipients may benefit from a transplant from older donors. Stephen Pastan, MD, Associate Professor of Medicine and Medical Director of the Kidney and Pancreas Transplant Program at Emory University School of Medicine, explained that a kidney from an older donor may not last as long—perhaps 5 years rather than 8—but getting a transplant from an older donor is still much better than staying on dialysis. There are several national efforts underway to increase access to transplantation and increase the number of organs available from both deceased and living donors.

Among the aims of the US Department of Health and Human Services Advancing American Kidney Health program launched in 2019 are increasing the number of donor kidneys available, reforming the organ procurement system, and removing financial and other barriers to living organ donation. The United Network for Organ Sharing is developing systems that would more quickly match donor kidneys to centers that will use them in order to decrease discards of donor kidneys that spend too much time on ice during the allocation process.

A report from the National Kidney Foundation’s Consensus Conference to Decrease Kidney Discards highlighted the need to change regulations or payer incentives that may unfairly penalize transplant centers that use lower quality kidneys, Cheng noted. She explained there can be "tension between what is best for the community and what is best for the individual patient." For example, using an older donor kidney in an older patient may be beneficial, but if it fails, an older patient may be less likely to get a second chance. "It’s a great idea to try to expand the usage of [ marginal] kidneys," Cheng said. "But there are a lot of just unknowns and ethical questions in finding the proper patients to get these organs to. I’ve personally in my practice seen great successes with these and I’ve also seen some really bad failures."

References:

ASN Executive Vice President Tod Ibrahim Named President of CMSS

Tod Ibrahim, ASN executive vice president, has been named president of the Council of Medical Specialty Societies (CMSS). His term took effect in November 2019.

“CMSS is uniquely positioned to help address pressing clinical topics, research-related issues, and educational topics common to its members,” Ibrahim said. “There is an opportunity to think creatively across specialties, and that was really appealing to me.”

Founded in 1965, CMSS provides an independent forum for the discussion by medical specialists of issues of national interest and mutual concern. The organization currently has 46 national medical society members representing more than 800,000 physicians. ASN has been a member of CMSS for nearly 10 years.

Ibrahim succeeds Ken Berka, MD, FAAFP, CPHMS, a past member of the board of directors of the American Academy of Family Physicians, and David B. Hoyt, MD, FACS, executive director of the American College of Surgeons. Dar-
Indication
Parsabiv™ (etelcalcetide) is indicated for the treatment of secondary hyperparathyroidism (HPT) in adult patients with chronic kidney disease (CKD) on hemodialysis.

Limitations of Use:
Parsabiv™ has not been studied in adult patients with parathyroid carcinoma, primary hyperparathyroidism, or with CKD who are not on hemodialysis and is not recommended for use in these populations.

Important Safety Information
Contraindication: Parsabiv™ is contraindicated in patients with known hypersensitivity to etelcalcetide or any of its excipients. Hypersensitivity reactions, including pruritic rash, urticaria, and face edema, have occurred.

Hypocalcemia: Parsabiv™ lowers serum calcium and can lead to hypocalcemia, sometimes severe. Significant lowering of serum calcium can cause QT interval prolongation and ventricular arrhythmia. Patients with conditions that predispose to QT interval prolongation and ventricular arrhythmia may be at increased risk for QT interval prolongation and ventricular arrhythmias if they develop hypocalcemia due to Parsabiv™. Closely monitor corrected serum calcium and QT interval in patients at risk on Parsabiv™.

Significant reductions in corrected serum calcium may lower the threshold for seizures. Patients with a history of seizure disorder may be at increased risk for seizures if they develop hypocalcemia due to Parsabiv™. Monitor corrected serum calcium in patients with seizure disorders on Parsabiv™.

Concurrent administration of Parsabiv™ with another oral calcimimetic could result in severe, life-threatening hypocalcemia. Patients switching from cinacalcet to Parsabiv™ should discontinue cinacalcet for at least 7 days prior to initiating Parsabiv™. Closely monitor corrected serum calcium in patients receiving Parsabiv™ and concomitant therapies known to lower serum calcium.

Measure corrected serum calcium prior to initiation of Parsabiv™. Do not initiate in patients if the corrected serum calcium is less than the lower limit of normal. Monitor corrected serum calcium within 1 week after initiation or dose adjustment and every 4 weeks during treatment with Parsabiv™. Measure PTH 4 weeks after initiation or dose adjustment of Parsabiv™. Once the maintenance dose has been established, measure PTH per clinical practice.

Worsening Heart Failure: In Parsabiv™ clinical studies, cases of hypotension, congestive heart failure, and decreased myocardial performance have been reported. Closely monitor patients treated with Parsabiv™ for worsening signs and symptoms of heart failure.

Upper Gastrointestinal Bleeding: In clinical studies, 2 patients treated with Parsabiv™ in 1253 patient years of exposure had upper gastrointestinal (GI) bleeding at the time of death. The exact cause of GI bleeding in these patients is unknown and there were too few cases to determine whether these cases were related to Parsabiv™.

Patients with risk factors for upper GI bleeding, such as known gastritis, esophagitis, ulcers or severe vomiting, may be at increased risk for GI bleeding with Parsabiv™. Monitor patients for worsening of common Parsabiv™ GI adverse reactions and for signs and symptoms of GI bleeding and ulcerations during Parsabiv™ therapy.

Adynamic Bone: Adynamic bone may develop if PTH levels are chronically suppressed.

Adverse Reactions: In clinical trials of patients with secondary HPT comparing Parsabiv™ to placebo, the most common adverse reactions were blood calcium decreased (64% vs. 10%), muscle spasms (12% vs. 7%), diarrhea (11% vs. 9%), nausea (11% vs. 6%), vomiting (9% vs. 5%), headache (8% vs. 6%), hypocalcemia (7% vs. 0.2%), and paresthesia (6% vs. 1%).

Please see Brief Summary of full Prescribing Information on adjacent page.

IV = intravenous; sHPT = secondary hyperparathyroidism; PTH = parathyroid hormone; P = phosphate; cCa = corrected calcium.

Reference: 1. Parsabiv™ (etelcalcetide) prescribing information, Amgen.
Please see package insert for full Prescribing Information.

INDICATIONS AND USAGE
PARSABIV is indicated for the treatment of secondary hyperparathyroidism (HPT) in adult patients with chronic kidney disease (CKD) on hemodialysis.

Limitations of Use:
PARSABIV has not been studied in adult patients with parathyroid carcinoma, primary hyperparathyroidism, or with chronic kidney disease who are not on hemodialysis and is not recommended for use in these populations.

CONTRAINDICATIONS
Hypersensitivity
PARSABIV is contraindicated in patients with known hypersensitivity to etelcalcetide or any of its excipients. Hypersensitivity reactions, including urticarial rash, urticaria, and face edema, have occurred with PARSABIV (see Adverse Reactions (6.1) in PARSABIV full prescribing information).

WARNINGS AND PRECAUTIONS
Hypocalcemia
PARSABIV lowers serum calcium (see Adverse Reactions (6.1) in PARSABIV full prescribing information) and can lead to hypocalcemia, sometimes severe. Significant lowering of serum calcium can cause paresthesias, myalgias, muscle spasms, seizures, QT interval prolongation, and ventricular arrhythmias. QT interval prolongation and ventricular arrhythmias

In the combined placebo-controlled studies, more patients treated with PARSABIV experienced a maximum increase from baseline of greater than 60 msec in the QTcF interval (50% placebo versus 1.2% PARSABIV). In these studies, the incidence of a maximum post-baseline prediscovery QTcF > 500 msec in the placebo and PARSABIV groups was 1.9% and 4.8%, respectively (see Adverse Reactions (6.1) in PARSABIV full prescribing information). Patients with con genital long QT syndrome, history of QT interval prolongation, family history of long QT syndrome or sudden cardiac death, and other conditions that predispose to QT interval prolongation and ventricular arrhythmias may be at increased risk for QT interval prolongation and ventricular arrhythmias if they develop hypocalcemia due to PARSABIV. Closely monitor corrected serum calcium and QT interval in patients at risk receiving PARSABIV.

Seizures
Significant reductions in corrected serum calcium may lower the threshold for seizures. Patients with a history of seizure disorder may be at increased risk for seizures if they develop hypocalcemia due to PARSABIV. Monitor corrected serum calcium in patients with seizure disorders receiving PARSABIV.

Concurrent administration of PARSABIV with another oral calcium-sensing receptor agonist could result in severe, life-threatening hypocalcemia. Patients switching from cinacalcet to PARSABIV should discontinue cinacalcet for at least 7 days prior to initiating PARSABIV (see Dosage and Administration (2.4) in PARSABIV full prescribing information). Closely monitor corrected serum calcium in patients receiving PARSABIV and concomitant therapies known to lower serum calcium.

Measure corrected serum calcium prior to initiation of PARSABIV. Do not initiate in patients if the corrected serum calcium is less than the lower limit of normal. Monitor corrected serum calcium within 1 week after initiation or dose adjustment and every 4 weeks during treatment with PARSABIV (see Dosage and Administration (2.3) in PARSABIV full prescribing information). Educate patients on the symptoms of hypocalcemia, and advise them to contact a healthcare provider if they occur. If corrected serum calcium falls below the lower limit of normal or symptoms of hypocalcemia develop, start or increase calcium supplementation (including calcium, calcium-containing phosphate binders, and/or vitamin D sterols or increases in dialysate calcium concentration). PARSABIV dose reduction or discontinuation of PARSABIV may be necessary (see Dosage and Administration (2.3) in PARSABIV full prescribing information).

Worsening Heart Failure
In clinical studies with PARSABIV, cases of hypertension, congestive heart failure, and decreased myocardial performance have been reported. In clinical studies, heart failure requiring hospitalization occurred in 2% of PARSABIV-treated patients and 1% of placebo-treated patients. Reductions in corrected serum calcium may be associated with congestive heart failure; however, a causal relationship to PARSABIV could not be completely excluded. Closely monitor patients treated with PARSABIV for worsening signs and symptoms of heart failure.

Upper Gastrointestinal Bleeding
In clinical studies, two patients treated with PARSABIV in 1253 patient-years of exposure had upper gastrointestinal (GI) bleeding noted at the time of death while no patient in the control groups in 384 patient-years of exposure had upper GI bleeding noted at the time of death. The exact cause of GI bleeding in these patients is unknown, and there were too few cases to determine whether these cases were related to PARSABIV.

Patients with risk factors for upper GI bleeding (such as known gastritis, esophagitis, ulcers, or severe vomiting) may be at increased risk for GI bleeding while receiving PARSABIV treatment. Monitor patients for worsening of common GI adverse reactions of nausea and vomiting associated with PARSABIV (see Adverse Reactions (6.1) in PARSABIV full prescribing information) and for signs and symptoms of GI bleeding and ulcerations during PARSABIV therapy. Promptly evaluate and treat any suspected GI bleeding.

Adynamic Bone
Adynamic bone may develop if PTH levels are chronically suppressed. If PTH levels decrease below the recommended target range, the dose of vitamin D sterols and/or PARSABIV should be reduced or therapy discontinued. After discontinuation, resume therapy at a lower dose to maintain PTH levels in the target range (see Dosage and Administration (2.1) in PARSABIV full prescribing information).

ADVERSE REACTIONS
The following adverse reactions are discussed in greater detail in other sections of the labeling:
- Hypocalcemia (see Warnings and Precautions (5.1) in PARSABIV full prescribing information)
- Worsening Heart Failure (see Warnings and Precautions (5.2) in PARSABIV full prescribing information)
- Upper Gastrointestinal Bleeding (see Warnings and Precautions (5.3) in PARSABIV full prescribing information)
- Adynamic Bone (see Warnings and Precautions (5.4) in PARSABIV full prescribing information)

Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

The data in Table 2 are derived from two placebo-controlled clinical studies in patients with chronic kidney disease and secondary hyperparathyroidism on hemodialysis. The data reflect exposure of 503 patients to PARSABIV with a mean duration of exposure to PARSABIV of 23.6 weeks. The mean age of patients was approximately 55 years, and 60% of the patients were male. The total patients, 67% were Caucasian, 28% were Black or African American, 2.6% were Asian, 1.2% were Native Hawaiian or Other Pacific Islander, and 1.6% were categorized as Other. Table 2 shows common adverse reactions associated with the use of PARSABIV in the pool of placebo-controlled studies. These adverse reactions occurred more commonly on PARSABIV than on placebo and were reported in at least 5% of patients treated with PARSABIV.

Table 2: Adverse Reactions Reported in ≥ 5% of PARSABIV-Treated Patients

<table>
<thead>
<tr>
<th>Adverse Reaction*</th>
<th>Placebo (N = 513)</th>
<th>PARSABIV (N = 503)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood calcium decreaseda</td>
<td>10%</td>
<td>64%</td>
</tr>
<tr>
<td>Muscle spasms</td>
<td>7%</td>
<td>12%</td>
</tr>
<tr>
<td>Diaphoresis</td>
<td>9%</td>
<td>11%</td>
</tr>
<tr>
<td>Nausea</td>
<td>6%</td>
<td>11%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>5%</td>
<td>9%</td>
</tr>
<tr>
<td>Headache</td>
<td>6%</td>
<td>8%</td>
</tr>
<tr>
<td>Hypocalcemiaa</td>
<td>0.2%</td>
<td>7%</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>1%</td>
<td>6%</td>
</tr>
</tbody>
</table>

* Included adverse reactions reported with at least 1% greater incidence in the PARSABIV group compared to the placebo group

a Asymptomatic reductions in corrected serum calcium between 7.5 and < 8.3 mg/dL (that required medical management)

Upper gastrointestinal bleeding associated with PARSABIV and ulcerations during PARSABIV therapy.
Other adverse reactions associated with the use of PARSABIV but reported in < 1% of patients in the PARSABIV group in the two placebo-controlled clinical studies were:

- Hypokalemia: 3% and 4% for placebo and PARSABIV, respectively.
- Hypocalcemia: 3% and 4% for placebo and PARSABIV, respectively.
- Neutropenia: 3% and 4% for placebo and PARSABIV, respectively.
- Proteinuria: 3% and 4% for placebo and PARSABIV, respectively.
- Hypophosphatemia: 3% and 4% for placebo and PARSABIV, respectively.

Description of Selected Adverse Reactions

Hypocalcemia

In the combined placebo-controlled studies, a higher proportion of patients on PARSABIV developed at least one corrected serum calcium value below 7.0 mg/dL (7.6% PARSABIV, 9.1% placebo, below 7.5 mg/dL (27% PARSABIV, 5.5% placebo), and below 8.3 mg/dL (79% PARSABIV, 19% placebo). In the combined placebo-controlled studies, 1% of patients in the PARSABIV group and 0% of patients in the placebo group discontinued treatment due to an adverse reaction attributed to a low corrected serum calcium.

In the combined placebo-controlled studies, 19% of patients treated with PARSABIV and 8% of patients treated with placebo had at least one measured phosphorus level below the lower normal limit (i.e., 2.2 mg/dL).

QTc Interval Prolongation Secondary to Hypocalcemia

In the combined placebo-controlled studies, more patients treated with PARSABIV experienced a maximum increase from baseline of greater than 60 msec in the QTcF interval (0% placebo versus 1.2% PARSABIV). The patient incidence of maximum post-baseline predialysis QTcF > 500 msec in the placebo and PARSABIV groups was 1.9% and 4.6%, respectively.

Hypersensitivity

In the combined placebo-controlled studies, the subject incidence of adverse reactions potentially related to hypersensitivity was 4.4% in the PARSABIV group and 3.7% in the placebo group. Hypersensitivity reactions in the PARSABIV group were pruritic rash, urticaria, and face edema.

Immunogenicity

As with all peptide therapeutics, there is potential for immunogenicity. The detection of anti-drug binding antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to etelcalcetide with the incidence of antibodies to other products may be misleading.

In clinical studies, 7.1% (7 out of 99) of patients with secondary hyperparathyroidism treated with PARSABIV for up to 6 months tested positive for binding anti-etelcalcetide antibodies. Fifty-seven out of 71 had pre-existing anti-etelcalcetide antibodies.

No evidence of altered pharmacokinetic profile, clinical response, or safety profile was associated with pre-existing or developing anti-etelcalcetide antibodies. If formation of anti-etelcalcetide binding antibodies with a clinically significant effect is suspected, contact Amgen at 1-866-77-MAN (1-866-772-6234) to discuss antibody testing.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

There are no available data on the use of PARSABIV in pregnant women. In animal reproduction studies, effects were seen at doses associated with maternal toxicity that included hypocalcemia. In a pre- and post-natal study in rats administered etelcalcetide during organogenesis through delivery and weaning, there was a slight increase in perinatal pup mortality, delay in parturition, and transient effects on pup growth at exposures 1.8 times the human exposure for the clinical dose. There were no effects on embryo-fetal development in Sprague-Dawley rats administered etelcalcetide at 0.75, 1.5, and 3 mg/kg/day by the intravenous route during organogenesis (pre-mating to gestation day 17) at exposures up to 1.8 times human exposures at the clinical dose of 15 mg three times per week based on AUC. No effects on embryo-fetal development were observed in New Zealand White rabbits at doses of etelcalcetide of 0.375, 0.75, and 1.5 mg/kg by the intravenous route (gestation day 7 to 118, representing up to 4.3 times human exposures based on AUC). In separate studies at higher doses of 4.5 mg/kg in rats (gestation days 6 to 17) and 2.25 mg/kg in rabbits (gestation days 7 to 20), representing 2.7 and 7 fold clinical exposures, respectively, there was reduced fetal growth associated with maternal toxicities of hypocalcemia, tremoring, and reductions in body weight and food consumption.

In a pre- and post-natal development study in Sprague-Dawley rats administered etelcalcetide at 0.75, 1.5, and 3 mg/kg/day by the intravenous route (gestation day 7 to lactation day 20), there was a slight increase in perinatal pup mortality, delay in parturition, and transient reductions in post-natal growth at 3 mg/kg/day (representing 1.8-fold human exposures at the clinical dose of 15 mg three times per week based on AUC), associated with maternal toxicities of hypocalcemia, tremoring, and reductions in body weight and food consumption. There were no effects on sexual maturation, neurobehavioral, or reproductive function at up to 3 mg/kg/day, representing exposures up to 1.8-fold human exposure based on AUC.

Lactation

Risk Summary

There are no data regarding the presence of PARSABIV in human milk or effects on the breastfed infant or on milk production. Studies in rats showed [14C]-etelcalcetide was present in the milk at concentrations similar to plasma. Because of the potential for PARSABIV to cause adverse effects in breastfed infants including hypocalcemia, advise women that use of PARSABIV is not recommended while breastfeeding.

Data

Presence of milk was assessed following a single intravenous dose of [14C]-etelcalcetide in lactating rats at maternal exposures similar to the exposure at the human clinical dose of 15 mg three times per week. [14C]-etelcalcetide-derived radioactivity was present in milk at levels similar to plasma.

Pediatric Use

The safety and efficacy of PARSABIV have not been established in pediatric patients.

Geriatric Use

Of the 503 patients in placebo-controlled studies who received PARSABIV, 177 patients (35.2%) were ≥ 65 years old and 72 patients (14%) were > 75 years old.

No clinically significant differences in safety or efficacy were observed between patients ≥ 65 years and younger patients (≥ 18 and < 65 years old). No differences in plasma concentrations of etelcalcetide were observed between patients ≥65 years and younger patients (≥ 18 and < 65 years old).

OVERDOSAGE

There is no clinical experience with PARSABIV overdose. Overdose of PARSABIV may lead to hypocalcemia with or without clinical symptoms and may require treatment. Although PARSABIV is cleared by dialysis, hemodialysis has not been studied as a treatment for PARSABIV overdose. In the event of overdose, corrected serum calcium should be checked and patients should be monitored for symptoms of hypocalcemia, and appropriate measures should be taken [see Warnings and Precautions (5.1) in PARSABIV full prescribing information].

PARSABIV™ (etelcalcetide)

Manufactured for:
KAI Pharmaceuticals, Inc., a wholly owned subsidiary of Amgen, Inc.
One Amgen Center Drive
Thousand Oaks, California 91320-1799

Patent: http://pat.amgen.com/Parsabiv/

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Data

Animal Data

There were no effects on embryo-fetal development in Sprague-Dawley rats when etelcalcetide was dosed at 0.75, 1.5, and 3 mg/kg/day by the intravenous route during organogenesis (pregnancy to gestation day 17) at exposures up to 1.8 times human exposures at the clinical dose of 15 mg three times per week based on AUC. No effects on embryo-fetal development were observed in New Zealand White rabbits at doses of etelcalcetide of 0.375, 0.75, and 1.5 mg/kg by the intravenous route (gestation day 7 to 118, representing up to 4.3 times human exposures based on AUC). In separate studies at higher doses of 4.5 mg/kg in rats (gestation days 6 to 17) and 2.25 mg/kg in rabbits (gestation days 7 to 20), representing 2.7 and 7 fold clinical exposures, respectively, there was reduced fetal growth associated with maternal toxicities of hypocalcemia, tremoring, and reductions in body weight and food consumption.

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Patent: http://pat.amgen.com/Parsabiv/

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Fistula Creation
Continued from page 1
sion in conflicting ways, and providing no firm answers. A study from Canada provided more observational evidence that the creation of an AVF slows a patient’s slide toward dialysis, whereas one from Sweden found the same benefits from the placement of either an AVF or a peritoneal dialysis catheter.

The first report, published in November 2019 in *BMC Nephrology* by Annie-Claire Nadeau-Fredette, MD, et al., was a retrospective cohort study of 146 patients in Quebec whose estimated glomerular filtration rates (eGFRs) were followed pre- and post-AVF creation. The study found that “AVF creation was associated with a significant reduction in eGFR decline.” The results echo the findings of several other observational studies.

But a somewhat contrasting study from the Karolinska Institute in Sweden, published in October 2019 in *Nephrology Dialysis Transplantation* by Ulrika Hahn Lundstrom et al., compared the effects of AVF placement with peritoneal dialysis catheter placement in 744 pre-dialysis patients. The study found that “both forms of access were associated with reduced eGFR decline [with] no significant difference in eGFR decline” between the two procedures.

Reasons for eGFR benefit
Two broad categories of explanations have been proposed for how AVF placement could contribute to flattened eGFR decline: first, by contributing to physiological changes that benefit kidney function, and second, through ancillary improvements in care or patient actions.

Several physiological reasons—or at least possibilities—have been proposed for how AVF placement could be associated with the flattening of decline in kidney function, according to Nadeau-Fredette, of the Hopital Maisonneuve-Rosemont, Montreal, Quebec, Canada, and lead author of the AVF study.

One possibility is an effect from remote ischemic pre-conditioning (RIPC). “Recent studies demonstrated that RIPC, induced by repeated cycle(s) of inflating and deflating blood pressure cuffs, could enhance renal protection against ischemic injuries through various humoral, anti-inflammatory, anti-oxidant, and anti-apoptotic effects,” Nadeau-Fredette et al. write. “Local limb ischemia induced by clamping of arteries and ligature of small arterioles during AVF creation could create acute changes similar to those observed with RIPC.”

Another possibility is that creation of a fistula increases blood flow with effects extending to cardiac output. “AVF enhances cardiac output through increased heart rate, cardiac contractility and venous return, and lowers systemic peripheral resistance and arterial rigidity through endothelial changes induced by increased wall stress. The enhanced cardiac output and lower systemic peripheral resistance both favor renal perfusion,” the *BMC Nephrology* authors write.

But they also note that “it is possible that the observed effect of AVF on eGFR was mediated by improved compliance to drug and medical follow-up or natural stabilization of the kidney disease.”

Patient compliance and other effects
The study from the Karolinska Institute calls into question the impact of a physiological reason for stabilization of eGFR because the results were the same for the AVF and peritoneal dialysis catheter groups, but rather appears to bolster a “process of care” and compliance explanation, according to Prabir Roy-Chaudhury, MD, of the University of North Carolina Kidney Center in Chapel Hill.

Because patients resist holding the AVF surgical procedure, many nephrologists have looked to the results of observational studies that led to the hypothesis that AVF creation could affect kidney function—and even lead to benefits that could postpone the need for dialysis.

Roy-Chaudhury notes that as their disease progresses, patients will have more interactions with their healthcare providers. Patients resist the idea of going on dialysis, and don’t want to give in to their situation, but faced with the grim reality of having a procedure, their compliance might increase: “When the patient asks, ‘Is there any chance that I can prolong the time to dialysis even with the fistula placed?’ The physician is going to say, ‘Do all the things that you were doing before,’ which the patient may not have been doing. So now suddenly the patient starts doing all of those important things they have been neglecting, like taking their medicine, controlling their blood pressure, coming to appointments, and listening to the nurse.”

Similarly, the patient receives stepped-up care and closer attention from providers when preparing to have a procedure, which could also have beneficial effects on the patient’s condition. “It could be a result of the process of care, . . . which is important because it means that one way of reducing the decline of GFR is to enhance the process of care,” Roy-Chaudhury said.

Another confounding factor could be that the reasons and timing of preparing for dialysis play into a statistical phenomenon known as regression to the mean related. “The accelerated decline in kidney function leads to the decision to begin dialysis and implant a fistula, but such declines tend not to be linear. The decline tends not to occur at a consistent rate, but flattens out over time—regresses to the mean rate of decline,” Roy-Chaudhury told *ASN Kidney News*.

Effects of AVF maturation
Cuba P. Kovesdy, MD, of the University of Tennessee Health Science Center in Memphis, said there are now three or four observational studies that show an association of AVF placement with the benefit of a flatter trajectory of eGFR decline. The Swedish study shows no difference between AVF and catheters, but is like the Canadian study in that both “show a benefit from intervention,” Kovesdy said.

Kovesdy and colleagues published the largest study to date of the potential AVF effect in *Nephrology Dialysis Transplantation* in 2017. They compared more than 3000 patients with chronic kidney disease who had a pre-dialysis AVF or arteriovenous graft (AVG) with a 3500-patient comparator cohort who started dialysis with a central venous catheter. They found a deceleration of eGFR decline in the AVF/AVG group compared with an acceleration of eGFR decline in the catheter group.

The benefit in the AVF/AVG group occurred independent of the AVF/AVG maturation, however, which led the researchers to “consider the possibility that the deceleration of eGFR decline … may be attributable to factors unrelated to the physiological effects of a mature vascular access, such as more attentive nephrologist care and improved patient health status or behavioral compliance with therapy. Nonetheless, there still seem to be other plausible physiological mechanisms that could explain the potential renoprotective effects of AVF/AVG creation even in those patients whose vascular access is not mature enough for successful hemodialysis cannulation.”

These findings did not support that these physiological mechanisms were related to cardiac improvements, but the researchers noted the “growing evidence from experimental and clinical studies” of benefits from RIPC. “The process of AVF surgery involves ‘repetitive clamping of the feeding artery and permanent ligation of small arterial branches. It has been postulated that even a brief ischemic stimulus of a remote site releases RIPC-induced humoral factors such as adenosine, erythropoietin, or nitric oxide into the systemic circulation, which subsequently protects other target organs, including the kidney,” the researchers wrote.

This local limb ischemia would occur in all patients who underwent an AVF procedure, so the potential benefit would apply regardless of whether the fistula matured.

No definitive answers
Kovesdy bemoaned the “inertia or lack of trust” encountered when trying to convince a patient it is time to place an AVF to prepare for dialysis, and sees the advantage of having another reason to encourage a patient to proceed. “This is only observational data, so the level of evidence is not high enough to truly implicate at this point. And there are several aspects of this data which suggest that it may indeed be some kind of an unmeasured confounder” leading to the benefit, he said.

Nadeau-Fredette said that she would like to see more patients using AVFs because “it is the best access,” and a link to another benefit might help convince them—but the evidence of cause and effect is not there. “This is only observational, so I cannot say that it is directly related. There are some hemodynamic reasons that could be involved, but it is very difficult to know if it is really the cause or just kind of an observation,” she said.

There is one point on which everyone agrees: More direct evidence on the level that randomized clinical trials could provide would be a tremendous help. But it would be ethically difficult to design a clinical trial in which a tranche of patients were denied the recognized standard of care of AVF placement.■
Changes to Organ Procurement Organization Measures Garner ASN’s Support, with Recommendations for Improvement

By David White

The American Society of Nephrology (ASN) provided comments of support and recommendations for improvement in February 2020 on the proposed rule for Organ Procurement Organizations (OPOs) Conditions for Coverage: Revisions to the Outcome Measure Requirements for Organ Procurement Organizations proposed by the Centers for Medicare & Medicaid Services (CMS). The proposed rule intends to require transparent, verifiable, and uniform metrics by which CMS can evaluate OPO performance.

ASN supported the proposal, writing “[W]ith 115,000 Americans waiting for an organ, ASN supports the proposed rule to establish both transparent, uniform metrics to help assess the performance of each of the 58 OPOs and clear procedures for evaluating those organizations including processes for improvement and re-certification. ASN believes that reforming the current system of OPO performance oversight is necessary to enable the Advancing American Kidney Health goal of doubling the number of kidneys available for transplant by 2030 as well as to approach the proposed target transplant rate described in the ESRD Treatment Choices proposed model and the four tracks of the voluntary model.”

In July 2019, President Donald J. Trump issued the Executive Order 13879 titled Advancing American Kidney Health (1), aspects of which are addressed in the proposed rule. The Executive Order specifically calls on the Secretary of Health and Human Services to “propose a regulation to establish rules. The Executive Order specifically calls on the Secretary of Health and Human Services to “propose a regulation to establish rules for OPO recertification with two new outcome measures that would be used to assess an OPO's performance: “donation rate” and “organ transplantation rate,” effective beginning in 2022. The “donation rate” would be measured as the number of actual deceased donors as a percentage of total inpatient deaths in the donation service area (DSA) among patients 75 years of age or younger with any cause of death that would not be an absolute contraindication to organ donation. The “organ transplantation rate” would be measured as the number of organs procured within the DSA and transplanted as a percentage of total inpatient deaths in the DSA among patients 75 years of age or younger with any cause of death that would not be an absolute contraindication to organ donation (2).

Cause, Age, and Location Consistent (CALC) measure

CMS proposed two methodologies for calculating the denominator in these measures: 1) the Cause, Age, and Location Consistent (CALC) donation measure that uses ICD-10 codes to identify deaths that are consistent with donation (that is, inclusion criteria) and 2) an alternative where CMS would exclude ICD-10 codes that are absolute contraindications to organ donation (that is, exclusion criteria).

ASN supported using the inclusionary CALC metric described in the Proposed Rule, as opposed to the proposed denominator that uses exclusionary diagnosis. Although CMS has shown that the net result in terms of among-OPO comparisons is similar, “the CALC metric has superior face validity, because it restricts the denominator to inpatient deaths from causes that are consistent with donation, rather than the exclusionary measure, which includes causes of death that never lead to donation,” ASN commented.

As lead researcher on the CALC metric David Goldberg, MD, and his colleagues accurately summarize, “compared to the current metric that relies on eligible deaths, the benefits of our proposed donation metric are that it:

- Utilizes a uniform process of estimating the donation potential within each donor service area,
- Includes potential DCD donors that are excluded from the eligible death definition, and
- Provides a reliable year-to-year measure of OPO performance to track changes in performance.” (3)

The researchers also write, “[T]hese conclusions should provide CMS, and the transplant community, with confidence that the proposed CMS metric using CDC inpatient death data as a tool to compare OPO is not compromised by its lack of inclusion of ventilation or other comorbidity data.” (4)

Donation rate numerator (or definition of donor)

ASN encouraged CMS to avoid penalizing OPOs under the scenarios when extensive efforts are made to procure organs for transplant, but ultimately no organs are placed for transplant (so called “zero organ donors”). ASN outlined the following scenario as an example that could occur, and credit for the attempt would be denied if only donors from whom organs are transplanted are considered donors:

1. A deceased (brain-dead or donation after cardiac death) donor is identified that matches a locally available potential recipient.
2. There is preliminary determination of medical suitability, and preliminary offer acceptance by a transplant center.
3. The donor is taken to the operating room, but during organ procurement the transplant surgeon unexpectedly finds an unacceptable situation (such as unsuspected intra-abdominal cancer).
4. The surgeon appropriately cancels use of the organs for transplant.

ASN maintained that the effort and expense to reach this stage is unlikely to lead to “gaming” to obtain credit for donation noting “more aggressive pursuit of higher risk and older donors will likely lead to more identification of medical contraindications at later stages. Aggressive pursuit of donor organs will always be accompanied by some medically appropriate non-utilization.”

Risk adjustment

ASN supported CMS’ decision to not risk adjust based on race, quoting Janice F. Whaley, MPH, CTBS, CPTC, Chief Executive Officer of Donor Network West from the organization’s comment letter to CMS in September 2019 on its proposed rule on “Organ Procurement Organizations Conditions for Coverage: Proposed Revision of the Definition of Expected Donation Rate.”

“As [P]ast-President of the Association for Multicultural Affairs in Transplant (AMAT) and deeply steeped in mi-
ASN believes that reforming the current system of OPO performance oversight is necessary to enable the Advancing American Kidney Health goal of doubling the number of kidneys available for transplant by 2030. . . .

Organ transplantation rates by type of organ
ASN supported reporting outcome measures of organ transplant rates by type of organ. The criteria for qualifying for a transplant not only differ based on transplant center, but also on the type of organ. In reporting these data, ASN suggested that CMS consider how to distinguish the rate of organs transplanted versus those that were expected to be transplanted by organ type as well. This ratio would likely differ based on type of procurement, such as thoracic and abdominal organ procurement; donor management factors prior to procurement as these can affect usability and transplant success; and other factors.

Other regulatory steps to improve access to transplantation are expected this year. Follow Kidney News for more details.

References

Nationwide Campaign Aims to Mobilize Public, Kidney Community to Encourage Early Detection and Management of Kidney Disease

A nation-wide public awareness campaign to promote early detection, treatment, and management of kidney disease is launching in March 2020 in conjunction with National Kidney Month. The campaign, called “Are You the 33%?”, is designed to engage every adult to learn more about their risk for kidney disease by taking a simple, one-minute online quiz at MinuteforYourKidneys.org.

One in three adults in the United States is at risk for kidney disease.

“Look around the next time you’re sitting in a school auditorium or even in a giant professional sports stadium; one-third of every adult in there with you is at risk of developing kidney disease,” said Kevin Longino, CEO of the National Kidney Foundation (NKF) and recipient of a kidney transplant.

Launched by NKF, the campaign is among the first steps in a collaborative partnership among the Department of Health and Human Services (HHS), NKF, and ASN to raise awareness about kidney disease and improve patient outcomes. The Public Awareness Initiative was outlined in the Executive Order on Advancing American Kidney Health, the historic action to transform kidney health signed by President Donald J. Trump in July 2019.

The National Kidney Foundation has entered into strategic alliances with CVS Kidney Care, Healthways and Laboratory Corporation of America in order to carry out the campaign with Otsuka America Pharmaceutical, Inc. serving as a Campaign Sponsor.

In its partnership with HHS and NKF, ASN will fulfill the Public Awareness Initiative outlined in the Executive Order by educating clinical professionals and spurring innovations by entities serving the kidney community. Officially launching in fall 2020, ASN’s campaign will target and inform kidney care professionals about how to succeed in a future where the practice of nephrology includes more home-based therapies and transplantations. In addition, ASN will build off its efforts in 2019 and continue to engage capital markets to dispel myths, encourage prioritizing the kidney space for investment, and advocate that nephrology is open for business.

The public awareness “Are you the 33%?” campaign will include “compelling visuals, a thought-provoking social media campaign, and a broadcast PSA launching later this month with television and film star Wilmer Valderrama, [and will focus] on the 33% of American adults at risk for developing dangerous, life-threatening kidney disease,” according to a press release issued by NKF: “Risk factors include diabetes, heart disease, high blood pressure, obesity and family history of kidney disease.”

The campaign microsite will be available in Spanish starting in September 2020.

“More than 90% of the 37,000,000 Americans and 850,000,000 individuals worldwide affected with kidney disease are unaware that they are even sick,” said Anupam Agarwal, MD, FASN, ASN President. “This silent epidemic often strikes without symptoms. Millions of people won’t know they have kidney disease until their kidneys stop working and it’s too late.”
Preventing Bloodstream Infections in Hemodialysis Patients

By Michele H. Mokrzycki

In 2017, approximately 459,000 patients in the United States received in-center hemodialysis (HD), and more than 108,000 new patients began renal replacement with HD (1). HD catheters were the most common form of vascular access in new patients, accounting for 80% of all accesses. Therefore, more than 86,000 new HD patients began treatment with a catheter in 2017 (1). Among prevalent HD patients, catheter use was lower: approximately 20%. Unfortunately, catheter use in patients receiving both incident and prevalent HD has remained unchanged over the past 6 years.

Patients receiving in-center HD are a unique patient population and are at risk for infections because of the shared treatment setting and frequent accessing of the bloodstream. Catheter-dependent patients are particularly vulnerable because of the potential for direct entry of skin bacteria from the catheter entrance site into the tunnel and bloodstream, and during catheter connection and disconnection. In fact, the rate of bloodstream infection is nine times higher for catheter-dependent HD patients than in those using arteriovenous fistulas (2).

Core interventions for preventing infections in HD

A recently published review, “Prevention of bloodstream infections in patients undergoing hemodialysis” by Fisher et al. (3), in the January 2020 issue of CJASN examines both established and novel strategies available for the prevention of bloodstream infections in patients receiving HD (Figure 1).

The CJASN review highlights the Centers for Disease Control and Prevention’s core interventions for preventing HD catheter infections, which are also available on the CDC’s website. The CDC’s core interventions were initially published in 2013 and were last updated in 2016 (4). An important recent additional recommendation to the updated 2016 CDC core interventions was on the preferred use of chlorhexidine as a skin antiseptic agent for care of the catheter exit site.

Chlorhexidine-alcohol antiseptic solution has been shown to be significantly superior to povidone iodine–alcohol in preventing catheter infections in the intensive care unit. In a 2015 study, patients randomized to the chlorhexidine-alcohol arm experienced an 80% lower rate of catheter-related bloodstream infections than did those in the povidone iodine–alcohol arm (5). The CDC also recommends the use of a topical antimicrobial ointment as an important part of routine care of the HD catheter exit site. Triple antibiotic ointment and povidone-iodine ointment are the recommended antimicrobial agents, and both are associated with marked reductions in bloodstream infections of approximately 75% to 93%. The application of mupirocin to the catheter exit site, although effective, may have the potential for microbial resistance with long-term use, and its routine use is not recommended.

New chlorhexidine-containing products

Chlorhexidine-based products are now widely used in the HD setting. They include chlorhexidine-impregnated sponges (Bisupalch CHG, Johnson and Johnson, Inc.) and dressings (Tegaderm CHG, 3M), which may be alternatives to antimicrobial ointments for routine catheter exit site care. More recently, a novel catheter hub device (ClearGuard HD Antimicrobial Barrier Cap, Pursuit Vascular, Inc.) has been shown to reduce central catheter–associated bloodstream infections in HD patients and was approved by the US Food and Drug Administration in 2018 (6–9). It is designed with a chlorhexidine-coated rod, which provides antiseptic delivery directly into the HD catheter lumen between HD sessions (6–9). Although the upfront costs of these novel products are higher, the long-term projected savings attributable to lower rates of bloodstream infections and hospitalizations may be substantial.

Progress in catheter lock research

Antibiotic catheter locking solutions have been used for prevention of bloodstream infections and are highly effective, achieving a reduction of 50% to 100% in infections. Gentamicin is the most frequently prescribed antibiotic catheter lock; however, a report of gentamicin resistance in one series, which used a relatively high concentration of gentamicin (4 mg/mL) has warranted caution about its routine use (10). More recent studies of gentamicin lock, using lower concentrations (0.32 mg/mL), reported either no change or a decline in gentamicin resistance during long-term follow-up and without loss of efficacy (11, 12).

To avoid the risk of selection for antibiotic-resistant microbes, recent efforts have focused on the development of novel nonantibiotic catheter locking agents, including tissue plasminogen activator, tauradine, ethanol, and sodium bicarbonate. The instillation of tissue plasminogen activator into the catheter lumen as a lock once weekly, in addition to heparin lock twice weekly, has been shown to significantly reduce bloodstream infection rates; however, the immediate costs are a concern and have hindered its routine use (13). Tauradine, which has a low potential for resistance, is widely used as a catheter locking agent in the European Union and is effective for prevention of HD catheter–related bloodstream infections, but it has not yet been approved for use in the United States. A phase 3 trial, the Lock-It 100 study of tauradine-heparin-citrate lock (Neutrolin, CorMedix, Inc.) in the United States, reported a significantly lower rate of catheter-associated bloodstream infec-

Figure 1. Strategies for the prevention of bloodstream infections in patients receiving hemodialysis

Continued on page 12
figure 3. Example of the electronic Chairside Checklist 2020, which is in development by the Nephrologists Transforming Dialysis Safety (NTDS) Vascular Access Workgroup of the American Society of Nephrology and the Centers for Disease Control and Prevention

Dialysis Care Checklist
*Required
Who is observing the procedure?*

- [ ] Technician
- [ ] Nurse
- [ ] Social Worker
- [ ] Dietician
- [ ] Physican
- [ ] PA/APRN

Procedure*

- [ ] Catheter Connection
- [ ] Catheter Disconnection
- [ ] Catheter Exit Site Care
- [ ] Watch Proper Procedure Videos
- [ ] View Checklist Results

References

Michele M. Morley, MD, FASN, is chair of the vascular access committee, Nephrologists Transforming Dialysis Safety Initiative of the American Society of Nephrology, and a professor of medicine at the Montefiore Einstein College of Medicine.
Community-Acquired Acute Kidney Injury in Asia

By Vivek Kumar and Vivekanand Jha

Asia is synonymous with diversity, which is reflected in the epidemiology of kidney diseases, especially acute kidney injury (AKI). In contrast to people in the industrialized developed countries, most Asian people, especially those living in rural areas with relatively limited access to healthcare, continue to bear a large burden of AKI. This condition develops in these communities secondary to locally prevalent health issues of public health importance.

The 0by25 Global Snapshot study by the International Society of Nephrology showed that 80% of the burden of AKI in low- and middle-income countries of Asia is community acquired. Community-acquired AKI (CA-AKI) predominantly affects young, previously healthy individuals who often work outdoors in rural areas and are exposed to a variety of occupational, environmental, or sociocultural risk factors that predispose or lead to the development of AKI. These factors are often the culmination of a complex interplay between geographic, ecological, social, and economic conditions prevalent in those regions. They include exposure to tropical infections like malaria, leptospirosis, dengue, or acute diarrheal illnesses; toxic envenomation after animal or insect bites (e.g., snakebite); the use of unproven traditional or local systems of medicine that frequently include nephrotoxic compounds; delays in seeking appropriate care; and lack of hygiene, sanitation, or an adequate supportive healthcare infrastructure.

This pattern of development for CA-AKI is in striking contrast to that for hospital-acquired AKI, which is seen in developed regions and high-income countries. The usual prototype of a patient at risk of AKI in such regions is an individual with preexisting comorbidities like chronic kidney disease, diabetes, or hypertension who is admitted to the hospital for complications related to chronic disease, or in whom AKI develops after a healthcare intervention like major surgery. The fact that mortality in children with AKI is 55 times higher in low- and middle-income countries than in high-income countries reflects the public health importance of addressing AKI in such settings.

Infections are the leading cause of CA-AKI in Asia. The tropical Asian climate favors the persistence and growth of microbes and disease vectors. Although most countries have undertaken community-based measures to control and prevent tropical infections through national programs and international collaborative efforts, the absolute burden still remains very high. At one end, Sri Lanka and the Maldives have recently declared malaria free, whereas at the other end, southeast Asia still reports the second highest number of malaria cases after Africa.

The epidemiology of infectious diseases has changed in Asia over recent decades, reflecting the changing host–pathogen interactions resulting from habitat destruction, industrialization, climate change, and indiscriminate use of drugs. Examples include the recognition of human Plasmodium knowlesi malaria, previously seen only in Old World monkeys in countries like Malaysia, Cambodia, and Indonesia; the identification of semi-domestic farm animals as maintenance or accidental hosts for leptospirosis in Sri Lanka; the dramatic increases in dengue viral infections; and the reemergence of rickettsial diseases like scrub typhus across India and China. All of these infections can cause AKI.

Other important risks for CA-AKI are animal or insect bites—occupational hazards for those living in rural areas and working outdoors for their livelihood. South Asia and southeast Asia report the highest number of snakebite-related envenomation and deaths in the world. AKI is common in vesiculopapular viper bites. Stinging insects like wasps, hornets, and bees can also cause AKI, especially when a swarm attacks an individual and injects large doses of venom.

Finally, AKI after the consumption of exotic tropical plants continues to be encountered in Asia. The development of acute oxalate nephropathy leading to AKI after star fruit juice consumption is a classic example. Other plants whose consumption has been reported to lead to AKI include Gloriosa superba and Cleistanthus collinus. The unregulated and easy availability of chemicals, insecticides, and pesticides allows their abuse for homicidal or suicidal intent. AKI can develop after the ingestion of copper sulfate, paraziqu, or aluminum phosphate. A lack of healthcare facilities and reliance on unproven traditional or indigenous medicines owing to social or cultural beliefs, frequently expose underprivileged people to local drugs that contain nephrotoxic compounds and heavy metals.

AKI in obstetric patients in the settings of puerperal sepsis, unsupervised pregnancies, unsafe deliveries, or illegal abortions by untrained personnel is still common among young women from poor socioeconomic groups. Acute cervical necrosis is a dreaded complication especially associated with obstetric AKI, which portends poor renal recovery.

Despite the nonmodifiable nature of a few risk factors (e.g., geographic and ecological factors), a vast majority of CA-AKI cases in Asia are potentially preventable. Concerted efforts over three decades in Bangladesh have almost eliminated a mortality rate of 27% that was previously seen with AKI and acute diarrheal illnesses during floods. Such successes underlie the need to adopt public health approaches to the elimination of preventable mortality due to AKI—the mission behind the 0by25 initiative of the International Society of Nephrology. Awareness among the general public, focused social groups, administrative stakeholders, and various healthcare professionals, and collaborative efforts to implement measures for preventing CA-AKI by early identification in the community and timely referral to appropriate healthcare facilities, are keys to improving outcomes.

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Undergoing home dialysis in a shared house with other patients of Māori or Pacific ethnicity without medical supervision provided patients with flexibility and support, and enabled them to overcome obstacles to home dialysis, according to a recent study.

New Zealand, where the study was conducted, has long embraced home dialysis. But not all patients are able to or want to do dialysis at home. To help meet their needs, an initiative launched in 2004 to set up community dialysis homes across the country where patients can go to dialyze on their own schedule. The local kidney societies own the homes and manage their day-to-day operations with help from the patients, explained lead author Rachael Walker, PhD, associate professor of Postgraduate Nursing Programs and a nurse practitioner at the Eastern Institute of Technology in Napier, New Zealand. The primary dialysis provider in the area installs the machines and maintains them.

“It’s a way to provide independent hemodialysis close to the patient’s own home, when otherwise they wouldn’t have access to appropriate housing or utilities that would enable them to do home dialysis,” she said. She explained that renters may not be able to install the necessary plumbing, some individuals may lack the room for the machines or supplies, or the costs may be prohibitive. Additionally, many patients may wish to dialyze away from home to maintain their privacy or reduce their family’s exposure to their care.

Walker described a qualitative interview study with 25 patients of Māori or Pacific ethnicity who use the community dialysis houses. The study, which was published in Kidney Medicine, found that patients said the model reduced the burden on their families and offered freedom and flexibility, control of their health, and community support. “Being able to come whenever you feel like it instead of having to fit into the hospital routine,” was important to one woman in her 40s who participated in the study. “I come whenever it suits me. Those reasons make dialysis a lot more double and livable and part of your life as opposed to attending a dialysis appointment. It makes it feel like it is just one section of your life rather than a hospital taking over your life.”

People who are Māori or other Pacific ethnicities are disproportionately affected by kidney failure. They are also under-represented among the ranks of patients on home dialysis, Walker noted. Yet the study found this model worked well for them.

“The community houses, as well as meeting their cultural preferences, allow the patients to achieve best practice by actually enabling them to have more dialysis hours,” she said. “The majority of the patients were doing over 20 hours of dialysis a week.”

Having more flexibility with timing also allowed more than half of the patients to work, which is often impossible for patients on hospital-based dialysis, noted Walker. Additionally, they found the group environment more supportive, less lonely, and they had fewer concerns about safety. More experienced patients often helped less experienced ones, she said.

“The houses provided more psychosocial support and also allowed them to be able to continue employment, and social, cultural, and community responsibilities and preferences,” Walker said.

Jenny Shen, MD, assistant professor of medicine in the Division of Nephrology at the David Geffen School of Medicine at the University of California–Los Angeles, said community home dialysis...
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Maternal Diabetes Increases Early CVD Risk in Offspring

Children born to mothers with gestational or pregestational diabetes are at increased risk of developing cardiovascular disease (CVD) at follow-up through young adulthood, reports a study in the British Medical Journal.

The prevalence of CVD among children and young adults has increased in recent decades. Rates of pregestational and gestational diabetes have been rising as well; a growing body of evidence suggests that offspring of women with diabetes are at increased risk of metabolic syndrome and congenital heart disease. This population-based study sought to determine the extent to which exposure to maternal diabetes increases the lifetime risk of diabetes in offspring.

The BMJ study used Danish national health registry data on liveborn children without congenital heart disease between 1977 and 2016. The researchers identified three groups of children exposed to maternal diabetes during gestation: type 1 diabetes, 22,055 children (0.9%); type 2 diabetes, 6537 children (0.3%); and gestational diabetes, 26,272 children (1.1%).

Mothers with diabetes were more likely to be older, to have higher education, to have higher parity, to live alone, and to smoke less during pregnancy.

Follow-up data for up to 40 years were analyzed to examine associations between maternal diabetes and early-onset CVD, defined by hospital diagnosis. Analyses included adjustment for potential confounders including calendar year, sex, singleton birth, maternal risk factors, and paternal history of CVD before childbirth. Cumulative incidence of early-onset CVD was averaged across individuals and adjusted for competing causes of death.

During follow-up, CVD was diagnosed in 11,533 offspring whose mothers had diabetes and 91,311 without such exposure: rates per 1000 person-years were 2.02 versus 2.01, respectively. The offspring exposed to maternal diabetes were more likely to have a parental history of CVD and were also at higher risk of developing diabetes, obesity, hypertension, hypercholesterolemia, and chronic kidney disease.

Exposed offspring had a significantly higher overall risk of CVD: hazard ratio (HR) 1.29. The increase in CVD risk was greater for offspring exposed to pregestational diabetes, with a HR 1.34; but remained significant for those exposed to gestational diabetes, HR 1.19.

At age 40, cumulative incidence of CVD was 13.07% in the exposed group versus 4.72% in those not exposed to maternal diabetes. Exposure was associated with increased risk of most types of CVD: HR 1.45 for heart failure, 1.78 for hypertensive disease, 1.82 for deep vein thrombosis, and 1.91 for pulmonary embolism [Yu Y, et al. Maternal diabetes during pregnancy and early onset of cardiovascular disease in offspring: population based cohort study with 40 years of follow-up. BMJ 2019; 367:l6398].

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The most common adverse reactions reported with AURYXIA in clinical trials were:

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DRUG INTERACTIONS: When clinically significant drug interactions are expected, e.g., Ciprofloxacin or Doxycycline, separate timing of administration

To report suspected adverse reactions, contact Akebia Therapeutics, Inc. at 1-844-445-3799

Please see the Brief Summary including patient counseling information on the following page

Approval for First Triple Combination Pill for Type 2 Diabetes

The US Food and Drug Administration (FDA) recently approved a new pill that contains three type 2 diabetes medications: Tijardy XR (extended release). The triple-combination pill is marketed through a partnership of Boehringer Ingelheim and Eli Lilly and includes the following medications:

- the SGLT-2 inhibitor empagliflozin, with the dose to be defined
- the DPP-4 inhibitor linagliptin, and
- metformin hydrochloride extended release formulation (ER).

Empagliflozin (brand name Jardiance), and Linagliptin (Tradjenta) are each manufactured and sold through a partnership between Boehringer Ingelheim (Ridgefield, CT) and Eli Lilly (Indianapolis, IN).

Metformin hydrochloride ER has been available since 1995 in the United States and is sold under brand names (e.g., Glucophage) and generic formulations. It is the most commonly prescribed oral treatment for type 2 diabetes (1).

Multiple medications may be needed to treat type 2 diabetes. The triple combination pill simplifies patient management of their diabetes.

Many adults living with type 2 diabetes who are already on a treatment plan including multiple medications still struggle to keep their blood sugar under control, and may require additional agents to reach their A1C targets, said Ralph DeFronzo, MD. professor and diabetes division chief at University of Texas Health in San Antonio. “Adding new medicines to an individual’s plan can be challenging for some, which is why new treatment options that can help improve blood sugar without the burden of an increased pill count are important….”

Having three different diabetes medications in a single tablet is an important advance in diabetes treatment.”

The side effects list for Tijardy XR incorporates effects of the individual drugs involved, according to a media release from Boehringer Ingelheim. Common side effects include upper respiratory tract infection, urinary tract infections, stuffy or runny nose and sore throat, constipation, headache, and gastroenteritis. Among the serious side effects of the new triple-combination drug are lactic acidosis; pancreatitis; heart failure; a rare but serious bacterial infection of the peritoneum, necrotizing fasciitis; acute kidney injury; serious urinary tract infections; nephrotoxicity; dehydration; and hypoglycemia.
Whether you’re actively seeking new employment, or seeing what opportunities are currently available, ASN provides you the most comprehensive list of positions in kidney medicine and research.

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The Science of Learning: How it Can Help Improve Nephrology Education

“Leveraging the Science of Learning to Elevate Your Teaching” was the topic of an inaugural faculty development workshop for medical educators at Kidney Week 2019. The workshop showcased high-yield strategies to optimize participants’ teaching, enhance the experience of learners, and translate teaching innovations into education scholarship for dissemination and academic credit. Advancing education in nephrology has long been a focus of ASN Past President Mark E. Rosenberg, MD, FASN.

Suzanne Norby, MD, FASN, chair of the ASN Continuous Professional Development Committee, and Melanie Hoenig, MD, developed and moderated the session, which featured a cast of education rock stars and provided an opportunity for participants to brainstorm together and network. Norby is affiliated with the Mayo Clinic College of Medicine and Science Division of Nephrology & Hypertension in Rochester, MN, and Hoenig is affiliated with Beth Israel Deaconess Medical Center in Boston.

Keynote speaker Peter Brown, author of *Make It Stick: The Science of Successful Learning*, shared big ideas, including the role of retrieval in learning. He explained that long-term memory develops from encoding, consolidation, and then retrieval—in other words, “get it out to get it in.” He stressed the effectiveness of low-stakes spaced quizzes and of mixed practice: the process of alternating different topics and skills during the same study session. Although these strategies may take some learners out of their comfort zones, this can be desirable to promote growth, Brown said.

Exploring approaches to unpack the core concepts in teaching kidney physiology was the focus of Joel Michael, PhD, an educator and physiologist from Rush University, who has worked with the National Science Foundation and the American Physiological Society to improve learning in physiology. He noted that different aspects of physiology and pathophysiology are too often taught in silos, making it difficult for learners to absorb material. When different symbols and terminology are used to reflect the same concept, the parallels can be unrecognizable for students, he said. For example, Fick’s Law, Poiseuille’s law, and airflow in airways are all examples of flow-down gradients, but this key concept can be missed by students. Communication among educators is the key to limiting this confusion and facilitating students’ ability to make these connections.

Kris Gorman, an education program specialist from the University of Minnesota’s Center for Educational Innovation, helped the group contemplate metacognition. Metacognition means “thinking about thinking” and is used to consider how to assess cognitive processes and promote higher-order thinking skills. Gorman demonstrated how these strategies may be used both in the classroom and in the clinical arena to encourage learning.

To address the challenge of engaging digital natives and meet their learning needs, David Roberts, MD, dean of external education at Harvard Medical School, spoke about harnessing technology in medical education. He emphasized that good teaching is still about the content: technology is only a tool. When electronic content is created, however, it should be accessible on all platforms, especially by cell phones. He acknowledged that because modern learners are so accustomed to finding instant answers on the internet, they have had fewer opportunities to experience the “productive frustration” that can lead to learning, reinforcing Brown’s point about thoughtfully leading learners out of their comfort zones.

Because the impact of the learning environment should always be considered in the complex system of medical education, Thomas Viggiano, MD, former associate dean of faculty affairs at Mayo Clinic Alix School of Medicine, highlighted the challenges learners face in clinical settings and how these challenges may affect the decision to pursue nephrology. He also offered solutions to common learning environment problems, including creating a positive and supportive climate when teachers work with learners at all levels.

Grace Huang, editor-in-chief of MedEdPortal, noted the importance of educators disseminating their teaching successes and promoting scholarship, including publication in the medical education literature. She said there are a surprising number of journals and sites interested in publishing medical education content.

To conclude the session, Hoenig and Gorman facilitated small-group discussions to stimulate formulation of tangible ways participants can apply concepts from the workshop in their own teaching practices. Participants who shared their ideas will receive an e-mail from Norby and Hoenig asking how they implemented their strategies.

Kidney Education Website Goes “Viral,” Generating Over 60 Million Hits Worldwide

By Karen Blum

About 15 years ago, nephrologist Sanjay Pandya, MD, noticed that his patients were facing difficulties understanding their kidney diseases, including what to eat or not eat, and what other care they needed. He thought that if there were a book that spelled everything out in a single source, it would be useful to his patients, and he could then reduce the amount of time he spent counseling about these topics.

So, in 2006, Pandya, who has a private practice in Gujarati, India, wrote a book, “Save Your Kidneys,” in his native Gujarati language. The 200-page text, given free to patients, contained basic information about kidneys and how they function, advice on how to help prevent kidney disease, information about various kidney diseases and their causes and treatment, and comprehensive information about dialysis and transplantation. The book became so popular that he then thought to prepare a second version translated into Hindi, the national language of India, to make the information accessible to a wider audience. That, too, became popular among patients.

Then he dreamed bigger, and by 2010 had created the nonprofit Kidney Education Foundation and posted the information to a website he established, called KidneyEducation.com. Shortly thereafter, he developed an English version of the information. That’s when things really took off. Tushar Vacharajani, MD, a nephrologist in Cleveland, joined the project as an international liaison officer and, with Pandya, contacted other nephrologists around the globe asking for help.

Within a span of about eight years, they amassed a team of about 100 nephrologists, who together have made the information available in 37 languages, including Italian, Chinese, Spanish, French, Arabic, Russian, Portuguese, German, and Japanese, through KidneyEducation.com. The project has attracted the attention of some notable leaders in the world kidney community, including Giuseppe Remuzzi, a past president of the International Society of Nephrology, who prepared the Italian version of the book and website, and Guillermo Garcia-Garcia, a past president of the International Federation of Kidney Foundations, who prepared the Spanish versions. Books in Chinese were printed and distributed free to patients by Ho Chung Ping in Hong Kong. The educational resource is now available to read online, through the WhatsApp mobile application, and through free book downloads.

The website has been accessed over 60 million times, Pandya said. In 2017, the Golden Book of World Records awarded the foundation a certificate for having an e-book in the most languages.

The number of patients suffering from chronic kidney disease is on the rise, Pandya noted. However, he said, ig-
Creating a New Paradigm in Medical Education: The Nephrology Fellow Guidebook

By Sayna Norouzi

Medicine has become ever more complex. We deal with ever-increasing patient workloads and convoluted medical systems (1). As a result, medical education can sometimes take a back seat in the face of these challenges. Does this sound like a familiar scenario to you? Perhaps it’s time to change the paradigm of medical education.

I am a second-year nephrology fellow with a great passion for teaching. I strongly believe that we as fellows can continue to facilitate change in the medical education paradigm. We are in-house every day, working closely with residents and medical students. We can improve the environment, reform habits, and refine the overall education model; we are the foundation of the future. So, what can we do to facilitate change in the medical education system? Even in a small way.

Develop passion and a progressive mindset about medical education

We need to continually make learning interactive and engaging. The right mindset is the crucible to make changes and improve the medical education system. Even in a short interaction with a trainee about a consult, it is important to endeavor to leave the trainee with a stimulating pearl that can become a topic for future conversation.

Actively involve yourself in medical education and continually refine your teaching skills

Although being passionate about a mission is essential, passion alone is not enough. During my training I have actively worked to develop my teaching skills by delivering lectures to medical students and residents. I have tried to expand my skill sets by learning how to make animated videos, writing short blogs, micro-mentoring, and developing apps and websites. Learning a new skill can sound intimidating, but it can also become a very empowering tool for connecting with trainees.

Use social media as a teaching platform

The medical community on social media (#medtwitter) is growing exponentially. Being part of the #medtwitter family helped me connect with others who have similar interests and goals and led to collaborations with other institutions. As we all know, being active as a physician on social media comes with some rules. To better understand the medical media world, I did a one-year internship as part of the Nephrology Social Media Collective and later joined the executive team. Apply for internships, workshops, and volunteer activities to improve or add to your skill sets. These opportunities will keep you updated and help you have an open mind for new methods of teaching.

“Let the beauty of what you love be what you do”

This quotation is from the great poet Rumi.

Even though the role of educator comes with a lot of responsibilities, being an educator in your institution is a wonderful and fulfilling experience that provides the opportunity to guide and build relationships with trainees. You earn trainees’ trust and respect, which pushes you to stay updated, humble, and resourceful.

 Maintaining a positive and approachable attitude goes a long way. It’s certainly not too hard for a nephrology fellow to have a lovable personality. We can all agree on that, can’t we?

Sayna Norouzi, MD, is a nephrology fellow at the Baylor College of Medicine.

Reference


**Figure 1. Trends in inpatient admission comorbidity and electronic health data: implications for resident workload intensity**

**Background:** There is increasing concern about resident workload compression

**Goal:** Evaluate the following admissions components that impact physician workload:

- EHR data burden
- Patient comorbidities

**Setting:** 15 year retrospective study at a Veterans Affairs Hospital (2000-15)

Clark AV, et al. Aug 2018

Visual Abstract by @WrayCharles

Reprinted with permission from Clark et al. (1). (Visual abstract by @WrayCharles.)
**Findings**

**High Diabetes Rates in Hispanic and Asian Americans**

Hispanic Americans have the highest racial/ethnic prevalence of diabetes, while diabetes prevalence is similar in Asian and black Americans, according to a nationally representative study in *The Journal of the American Medical Association*. The study included data on 7755 US adults aged 20 years or older (mean 47.5) from the National Health and Nutrition Examination Surveys 2011–16. Participants were asked if they had been diagnosed with diabetes by a physician; undiagnosed diabetes was assessed by measurement of hemoglobin A1c, fasting plasma glucose, or 2-hour fasting plasma glucose. Racial/ethnic differences in diabetes prevalence were assessed, including selected subgroups within the Hispanic and Asian populations.

Sixty-five percent of participants were non-Hispanic white, 15% non-Hispanic black, 6% non-Hispanic Asian, and 3% other race/ethnicity. Crude prevalence of diabetes was 14.6% overall, including diagnosed diabetes in 10.0% of participants and undiagnosed diabetes in 4.6%. Another 37.5% of participants had prediabetes. There were significant racial/ethnic variations in age, body mass index, and education.

After adjustment for age and sex, weighted total diabetes prevalence was 12.4% for white adults compared to 22.1% for Hispanic, 20.4% for black, and 19.1% for Asian adults. Within the Hispanic population, total diabetes prevalence was 24.6% for the Mexican, 21.7% for Puerto Rican, 20.5% for Cuban/Dominican, 19.3% for Central American, and 12.3% for South American subgroups. Prevalence was 22.4% for Southeast Asian, 22.3% for South Asian, and 14.0% for East Asian subgroups.

Non-white racial/ethnic groups had higher prevalences of undiagnosed diabetes: 3.9% for white, 5.2% for black, and 7.5% for Hispanic and Asian Americans. A high percentage of cases of undiagnosed diabetes were identified by 2-hour fasting plasma glucose.

Hispanic and Asian individuals now account for 23% of the US population. Both of these racial/ethnic groups have been reported to have a higher prevalence of diabetes compared with European and African populations. The new study of racial/ethnic differences includes current, nationally representative estimates of diabetes prevalence among Hispanic and Asian Americans.

The results suggest that Hispanic Americans have the highest total prevalence of diabetes. Asian and black Americans also have increased diabetes prevalence, compared to their white counterparts.

The study also identifies differences in prevalence among Hispanic and Asian population subgroups. The researchers suggest that racial/ethnic differences in undiagnosed diabetes might be related to underlying physiologic causes [Cheng Y], et al. Prevalence of diabetes by race and ethnicity in the United States, 2011–2016. *JAMA* 2019; 322:2389–2398].

**Treatment for HCV Slows Progression of CKD**

Direct-acting antiviral therapy for hepatitis C virus (HCV) slows the decline in kidney function for patients with chronic kidney disease (CKD), reports a study in *Kidney International*. The retrospective study included 1178 HCV-infected patients who started DAA therapy between 2013 and 2017. All included patients were compliant with DAA treatment, had not undergone organ transplantation or started dialysis, and had available data on baseline cre...


It’s time for kidney talk

When you see unexplained signs of kidney disease, think Alport syndrome. It can filter through a family.

Incurable disease
- Alport syndrome (AS) is a permanent, hereditary condition responsible for a genetically defective basement membrane, causing chronic kidney inflammation, tissue fibrosis, and kidney failure.
- Across the entire range of AS genotypes, patients are at risk of progressing towards end-stage kidney disease (ESKD).

Hidden signs
- Patients often go undiagnosed, as the clinical presentation of AS is highly variable and family history may be unavailable.
- Persistent, microscopic hematuria is the cardinal sign of AS and should prompt immediate diagnostic investigation—particularly when combined with any family history of chronic kidney disease.

Early action
- Expert guidelines published in the Journal of the American Society of Nephrology now recommend genetic testing as the gold standard for diagnosing Alport syndrome.
- Early AS detection via genetic diagnosis, and its ability to guide a patient’s treatment decisions, demonstrates the powerful impact of precision medicine in nephrology.

Reata and Invitae have collaborated to offer no-charge genetic testing for rare chronic kidney disease or contact Invitae client services at clientservices@invitae.com or 800-436-3037.

Abnormal kidney function can have a strong family connection—Alport syndrome

Learn more about Alport syndrome at ReataPharma.com.

Peripheral Artery Disease Increases Adverse Outcomes in CKD

Patients with moderate to severe kidney disease have a higher risk of peripheral artery disease (PAD) with an increased risk of lower-limb complications and other adverse outcomes, reports a study in the American Journal of Kidney Diseases.

The retrospective analysis used administrative data on nearly 454,000 adult residents of Manitoba, Canada, who had at least one serum creatinine measurement between 2007 and 2014. Based on hospital discharge diagnostic codes and medical claims, 4.5% of patients had a diagnosis of PAD. Associations between PAD and CKD were analyzed, including the impact on lower-limb complications, cardiovascular events, and mortality.

Patients with PAD were older (69.0 versus 50.7 years) and more likely to be male (52.4% versus 44.8%). Grade 3 to 5 CKD was present in 30.0% of patients with PAD, compared to 10.1% of the non-PAD group. Rates of grade 5 CKD requiring dialysis were 3.1% versus 0.4%, respectively. Peripheral arterial disease was also associated with high rates of other comorbid conditions, including chronic pulmonary disease, diabetes, and cardiovascular/cerebrovascular disease.

Patients with PAD were at increased risk for all-cause mortality, cardiovascular events, and lower-limb complications, in all eGFR categories. The risk of lower-limb complications was 10 to 12 times higher for patients with grade 5 CKD requiring dialysis, compared to patients with normal kidney function who were free of PAD. Among patients with CKD grade 3 to 5, the hazard ratio for lower-limb complications increased from 2.12 for patients without CKD to 6.61 for those with CKD.

Peripheral artery disease is a common and burdensome complication among patients with CKD—largely related to foot complications. Few studies have examined the prevalence of PAD and associated adverse outcomes among patients with CKD not requiring kidney replacement therapy.

The new findings show a high prevalence of PAD among patients with grade 5 or higher CKD. The presence of PAD in patients with CKD is a "potent risk factor" for lower-limb complications, cardiovascular events, and death. The authors call for trials of screening and treatment strategies to address the "extreme risk" of lower-limb amputation or ulceration in dialysis patients with PAD (Bourrier M, et al. Peri- eral artery disease: its adverse consequences with and without CKD. Am J Kidney Dis 2019; DOI: 10.1053/j. ajkd.2019.08.028).
ASN Communities is the online place to go for members to collaborate, discuss challenging issues, and network with other kidney professionals.

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