Patients with CKD and Diabetes Have High Rates of Cardiac Rhythm Abnormalities

The leading cause of morbidity and mortality in patients with chronic kidney disease (CKD) is cardiovascular disease. Patients with CKD are also at increased risk of cardiac rhythm abnormalities including atrial fibrillation and ventricular arrhythmias compared with the general population. Cardiac rhythm abnormalities lead to poor clinical outcomes, including higher rates of death and sudden cardiac death. Identification of preclinical cardiac arrhythmias may provide opportunities for early therapy to improve the poor outcomes in patients with CKD.

Nazem Akoum, MD, and colleagues recently conducted a prospective observational study utilizing mobile cardiac telemetry monitors to study the rate of cardiac rhythm abnormalities. The study cohort included patients with moderate-to-severe CKD (estimated glomerular filtration rate 15 to 60 mL/min/1.73 m² not requiring dialysis) and type 2 diabetes. The researchers sought to test the hypothesis that, as in the dialysis population, rates of preclinical cardiac arrhythmias would be high in the study cohort. Results were reported in the *Clinical Journal of the American Society of Nephrology* [2019;14(4):549-556].

The observational study CANDY (Continuous Glucose Monitoring to Assess Glycemia in CKD) was conducted.

CREDENCE Trial: Canagliflozin Improved Renal Outcomes in Patients with Type 2 Diabetes

The substantial increase in the prevalence of end-stage renal disease worldwide is accounted for, in part, by the increasing prevalence of type 2 diabetes. It is estimated that more than 3 million people are being treated for kidney failure worldwide, a number that is expected to increase to more than 5 million by 2035. Currently renin-angiotensin system blockade is the only approved treatment for renoprotection in patients with type 2 diabetes.

In previous trials of inhibitors of sodium-glucose cotransporter 2 (SGLT2),...

Cognitive Impairment Influences Likelihood for Transplant Listing

Patients with end-stage renal disease (ESRD) on dialysis and patients who have received a kidney transplant may experience cognitive impairment, negatively affecting activities of daily living, quality of life, regimen adherence, healthcare costs, morbidity, and mortality. The treatment of choice for ESRD is kidney transplantation, which is associated with improved survival and quality of life.

Patients seeking to be put on the transplant list must undergo an evaluation process that includes multiple tests and clinic visits. Cognitive impairment can influence physicians’ perceptions and patients’ ability to complete the pretransplant evaluation. There are few data available on the association of eligibility for kidney transplant and cognition. Early detection of cognitive impairment can identify patients needing additional support or more detailed instructions as they work through the evaluation process.

Aditi Gupta, MD, and colleagues conducted a single-center longitudinal cohort study to examine how cognitive impairment is associated with the likelihood of being listed and time to listing for kidney transplant. Results of the study were reported in the *Clinical Journal of the American Society of Nephrology* [2019;14(4):S67-S75].

At the initial visit for evaluation for kidney transplant, the Montreal Cognitive
Updated KDIGO guidelines recommend limiting the use of calcium-based binders...

SWITCHING TO VELPHORO CAN MAKE A WORLD OF DIFFERENCE

**INDICATION**
Velphoro® (sucroferric oxyhydroxide) is a phosphate binder indicated for the control of serum phosphorus levels in patients with chronic kidney disease on dialysis.

**IMPORTANT SAFETY INFORMATION**
- Velphoro chewable tablets must be administered with meals. Velphoro should be chewed or crushed. Do not swallow whole.
- Patients with peritonitis during peritoneal dialysis, significant gastric or hepatic disorders, following major gastrointestinal (GI) surgery, or with a history of hemochromatosis or other diseases with iron accumulation have not been included in clinical studies with Velphoro. Monitor effect and iron homeostasis in such patients.
- In a parallel design, fixed-dose study of 6 weeks duration, the most common adverse drug reactions to Velphoro chewable tablets in hemodialysis patients included discolored feces (12%) and diarrhea (8%).

**SWITCHING TO VELPHORO**

- Velphoro can be administered concomitantly with oral calcitriol, ciprofloxacin, digoxin, enalapril, furosemide, HMG-CoA reductase inhibitors, hydrochlorothiazide, losartan, metoprolol, nifedipine, omeprazole, quinidine and warfarin. For oral medications where a reduction of bioavailability would be clinically significant consider separating the timing of administration. Consider monitoring clinical responses or blood levels of the concomitant medications.

Please see Brief Summary on adjacent page or visit www.Velphoro.com for full Prescribing Information.

* A retrospective analysis of pharmacy data assessed the real-world effectiveness of Velphoro in 1,029 adult in-center hemodialysis patients who were switched to Velphoro during routine care. The study compared the proportion of patients with phosphorus levels ≤5.5 mg/dL and the mean prescribed phosphate binder pills/day at baseline (3 months prior to Velphoro; binders included sevelamer carbonate, calcium acetate, and lanthanum carbonate) and during Velphoro follow-up (6 months after switch to Velphoro, n=424). This was a noninterventional analysis and did not impact prescriptions or prescribing patterns.


Velphoro is a registered trademark of Vifor Fresenius Medical Care Renal Pharma Ltd.
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Waltham, MA 02451

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**INDICATIONS AND USAGE**

Velphoro (sucroferric oxyhydroxide) is a phosphate binder indicated for the control of serum phosphorus levels in patients with chronic kidney disease on dialysis.

**DOSE AND ADMINISTRATION**

Velphoro tablets must be chewed and not swallowed whole. To aid with chewing and swallowing, tablets may be crushed.

The recommended starting dose of Velphoro is 3 tablets (1,500 mg) per day, administered as 1 tablet (500 mg) 3 times daily with meals. Adjust by 1 tablet per day as needed until an acceptable serum phosphorus level is reached, with regular monitoring afterwards. Titrate as often as weekly.

**DOSE FORMS AND STRENGTHS**

Velphoro (sucroferric oxyhydroxide) chewable tablet 500 mg.

**CONTRAINDICATIONS**

None.

**WARNINGS AND PRECAUTIONS**

Patients with peritonitis during peritoneal dialysis, significant gastric or hepatic disorders, following major gastrointestinal surgery, or with a history of hemorrhochromatosis or other diseases with iron accumulation have not been included in clinical studies with Velphoro. Monitor effect and iron homeostasis in such patients.

**ADVERSE REACTIONS**

In a parallel design, fixed-dose study of 6 weeks duration, the most common adverse drug reactions to Velphoro chewable tablets in hemodialysis patients included discolored feces (12%) and diarrhea (6%).

The following adverse reactions were identified during post approval use of Velphoro and were reported voluntarily from a population of uncertain size.

Gastrointestinal Disorders: tooth discoloration

Skin and Subcutaneous Tissue Disorder: rash

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Medical Care North America at 1-800-323-5188 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

**DRUG INTERACTIONS**

Velphoro can be administered concomitantly with oral calcitriol, ciprofloxacin, digoxin, enalapril, furosemide, HMG-CoA reductase inhibitors, hydrochlorothiazide, losartan, metoprolol, nifedipine, omeprazole, quinidine and warfarin.

Velphoro can be administered concomitantly with oral calcitriol, ciprofloxacin, digoxin, enalapril, furosemide, HMG-CoA reductase inhibitors, hydrochlorothiazide, losartan, metoprolol, nifedipine, omeprazole, quinidine and warfarin.

Take acetylsalicylic acid, cephalexin and doxycycline at least 1 hour before Velphoro.

Take levethyroxcine at least 4 hours before Velphoro.

Take levethyroxcine at least 4 hours before Velphoro.

For oral medications not listed above where a reduction of bioavailability would be clinically significant consider separation of the timing of administration. Consider monitoring clinical responses or blood levels of the concomitant medication.

**USE IN SPECIFIC POPULATIONS**

**Pregnancy**

Pregnancy Category B: Reproduction studies have been performed in rats and rabbits at doses up to 16 and 4 times, respectively, the human maximum recommended clinical dose on a body weight basis, and have not revealed evidence of impaired fertility or harm to the fetus due to Velphoro. However, Velphoro at a dose up to 16 times the maximum clinical dose was associated with an increase in post-implantation loss in pregnant rats. Animal reproduction studies are not always predictive of human response.

There are no adequate and well-controlled studies in pregnant women.

**Labor and Delivery**

No Velphoro treatment-related effects on labor and delivery were seen in animal studies with doses up to 16 times the maximum recommended clinical dose on a body weight basis. The effects of Velphoro on labor and delivery in humans are not known.

**Nursing Mothers**

Since the absorption of iron from Velphoro is minimal, excretion of Velphoro in breast milk is unlikely.

**Pediatric Use**

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

**Geriatric Use**

Of the total number of subjects in two active-controlled clinical studies of Velphoro (N=835), 29.7% (n=248) were 65 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects.

**OVERDOSAGE**

There are no reports of overdosage with Velphoro in patients. Since the absorption of iron from Velphoro is low, the risk of systemic iron toxicity is low. Hypophosphatemia should be treated by standard clinical practice.

Velphoro has been studied in doses up to 3,000 mg per day.

**HOW SUPPLIED/STORAGE AND HANDLING**

Velphoro are chewable tablets supplied as brown, circular, bi-planar tablets, embossed with “PA 500” on 1 side. Each tablet of Velphoro contains 500 mg iron as sucroferric oxyhydroxide. Velphoro tablets are packaged as follows:

NDC 4950-645-51 Bottle of 90 chewable tablets

**Storage**

Keep the bottle tightly closed in order to protect from moisture.

Store at 25°C (77°F) with excursions permitted to 15 to 30°C (59 to 86°F).

**PATIENT COUNSELING INFORMATION**

Inform patients that Velphoro tablets should be chewed or crushed. Do not swallow whole [see Dosage and Administration]. Velphoro tablets should be taken with meals.

Instruct patients on concomitant medications that should be dosed apart from Velphoro [see Drug Interactions].

Inform patients that Velphoro can cause discolored (black) stool, but this discoloration of the stool is considered normal with oral medications containing iron.

Inform patients that Velphoro can stain teeth.

Inform patients to report any rash to their healthcare professional.

Distributed by:

Fresenius Medical Care North America
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Waltham, MA 02451

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From the Chair

Time for a Dialysis Moon Shot

Two articles—in February 2019 by Mahesh Krishnan and Kent Thiry1 and by Ron Shinkman in June 20162—both published as New England Journal of Medicine Catalyst essays, coupled with a powerful critique in 2010 by Robin Fields in the Atlantic3, discuss the current state of dialysis care in the United States. Krishnan and Thiry, both senior leaders at DaVita, argue that innovation is alive in dialysis care and that much progress has been made. In contrast, Shinkman and Fields both make the case that low quality care and poor outcomes are commonplace and that dialysis is broken.

Krishnan and Thiry cite implementation science as a form of innovation that has produced results: “Dialysis care also has improved significantly over the past century through implementation science, providing dialysis patients with broader access to care, improved outcomes, and a better overall experience.” They point to a reduction in mortality as evidence that the current system is working.

In her article in the Atlantic2 titled “God Help You. You’re on Dialysis,” Robin Fields writes: “Yet the United States continues to have one of the industrialized world’s highest mortality rates for dialysis care. Even taking into account differences in patient characteristics, studies suggest that if our system performed as well as Italy’s or France’s, or Japan’s, thousands fewer kidney patients would die each year.” Fields provides examples of poor quality of care in dialysis facilities and makes a powerful case for the system being broken.

A speech by Alex M. Azar II, secretary of the Department of Health and Human Services (HHS), in March 2019 at the 6th Annual National Kidney Foundation (NKF) Kidney Patient Summit4 pushes for reform. Secretary Azar says that dialysis care does lack innovation. Coming from the US Government, his statement is striking. He points to incentives currently in place supporting the status quo, and says that HHS will aim to prioritize reform in Medicare reimbursement in order to incentivize more treatment options and greater innovation.

Changes in dialysis care and reimbursement are long overdue. In addition to the views of patients and families reported in the media, nephrologists like myself see that dialysis care needs reform. The steep cost of treatment (Medicare’s cost of treatment each year for just dialysis care is about $34 billion) has not been matched by improvements in the quality of life of patients on dialysis, nor by the development of new treatments. Krishnan and Thiry can argue that innovation in developing new devices has been constrained by regulation, but the fact is that very little has changed in dialysis care over the past two decades. This is amid healthy profits for large dialysis organizations that care for the majority of dialysis patients—just look at the balance sheet of DaVita or Fresenius.

Over the past few decades, the nephrology community has not been standing still. The National Institutes of Health has invested millions of dollars to fund both mechanistic studies and trials evaluating the effects of various interventions. Companies have developed new medicines. Dialysis companies have improved processes, including greater integration of care. The American Society of Nephrology has stepped in to develop synergies by launching the Kidney Health Initiative. And, the NKF has continued to push educational initiatives. All of this is laudable. Still, progress has been slow.

What the dialysis world needs is a “shot in the arm.” It needs the equivalent of the Cancer Moonshot, a $1.8 billion dollar initiative approved in December 2016 to find a cure for cancer. The Dialysis Moonshot could focus on strategies to improve the quality of life and clinical outcomes in dialysis patients. A focused effort that is well funded could make the difference. A blue ribbon panel could develop a list of priorities for the Dialysis Moonshot. Given the large cost of dialysis care, a $2 billion investment is a relatively small price to pay for future large benefits.

The fact is that we need a Dialysis Moonshot because current approaches are not working. Many therapeutic interventions that seem to be efficacious in nondialysis patients don’t seem to be effective in dialysis patients. Take, for example, the use of statins in dialysis patients. Despite cardiovascular events being the leading cause of death in dialysis patients, statins, which have been proven to be effective in nondialysis CKD patients and those with normal kidney function, do not seem to be effective in dialysis patients. Correcting anemia with erythropoietin, repairing abnormalities in metabolic bone disease parameters, and treating hypertension are all also challenging in dialysis patients.

New approaches are needed. As Albert Einstein is quoted as saying: “The definition of insanity is doing the same thing over and over again, but expecting different results.”

REFERENCES
agents developed to lower blood glucose levels in patients with type 2 diabetes, researchers found reductions in cardiovascular events with SGLT2 inhibitors. Secondary analyses suggested that there might be improvement in renal outcomes with SGLT2 inhibition.

The CREDENCE (Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation) trial was designed to examine the effects of the SGLT2 inhibitor canagliflozin on renal outcomes in patients with type 2 diabetes and albuminuric chronic kidney disease (CKD). Vladko Perkovic, MBBS, PhD, and colleagues reported results of the CREDENCE trial online in the New England Journal of Medicine [doi:10.1056/NEJMo1811744].

In this double-blind, randomized trial, patients with type 2 diabetes and albuminuric CKD were assigned to either canagliflozin 100 mg daily or placebo. All patients had estimated glomerular filtration rate (eGFR) of 30 to <90 mL/min/1.73 m² and albuminuria, defined as ratio of albumin (mg) to creatinine (g), >300 to 5000. The primary outcome of interest was a composite of end-stage renal disease (ESRD), defined as dialysis, transplantation, or sustained eGFR of <15 mL/min/1.73 m²; a doubling of serum creatinine level; or death from renal or cardiovascular causes.

Secondary outcomes were prespecified for sequential hierarchical testing: (1) composite of cardiovascular death or hospitalization for heart failure; (2) composite of cardiovascular death, myocardial infarction (MI), or stroke; (3) hospitalization for heart failure; (4) composite of ESRD, doubling of the serum creatinine level, or renal death; (5) cardiovascular death; (6) death from any cause; and (7) composite of cardiovascular death, MI, or hospitalization for heart failure or for unstable angina. All other efficacy outcomes were exploratory.

A total of 12,900 patients were screened from March 2014 through May 2017. Of those, 4401 underwent randomization at 690 sites in 34 countries. The two groups were similar in baseline characteristics: mean age was 63 years, 33.9% were women, mean glycated hemoglobin value was 690 sites in 34 countries. The two groups were similar in baseline characteristics: mean age was 63 years, 33.9% were women, mean glycated hemoglobin value was 6.6% and the median urinary albumin-to-creatinine ratio was 927.

By July 2018, the requisite number of primary outcome events to trigger the interim analysis were accrued. The data monitoring committee advised the CREDENCE steering committee members that the prespecified efficacy criteria for early cessation had been reached and recommended that the trial be stopped. Patients were recalled for final visits and the trial was concluded. At trial conclusion at a median follow-up of 2.62 years, 27.3% (n=1201) of patients in the two groups had discontinued therapy. During follow-up, trial adherence rate was 84%.

In the canagliflozin group, the event rate of the primary composite outcome of ESRD, doubling of serum creatinine level, or renal or cardiovascular death was significantly lower than in the placebo group: 4.2 per 1000 patient-years versus 6.2 per 1000 patient-years, respectively. The relative risk in the canagliflozin group was 30% lower than in the placebo group: hazard ratio (HR), 0.70; 95% confidence interval (CI), 0.59-0.82; P<.0001. Across regions and other prespecified groups, the effects were consistent, as they were for the components of ESRD (HR, 0.68; 95% CI, 0.54-0.86; P=.002).

The effects were also consistent across renal components: doubling of serum creatinine level, HR, 0.69; 95% CI, 0.57-0.83; P<.001 and the exploratory outcome of dialysis, kidney transplantation, or renal death, HR, 0.72; 95% CI, 0.54-0.97. Results were nearly identical in sensitivity analyses that included imputation of missing data (HR, 0.69; 95% CI, 0.59-0.82) or after adjustment for competing risks (HR, 0.70; 95% CI, 0.59-0.82).

When the secondary outcomes were tested in a hierarchical fashion, patients in the canagliflozin group also had a lower risk of several of prespecified outcomes, including composites of cardiovascular death or hospitalization for heart failure (HR, 0.69; 95% CI, 0.57-0.83; P<.001), cardiovascular death, MI, or stroke (HR, 0.80; 95% CI, 0.67-0.95; P=.01), and hospitalization for heart failure (HR, 0.61; 95% CI, 0.47-0.80; P=.001). In the canagliflozin group, the relative risk of the composite of ESRD, doubling of serum creatinine, or renal death was lower by 34% (HR, 0.66; 95% CI, 0.53-0.81; P<.001).

There were no significant differences between the two groups in the risk of cardiovascular death. The differences in all subsequent outcomes in the hierarchical testing sequence were not formally tested. The rates of adverse events and serious adverse events were similar overall in the two groups. There were no significant differences in the risk of lower limb amputation: 12.3 per 1000 patient-years in the canagliflozin group versus 11.2 per 1000 patient-years in the placebo group (HR, 1.11; 95% CI, 0.79-1.56). The rates of fracture were also similar in the two groups (HR, 0.98; 95% CI, 0.70-1.37). The rates of diabetic ketoacidosis were low overall, but higher in the canagliflozin group compared with the placebo group (2.2 per 1000 patient-years vs 0.2 per 1000 patient-years).

The researchers cited some limitations to the study, including stopping the trial early at a planned interim analysis, not measuring off-treatment eGFR levels in patients who had completed the trial, and excluding patients with very advanced kidney disease (eGFR <30 mL/min/1.73 m²). The researchers said, “In conclusion, among patients with type 2 diabetes and kidney disease, those in the canagliflozin group had a lower risk of kidney failure and cardiovascular events than those in the placebo group at a median follow-up of 2.62 years.”

TAKENAWAY POINTS

- The CREDENCE trial was designed to examine the effects of the sodium-glucose co-transporter 2 (SGLT2) inhibitor canagliflozin on renal outcomes in patients with type 2 diabetes and albuminuric chronic kidney disease.
- The primary outcome of interest was a composite of end-stage renal disease, a doubling of serum creatinine level or death from renal or cardiovascular causes.
- At a median follow-up of 2.62 years, the relative risk among patients in the canagliflozin group for the primary outcome was 30% lower than in the placebo group. There were no significant differences in the rates of amputation or fracture between the two groups.
Patients with CKD and diabetes continued from page 1

at the University of Washington. Participants were patients with type 2 diabetes mellitus and CKD. The arrhythmia study was a substudy of the CANDY study. Participants were offered mobile cardiac telemetry monitoring with the SEEQ device (SEEQ; Medtronic, Inc., Minneapolis, Minnesota) for a minimum of 7 days and up to 28 days. The SEEQ monitor is a patch that attaches to the patient’s pectoral area and provides a single-lead electrocardiogram recording.

Among the 38 substudy participants, 18 unique participants (47%) experienced 104 arrhythmic episodes. The overall rate of any cardiac arrhythmic episode in patients with CKD was 88.8 (95% confidence interval, 27.1-184.6) episodes per person-year.

Of the 81 patients with CKD in the CANDY study, 68 were approached to participate in the substudy. Of those, 56% (n=38) agreed to wear the SEEQ device and participate in the arrhythmia study, with no loss to follow-up. Of the 38 patients who agreed to participate, 50% (n=19) wore the SEEQ device for one monitoring period (mean, 13 days), 47% (n=18) for two monitoring periods (mean 14.1 days), and 3% (n=1) for three monitoring periods (22 days). Mean duration of overall monitoring per patient was 11.2 days.

Mean age of study participants was 68 years, 66% were men, and 84% were white. A total of 39% had a history of cardiovascular disease; heart failure was the most common type of cardiovascular disease. Seventy-one percent were obese, and mean estimated glomerular filtration rate was 38 mL/min/1.73 m². Ninety-two percent were taking antihypertensive medications: 76% were taking angiotensin-converting enzyme inhibitors/angiotensin receptor blockers and 55% were taking beta-blockers. Eighty-nine percent were on insulin, either alone or in combination with another oral hypoglycemic. Eleven percent were also taking thyroid supplementation.

Among the 38 substudy participants, 18 unique participants (47%) experienced 104 arrhythmic episodes. The overall rate of any cardiac arrhythmic episode in patients with CKD was 88.8 (95% confidence interval, 27.1-184.6) episodes per person-year. Atrial fibrillation and conduction abnormalities occurred at the highest rates. The rate of occurrence of conduction abnormalities was 26.5 per person-year (31 episodes among eight individuals). Second-degree atrioventricular block had the most episodes, but was limited to one participant. Compared with other cardiac arrhythmias, the lowest rate was seen in ventricular arrhythmias: there were 17 episodes of ventricular arrhythmias in nine unique individuals (24%). Premature ventricular complexes were the most common types of ventricular arrhythmias.

There were significant associations between age ≥65 years, body mass index ≥30 kg/m², use of beta-blocker/non-dihydropyridine (DHP) calcium channel blocker, and prior history of cardiovascular disease (coronary disease, heart failure, or stroke) and greater rates of cardiac arrhythmias of any type. Seven of the 58 participants had a previous diagnosis of atrial fibrillation (AF); of the remaining 31 participants, four (13%) received a new diagnosis of AF. Overall, there were 44 individual episodes of AF with a rate of 37.6 per person-year. There were no symptoms reported during any of the 44 AF episodes, and the duration of most of the episodes was between 5 minutes and 1 hour (59%), followed by 1 to 6 hours (38%) and >6 hours (2.7%).

Of the total cohort of 58 participants, 15 had known cardiovascular disease. Compared with the 23 patients without known cardiovascular disease, there appeared to be a trend toward higher rates of any arrhythmia overall and by subtype in the 15 participants with known cardiovascular disease. There also seemed to be a trend for a large variation in rate of AF and conduction abnormalities between the group with known cardiovascular disease and the group without known cardiovascular disease. Due to limited power, those analyses were exploratory.

Twenty-three participants (61%) were taking either beta-blockers or non-DHP calcium channel blockers. In analyses stratified by use of those agents, there appeared to be a trend toward higher rates of all arrhythmia types in the group taking either agent. The variation between the group taking the agents and the group not taking the agents appeared largest for risk of AF and conduction abnormalities.

The small sample size was among the limitations cited by the researchers. Others were only including participants with type 2 diabetes, lack of data on long-term outcomes, and lack of a control group.

The researchers said, “In conclusion, in this study of participants with moderate CKD and type 2 diabetes, we found subclinical cardiac arrhythmias to be common, as nearly half of the participants experienced cardiac arrhythmias detected by mobile cardiac telemetry. Subclinical cardiac arrhythmias may be important precursors to clinically significant cardiovascular events, including sudden cardiac death. Further data are needed to determine whether treatment of subclinical cardiac arrhythmias reduce cardiovascular complications and improve overall survival in this high-risk CKD population.”
Assessment (MoCA) was used to screen patients with ESRD for cognitive impairment. Patients were followed longitudinally for transplant eligibility, performed as a quality improvement project.

Exclusion criteria were any hearing or visual impairment that precluded taking the MoCA, inability to read, write, speak, or understand English, a previous chart diagnosis of dementia or mental retardation, or uncontrolled psychosis or active seizure disorder.

A total of 349 patients had MoCA assessment at the first visit and were included in the current analysis. Of those, 55% (n=193) had cognitive impairment (MoCA score ≤26). Mean age of the total cohort was 54 years, 42% (n=147) were men, and 73% (n=254) were white.

The patients were stratified into three groups based on their MoCA scores: severe cognitive impairment, MoCA ≤18 (n=21); mild-to-moderate cognitive impairment, MoCA 19-25 (n=172); and no cognitive impairment, MoCA ≥26 (n=156). There were differences in age, race, and history of smoking between those with no cognitive impairment and those with cognitive impairment. Those with cognitive impairment were older (62 and 55 years versus 51 years of age). Median time to active listing was higher for those with cognitive impairment in that age group with the exception of patients <50 years of age. Median time to active listing was longer for patients with cognitive impairment than for those with no cognitive impairment in that age group (10.6 months vs 6.3 months). Patients with cognitive impairment were declared ineligible sooner than those without cognitive impairment (8.6 months vs 15.4 months).

In the Cox proportional hazards model, MoCA score, sex, race, smoking, and diabetes were significant covariates associated with time to listing. There was an association between lower MoCA score and lower chances of active listing. Older patients and women also had a lower likelihood of listing.

By the end of 1 year after the initial pretransplant evaluation, 23.3% of patients with cognitive impairment were listed for transplant or had received a transplant, compared with 41% of patients with no cognitive impairment. Further, 43% of patients with cognitive impairment were declared ineligible or removed from the waitlist, compared with 32% of those with no cognitive impairment. There were no differences between patients who were declared ineligible within a month of the initial evaluation and those who were declared ineligible after a month, with the exception of a shorter time on dialysis for patients with mild-to-moderate cognitive impairment who were declared ineligible within a month (P<.01).

Study limitations cited by the authors included limiting the definition of cognitive impairment to results of the MoCA screening test rather than a detailed assessment of cognition with multiple neuropsychologic tests; using chart review to obtain medical history; and the single-center design of the study.

“In conclusion, cognitive impairment is common in patients presenting for transplant evaluation. Increasing age, history of smoking, and nonwhite race/ethnicity are associated with pretransplant cognitive impairment. Pretransplant cognition is associated with transplant eligibility. Cognitive impairment is associated with a lower likelihood of being listed for kidney transplant, and it is associated with a longer time to listing. Additional understanding of the reasons why cognitive impairment influences time to listing may improve transplant eligibility,” the researchers said.

There were differences in age, race, and history of smoking between those with no cognitive impairment and those with cognitive impairment.

Results of Kaplan-Meier analysis found that patients with higher MoCA scores were listed earlier; there was clear delineation between the three subgroups. When divided further by age and MoCA score, it took longer for active listing for patients with cognitive impairment than for those with no cognitive impairment in that age group with the exception of patients <50 years of age.

In the Cox proportional hazards model, MoCA score, sex, race, smoking, and diabetes were significant covariates associated with time to listing. There was an association between lower MoCA score and lower chances of active listing. Older patients and women also had a lower likelihood of listing.

By the end of 1 year after the initial pretransplant evaluation, 23.3% of patients with cognitive impairment were listed for transplant or had received a transplant, compared with 41% of patients with no cognitive impairment. Further, 43% of patients with cognitive impairment were declared ineligible or removed from the waitlist, compared with 32% of those with no cognitive impairment. There were no differences between patients who were declared ineligible within a month of the initial evaluation and those who were declared ineligible after a month, with the exception of a shorter time on dialysis for patients with mild-to-moderate cognitive impairment who were declared ineligible within a month (P<.01).

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“In conclusion, cognitive impairment is common in patients presenting for transplant evaluation. Increasing age, history of smoking, and nonwhite race/ethnicity are associated with pretransplant cognitive impairment. Pretransplant cognition is associated with transplant eligibility. Cognitive impairment is associated with a lower likelihood of being listed for kidney transplant, and it is associated with a longer time to listing. Additional understanding of the reasons why cognitive impairment influences time to listing may improve transplant eligibility,” the researchers said.
The National Kidney Foundation’s Spring Clinical Meetings 2019 were held in Boston in May. The meetings provided renal healthcare providers with the latest developments in all aspects of nephrology. Attendees included nephrologists in the private sector and academia, fellows and residents with interest in kidney disease, general internists, pharmacists, physician assistants, nurse practitioners, nurses and technicians, social workers, and renal and clinical dietitians.
Awareness of Proteinuria in the Community Setting: KDSAP Results

Boston—The Kidney Disease Screening and Awareness Program (KDSAP), working to increase early detection and improve awareness of kidney disease, provides free screening and education in the community setting. Proteinuria is an independent predictor of adverse clinical outcomes, yet due to the asymptomatic nature of proteinuria, early recognition is difficult; most individuals with proteinuria are not aware they have this condition.

Researchers, led by Min Zhuo, MD, collected and analyzed KDSAP data from October 2011 to May 2018. Two questions were used to assess awareness of proteinuria: [1] Have you ever had protein in the urine? and [2] Do you have kidney disease? Proteinuria awareness was defined as participants with trace or more protein on urine dipstick who answered yes to either of the two questions. Results of the analysis were reported during a poster session at the NKF Spring Clinical Meetings in a poster titled Degree of Proteinuria and Hematuria, as well as Ethnicity Are the Factors Predicting Awareness of Proteinuria in the Community: Results from Kidney Disease Screening and Awareness Program (KDSAP).

Of the 2432 KDSAP participants, 20% (n=461) had proteinuria. The overall awareness of proteinuria was 15.8% (n=46). Participants who were unaware of proteinuria were younger, more likely to be African American, have less self-reported family history of kidney disease and comorbidities, less microscopic hematuria, and milder proteinuria. There was an association between those with mild proteinuria [defined as tract or +1 proteinuria] and lower awareness [adjusted odds ratio [OR] 2.14: 95% confidence interval [CI] 1.11–4.18]. There was an association between African American race and less awareness of proteinuria [adjusted OR, 0.28: 95% CI, 0.10–0.69]. “Most KDSAP participants with proteinuria were unaware of the condition. Milder proteinuria, absence of microscopic hematuria, and African American [race] were associated with low proteinuria awareness,” the researchers said.

Source: Zhuo M, Song E, Moti S, et al. Degree of proteinuria and hematuria, as well as ethnicity are the factors predicting awareness of proteinuria in the community: Results from Kidney Disease Screening and Awareness Program (KDSAP). Abstract of a poster presented at the National Kidney Foundation 2019 Spring Clinical Meetings, May 8–12, 2019, Boston, Massachusetts.

Access to Care for Hemodialysis Patients During Natural Disasters

Boston—Among patients dependent on renal replacement therapy, the effects of missed treatments are severe, making access to care for in-center hemodialysis patients critical during and after a natural disaster. Stephanie Batresch (United Kingdom) and Vijay Lapsia, MD, [United States] conducted a review of existing literature to examine the state of the art in managing care of dialysis patients in the peri-disaster period. They reported results of the search during a poster session at the NKF Spring Clinical Meetings in a poster titled Present-Day Gaps in Emergency Preparedness for Dialysis Patients.

The search utilized the keywords hemodialysis, emergency preparedness, and disaster on PubMed. An internet search engine was used to gather additional relevant information. The researchers conducted the systematic review to grade each publication for relevance; key points were summarized.

Of the 50 studies identified in the initial search, 20 were directly relevant. More than one study concluded that visits to emergency departments increased following a natural disaster. Geriatric patients were particularly at risk of poor outcomes. One study cited limited accessibility of paper copies of emergency plans as a concern. Another concern was lack of availability of medical records, leading to confusion and the possibility of sub-optimal care. Another study demonstrated that in nephrology communities in areas not affected by the disaster, resources were typically overwhelmed.

Early restoration of electric and water lifelines was critical. A possible solution in disaster prone areas was increasing utilization of peritoneal dialysis. Results of a survey study found that dialysis patients who had informational social support from family or friends were better prepared for natural disasters.

“Present-day systems for dialysis patients during a natural disaster present many risks and gaps in healthcare, cause overcrowding in the emergency department after a disaster, prevent healthcare staff from giving proper care, increase mortality and morbidity, and overall worsen health conditions for patients. Scientific literature is very limited and the subject of emergency preparedness for dialysis patients needs to be studied in depth and issues related to resource accessibility and delivery in the peri-disaster period better understood.”


AKI Incidence in Patients Undergoing Total Hip Arthroplasty

Boston—Worldwide, the number of total hip arthroplasties being performed is increasing rapidly. Sohail Abdul Salim, MD, and colleagues recently conducted a literature search and meta-analysis to examine the incidence of acute kidney injury (AKI) in patients undergoing the procedure. They reported results of the meta-analysis during a poster session at the NKF Spring Clinical Meetings in a poster titled Incidence of Acute Kidney Injury in Patients Undergoing Total Hip Arthroplasty: A Meta-Analysis.

The literature search included MEDLINE, EMBASE, and the Cochrane Database from inception until July 2018. Studies assessing the incidence of AKI in patients undergoing total hip arthroplasty were included. AKI was defined using either RIFLE [Risk, Injury, Failure, Loss of kidney function, and End-stage renal disease], AKIN [Acute Kidney Injury Network], or KDIGO [Kidney Disease Improving Global Outcomes] criteria. The incidence of AKI in that patient population was estimated using a random-effects model.

The meta-analysis included 16 cohort studies representing 23,572 patients undergoing total hip arthroplasty. Overall, the pooled estimated incidence rates of AKI were 6.0% [95% confidence interval [CI] 3.6%–9.8%], the pooled estimated incidence rates of severe AKI requiring dialysis were 0.5% (95% CI 0.1%–2.3%). The pooled estimated incidence of AKI in patients undergoing total hip arthroplasty in the United States was 2.8% (95% CI 1.2%–6.6%).

In meta-regression of all included studies, there was significant negative correlation between incidence of AKI following total hip arthroplasty and the study year [slope = –0.37; P < 0.001]. There was no publication bias as assessed by the funnel plot and Egger’s regression asymmetry test with P=0.13 for the incidence of AKI in patients undergoing total hip arthroplasty.

“The overall estimated incidence rates of AKI and severe AKI requiring dialysis in patients undergoing total hip arthroplasty are 6.0% and 0.5%, respectively. There has been potential improvement in the AKI incidence for patients undergoing total hip arthroplasty over time,” the researchers said.


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Late-Breaker: Primary Results of AMBER: Patiromer plus Spironolactone for Blood Pressure Management

Boston—Treatment-resistant hypertension is a common complication of chronic kidney disease (CKD), yet the use of renin-angiotensin-aldosterone system inhibitor (RAAS) drugs may be limited in patients with CKD due to hyperkalemia. The PATHWAY-2 trial demonstrated that spironolactone was an effective fourth-line therapy for treatment-resistant hypertension; however, patients with advanced CKD were excluded from that trial.

The phase 2 AMBER study was designed to assess the use of the potassium binder patiromer concomitantly with spironolactone in patients with treatment-resistant hypertension and advanced CKD to prevent hyperkalemia and allow more persistent spironolactone use for blood pressure control. Rajiv Agarwal, MD, MBBS, FASN, reported results during a late-breaking poster session at the NKF Spring Clinical Meetings in a poster titled Patiromer to Enable Spironolactone in Patients with Resistant Hypertension and CKD: Primary Results of AMBER.

The multicenter, double-blind, placebo-controlled randomized controlled trial included a 4-week screening/run-in period and a 12-week treatment period. Eligible patients were adults with CKD and uncontrolled resistant hypertension (defined as unattended screening systolic automated office blood pressure 135-1260 mm Hg while on three anti-hypertensive drugs, including a diuretic and an angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker). Other inclusion criteria were estimated glomerular filtration rate 25 to ≤45 mL/min/1.72 m$^2$ and screening potassium level 4.3 to 5.1 mEq/L.

The primary efficacy end point is the between-group difference (spironolactone plus patiromer vs spironolactone + placebo) in the percentage of patients remaining on spironolactone at week 12. Secondary end points included the between-group difference in systolic automated office blood pressure change from baseline to week 12.

A total of 295 patients were randomized, creating a sample size that provides 80% power sufficient to detect a difference of ≥20% between treatment groups in the proportion of patients remaining on spironolactone at week 12 at $\alpha=0.05$. The database lock was January 31, 2019.

AMBER is the first randomized, controlled study of spironolactone in the treatment of resistant hypertension in patients with advanced CKD and will define the safety and effectiveness of spironolactone and if patiromer can facilitate the use of spironolactone to lower blood pressure in patients with resistant hypertension and CKD, the researchers said.

In late-breaking results, the researchers reported that the study “achieved statistical significance of its prespecified primary end point by demonstrating that a significantly higher proportion of patients taking Veltassa® (patiromer) remained on therapy through 12 weeks of treatment versus placebo with concomitant spironolactone in patients with resistant hypertension and CKD (86% vs 66%, P<.001, respectively). Safety results are consistent with existing Veltassa data, with no new safety issues identified.”


Association of Gestational Diabetes and CKD by Race/Ethnicity

**Boston**—Diabetes is a leading cause of chronic kidney disease (CKD). Women who develop gestational diabetes are at increased risk for diabetes and thus for CKD. Non-white women are at increased risk for diabetes. Albuminuria, and progression of CKD compared with non-Hispanic white women. Joanne Rodrigue, MPH, and colleagues conducted an analysis to examine the link between gestational diabetes and CKD based on race/ethnicity. Results were reported during a poster session at the NKF Spring Clinical Meetings in a poster titled Gestational Diabetes, Ethnicity, and Development of CKD.

CKD was defined as estimated glomerular filtration rate (eGFR) ≤60 mL/min/1.73 m² with an albumin-to-creatinine ratio ≥30 mg/g or eGFR 15 to 59 mL/min/1.73 m². Gestational diabetes was retrospectively recorded as a yes/no response. The study population included dialysis-dependent patients, including one that demonstrated IV iron was cost-effective compared with oral iron, particularly in patients ≥45 years of age.
Changes in Kidney Function in Elderly Patients with and without Nephrology Referral

Boston—With increases in life expectancy, there are more geriatric patients being referred to nephrology for management of chronic kidney disease (CKD). It is uncertain whether referral of geriatric patients improves outcomes. One recent study did not show any benefit of trending change in estimated glomerular filtration rate (eGFR) as a predictor of mortality in elderly patients. Results of a study conducted in the United Kingdom suggest that the majority of geriatric patients with CKD can be effectively managed in the primary care setting without a nephrology referral. There are few if any, data available from studies conducted in the United States.

Azza Abdel Hak, MD, and colleagues conducted a retrospective chart review of patients ≥80 years of age with eGFR <60 mL/min/1.73 m² who were seen at Thomas Jefferson University Hospital Philadelphia, Pennsylvania in 2009 and 2010. The researchers reported results of the chart review during a poster session at the NKF Spring Clinical Meetings in a poster titled A Study of Kidney Function Trends in Geriatric Patients with and without Nephrology Referral.

Demographics, including age, sex, and race, were collected at baseline. Creatinine, eGFR (calculated by CKD-Epidemiology Collaboration equation), and all-cause mortality were measured at baseline, and years 3 and 5. Patients were categorized into one of two groups, those with nephrology referral and those without nephrology referral. Differences between the two groups were compared using two-sample t tests and Chi-square tests as appropriate. Differences in creatinine and eGFR between the two groups were assessed using linear regression models. Binary outcomes, whether creatinine or eGFR changed from baseline by >25% at year 3 and >5% and were modeled using logistic regression analysis. The models were adjusted for age, sex, and race.

The nephrology group included 49 patients; the non-nephrology group included 71 patients. The eGFR in the nephrology group was significantly lower than in the non-nephrology group: 32.32 mL/min/1.73 m² versus 38.58 mL/min/1.73 m². There were no significant differences in 5-year increase of creatinine, 5-year decrease in eGFR, or 5-year all-cause mortality. Further, among patients with CKD stage 3, there were no significant differences in creatinine change or eGFR change between the two groups.

In conclusion, the researchers said, “This study did not show any beneficial gains of referral of senior patients with CKD to nephrology. It may be more appropriate to further study this pattern in the United States.” The researchers also noted that further study is needed to “develop a referral strategy that more closely reflects patient priorities.”


Vitality Scores among Peritoneal Dialysis Patients Differ Between Countries

Boston—There are few data available regarding fatigue in patients with end-stage renal disease treated with peritoneal dialysis. The 36-item Short Form Health Survey (SF-36) vitality scale has been used to establish hemodialysis patients’ perception of energy/fatigue. However, only a few small populations of peritoneal dialysis patients have been profiled using the scale. It is also unknown whether variations exist in vitality scores between countries.

Liz Wallim and colleagues defined the profiles of the vitality scores in large cohorts of incident peritoneal patients in Brazil and the United States. The researchers reported their findings during a poster session at the NKF Spring Clinical Meetings in a poster titled Fatigue in incident peritoneal dialysis patients in Brazil and the United States. The researchers reported results of the chart review during a poster session at the NKF Spring Clinical Meetings in a poster titled A Study of Kidney Function Trends in Geriatric Patients with and without Nephrology Referral.

The proportions of patients with a high level of fatigue were similar in Brazil and the United States (25.0% and 27.0% of patients reporting vitality scores, respectively).


Patient Perceptions of Their Experience at Dialysis Center

Boston—An understanding of the factors that drive dialysis patients’ experiences is crucial in providing care. It is unclear whether the in-center hemodialysis environment matters. Providers and Systems (ICH-CAHPS) survey reflects themes that contemporary hemodialysis patients have identified as important.

Kathryn S. Gray, HS, and colleagues at DaVita Clinical Research, Minneapolis, Minnesota, distributed an anonymous paper survey at 29 dialysis facilities. They reported results of the survey during a poster session at the NKF Spring Clinical Meetings in a poster titled Patient Reported Experience of Dialysis Care: Comparison to ICH-CAHPS.

The survey asked, “What are the three most important things about your experience at your dialysis center?” To enable theme identification and analysis, the researchers entered survey responses, along with all items from the ICH-CAHPS, into NVivo qualitative data analysis software (Burlington, MA). Of the 1000 surveys distributed, patients completed 734. Thirty themes were identified from the combination of ICH-CAHPS survey items and patient responses. Of the 30 themes, 21 were spontaneously mentioned by patients and were included on the ICH-CAHPS survey. Eight themes were mentioned by patients but were not reflected on ICH-CAHPS, and one theme was mentioned on ICH-CAHPS only.

In summary, the researchers said, “The ICH-CAHPS survey captures many but not all themes that patients report as being important to their experience; the frequency with which some themes are mentioned on ICH-CAHPS may not be reflective of their relative importance to patients. Development of survey instruments that reflect patient-identified themes may enable the provision of care that more closely reflects patient priorities.”

Management of Hyperkalemia with Patiromer in Real-World Setting

Boston—Csaba P. Kovacs, MD, and colleagues recently conducted a retrospective cohort study to examine the incidence of hyperkalemia following initiation of patiromer in patients with hyperkalemia on chronic hemodialysis. Results of the study were reported at the NKF Spring Clinical Meetings in a poster titled "Real-World Evaluation of Potassium Levels in Hemodialysis Patients Initiating Treatment with Patiromer.” Patiromer is a potassium binder indicated for the treatment of hyperkalemia.

The study utilized de-identified electronic health record data from January 2016 to December 2017 from a large dialysis organization in the United States. Hemodialysis patients with a baseline serum potassium ≥5.0 mEq/L who initiated treatment with patiromer were eligible for the study. Patients were followed from the index date (first order for patiromer) to 90 days post index, discontinuation or switch to another treatment, loss to follow-up, or December 31, 2017. Hyperkalemia (potassium ≥5.5 mEq/L) was classified using serum potassium in three sequential 30-day intervals after the index date. The study examined the percentage of patients with ≥1 serum potassium ≥5.5 mEq/L and 30-day hyperkalemic rate. The researchers identified 1166 eligible patients who initiated treatment with patiromer following a serum potassium measurement ≥5.0 mEq/L. Median age of the cohort was 65 years, 56% were women, and median follow-up was 90 days. Continuation of patiromer use was high. 96% of patients were treated through 30 days, 79% through 60 days, and 68% through 90 days. At baseline, median serum potassium was 6.0 mEq/L; 20% of patients had a dialysate potassium concentration ≥2 mEq/L. The rate of hypokalemia was less than 1% at 12, 2, and 3 months.

In summary, the researchers said, “Among chronic hemodialysis patients, real-world management of hyperkalemia with patiromer was associated with low hypokalemia rates.”


Pregnancy-Related Acute Kidney Injury and Socioeconomic Factors

Boston—in the United States, rates of pregnancy-related morbidity are increasing, and minority women are a higher risk than white women. Pregnancy-related acute kidney injury (Pr-AKI) has risen 300% from 1993 to 2014; however, there are few data available on racial trends in Pr-AKI. Kelly Beers, MD, and colleagues utilized a national representative dataset to examine trends in Pr-AKI by self-reported race. They reported results of the analysis during a poster session at the NKF 2019 Spring Clinical Meetings in a poster titled "Racial Disparities in Pregnancy-Related Acute Kidney Injury.”

Hospitalizations for pregnancy and diagnoses of AKI were identified using International Classification of Diseases codes. The researchers estimated trends in AKI and the impact of race on outcomes, then adjusted for socioeconomic and hospital-related factors.

From 2005 to 2014, there were 9,768,905 pregnancy hospitalizations, 70,582 of those had Pr-AKI (0.72 per 1000 hospitalizations). The patients with Pr-AKI were older, more likely to be black (Pr-AKI 29% vs non-AKI 12%, p=0.001) and have an All Patient Refined-Diagnosis Related Group mortality score of 4 (Pr-AKI 33% vs non-AKI 10%). There was an increase in hospitalization rate for Pr-AKI from 0.04% in 2005 to 0.12% in 2015. The increase was largest in blacks. There was an association between AKI and increased odds of preterm labor, miscarriage, mortality and discharge other than home. Proportions of all adverse outcomes were higher among black and Hispanic women hospitalized for Pr-AKI. This was attenuated following adjustment for socioeconomic factors; however, Hispanics women had higher odds of preterm labor, and both Hispanic and black women had higher odds of preeclampsia/eclosion compared with white women.

The researchers said, "Pr-AKI is increasing significantly and associated with adverse outcomes in pregnancy with a sharper rise in racial/ethnic minorities. Many of those differences are attenuated after adjustment for socioeconomic factors, although notable differences in preterm labor and pre- eclampsia remain. Our findings suggest that socioeconomic factors play a significant role in the increased risk of Pr-AKI among minority women.”


Remote Patient Monitoring vs Standard Communications in Patients on Peritoneal Dialysis

Boston—Timely communication between patients on peritoneal dialysis and providers can be enhanced using remote patient monitoring. Previous studies found an association between peritoneal dialysis modality longevity and remote patient monitoring compared with standard communications (no remote patient monitoring). Harold Giles, MD, and colleagues recently performed a retrospective analysis to assess trends in communication frequency in patients with peritoneal dialysis (PD) and standard communications in patients with hemodialysis (HD) from January 2016 to December 2017. The researchers reported a decrease in the proportion of patients with remote communications from 50% in January 2016 to 25% in December 2017 in the PD group and a decrease from 75% to 50% in the HD group. The proportion of patients with standard communications increased from 5% to 25% in both groups.

The researchers controlled for peritoneal PD mortality rate was lower in remote monitoring patients [HR 0.76, 95% CI 0.67-0.87] and there was a trend toward 19% higher transplantation rate in remote monitoring patients compared with standard communications [HR 1.19, 95% CI 1.08-1.30]. There was no difference in rates of transfer to hemodialysis (defined as transfer to hemodialysis with no return to peritoneal dialysis in 6 weeks). Baseline peritoneal dialysis Kt/V data were available for most patients: 97.8% for the remote patient monitoring group and 97.1% for the standard communications group. Prior analysis (without match) found a larger difference in days on peritoneal dialysis (106 vs 44 days). The magnitude of effect comparing remote patient monitoring compared with standard communications (defined as transfer to hemodialysis with no return to peritoneal dialysis in 6 weeks) was found to be statistically significant [HR 1.27 vs current HR 1.19]. In conclusion, the researchers said, “The association between remote patient monitoring of peritoneal patients and longevity on peritoneal dialysis was confirmed in this analysis with matched bootstrap sampling to control for peritoneal start year.”

Source: Giles H, L. J. Mullon C, et al. Remote patient monitoring (RPM) and longevity on peritoneal dialysis (PD): An Analysis Controlling for Confounding by PD Start Year. Data on peritoneal patients using the Liberty (c) for >20 days, from 2012 to 2017 were extracted. Remote monitoring patients were required to transmit data through a modem within 30 days of initiation of peritoneal dialysis. The researchers controlled for peritoneal start year via a 1:1 match of standard communications patients (n=12,032) and remote monitoring patients (n=714). Bootstrapping was used to create 1000 randomly selected standard communications cohorts; hazard ratios were averaged. Availability of baseline peritoneal dialysis Kt/V was used as a proxy for therapy adherence.

Patients continued peritoneal dialysis modality for an average of 625 days for remote monitoring patients and 581 days for patients in the standard communications group (difference, 44 days). Compared with standard communications, the rate of stopping peritoneal dialysis was 11% lower with remote patient monitoring [HR 0.89, 95% CI 0.81-0.97]. Mortality rate was lower in remote monitoring patients [HR 0.76, 95% CI 0.67-0.87] and there was a trend toward 19% higher transplantation rate in remote monitoring patients compared with standard communications [HR 1.19, 95% CI 1.08-1.30]. There was no difference in rate of transfer to hemodialysis (defined as transfer to hemodialysis with no return to peritoneal dialysis in 6 weeks).

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There was an increase in hospitalization rate for Pr-AKI from 0.04% in 2005 to 0.12% in 2015.
Using Ultrasound to Guide Cannulation in Hemodialysis Patients

Boston—The optimal vascular access for hemodialysis patients is a permanent arteriovenous fistula (AVF) or graft (AVG), providing the lowest risk for infections related to access. Cannulation of a vascular access can be a challenge, and a common complication of new AVFs or AVGs is infiltration of the access. Infiltration of the vascular access is associated with missed hemodialysis treatments, the need for urgent surgical procedures, and loss of access.

Clinicians at Fresenius Medical Care North America developed a pilot program to determine the value in utilizing ultrasound to guide cannulation using a handheld ultrasound device. Results of the quality improvement pilot program were reported by Sheetal Chaudhuri during a poster session at the NKF Spring Clinical Meetings in a poster titled “Access Cannulations in Hemodialysis Patients.”

The initiative was conducted at 14 clinics from April 2018 through June 2018. It was divided into two phases. Phase 1 consisted of data recording on standard-of-care cannulation success and infiltration rates prior to use of an ultrasound. Phase 2 included a 4-week period using an ultrasound to guide cannulations of the AVF/AVG and collect consistent data. Documentation of cannulation success and complications was achieved using an access grading tool portal. At the end of phase 2, the researchers compared rates of successful cannulations and infiltration complications between the two phases.

The analysis included data from 310 patients: 162 in phase 1 and 148 in phase 2. During the pilot program, there were 690 cannulations performed in phase 1 and 471 in phase 2. Compared with phase 1 (no ultrasound), the need for a second cannulation attempt was reduced by 31.90% in phase 2 (with ultrasound). Rates of infiltration were 69.2% lower in phase 2 versus phase 1.

“This analysis identifies that use of a handheld ultrasound for cannulation of AVFs/AVGs may improve success rates and decrease infiltrations. Further testing is needed in a larger number of patients to confirm these findings,” the researchers said.


Nephrology Care for Patients with Advanced CKD Not Undergoing Dialysis

Boston—There are few available data on how patterns of end-of-life care for patients with advanced chronic kidney disease (CKD) who opt to forgo maintenance dialysis are shaped by prior care from a nephrologist. Susan Wong, MD, MS, and colleagues at the US Veterans Administration (VA) Puget Sound Health Care System, Seattle, Washington, conducted an analysis of data on patients who did not pursue maintenance dialysis prior to death. The researchers reported results of the analysis during a poster session at the NKF Spring Clinical Meetings in a poster titled “Nephrology Care in Patients with Advanced Kidney Disease Not Treated with Maintenance Dialysis.”

The case series included 812 patients in the VA healthcare system between 2000 and 2011 with advanced CKD who did not pursue maintenance dialysis. The researchers compared differences in patterns of end-of-life care among patients with advanced CKD [estimated glomerular filtration rate (eGFR), <15 mL/min/1.73 m2] who had no nephrology clinic visits, those who had fewer than four nephrology clinic visits, and those who had four or more nephrology clinic visits during the year prior to cohort entry.

Of the total cohort, 46.8% had no visits to the nephrology clinic, 35.1% had fewer than four visits, and 18.1% had four or more visits. Median time from cohort entry to death for patients who had no nephrology clinic visits was 96 days, compared with 250 days for those who had fewer than four visits and 273 days for those who had four or more visits. Compared with the patients who had no visits to the nephrology clinic, those with four or more visits were more likely to have received a palliative care consultation (66.0% vs 47.1%; odds ratio [OR], 1.76; 95% confidence interval [CI], 1.15–2.7) and be enrolled in hospice care (54.4% vs 31.1%; OR, 2.16; 95% CI, 1.42–3.30) prior to death.

There were no differences in the proportion of patients who were hospitalized or had received an intensive procedure during the final month of life and had died in a hospital setting. Differences in time for cohort entry to death and rates of hospice enrollment between groups were attenuated in sensitivity analyses and were no longer statistically significant among patients with more rapid decline in eGFR (1 mL/min/1.73 m2).

In summary, the researchers said: “Receipt of more nephrology care was associated with a longer time between eGFR <15 mL/min/1.73 m2 to death and more frequent receipt of supportive care services such as palliative care and hospice care but not in patients with more rapid progression of their CKD. Our findings suggest potential value in initiating advance care planning and active nephrology management upstream in the illness trajectory of patients who are considering not undergoing dialysis.”

Epidemiology and Burden of Anemia in CKD: A Literature Review

Boston—According to Milena Anatchkova, PhD, and colleagues, there are no recent reviews describing the epidemiology and burden of anemia in patients with chronic kidney disease (CKD) in the United States. The researchers recently conducted a study designed to address this evidence gap by examining and summarizing existing evidence of the epidemiologic burden of anemia in CKD. Results of the study were reported during a poster session at the NKF Spring Clinical Meetings in a poster titled Targeted Review of the Epidemiology and Burden of Anemia in Chronic Kidney Disease.

The researchers utilized a targeted review approach to develop preselected criteria and outcomes. Searches were conducted in Medline, EMBASE, and proceedings from recent conferences to identify research into the epidemiologic burden of CKD anemia in the United States since 2013. The focus of the review was on natural disease history, incidence, prevalence, mortality, and disease severity.

A total of 667 publications were screened. Of those, 30 were included in the qualitative analysis. There were significant associations between anemia in CKD and female sex (n=4), older age (n=5), non-white race (n=4), and history of anemia (n=2). In ten studies of diverse populations, there was wide variation in prevalence of anemia in CKD (range: 15%-69%), prevalence rates were closely associated with older age and disease severity.

All-cause mortality was reported in four studies (range: 15%-35%). Of two studies examining associations between anemia and mortality, one reported a non-significant association. Findings for the association of mortality outcomes with anemia treatments (erythropoietin-stimulating agents and/or iron supplements) were mixed in nine studies. None of the studies reported data on the incidence of anemia in CKD.

In conclusion, the researchers said, “The literature review identified few studies and reports a wide range of prevalence data for anemia in CKD, with little insight relating to the relationship between mortality and anemia, and possible factors associated with natural disease history. Given the sparse data, epidemiologic burden remains a gap in peer-reviewed literature, especially with respect to incidence of anemia in CKD in the United States over the last 5 years.”


Registry Identifies CKD Patients at High Risk of Progression to ESRD

Boston—Due to the difficulty in predicting which patients with chronic kidney disease (CKD) will progress to end-stage renal disease (ESRD), current standard of care for patients prior to ESRD is suboptimal. There are prediction tools available, but, according to Jamie Green, MD, and colleagues, they have not been widely implemented into clinical care. The research team worked to (1) develop a CKD registry to identify patients at high risk of progression to ESRD and (2) enroll patients at high risk of disease progression in a clinical program to improve care pre-ESRD. The registry was described during a poster session at the NKF Spring Clinical Meetings in a poster titled Clinical Implementation of a Chronic Kidney Disease (CKD) Registry with Risk Prediction.

The CKD registry was developed as part of a clinical trial conducted at eight nephrology clinics in a large integrated health system in Pennsylvania. Based on electronic health records, patients not on dialysis with CKD stages G3A3, G3bA2-A3, G4A1-A3, and G5A1-A3 were eligible for inclusion in the registry. Patients remained in the registry until they reached 6-months following initiation of renal replacement therapy.

The validated Kidney Failure Risk Equation used to predict risk was embedded in the registry. Patients were stratified according to risk of progression to kidney failure within 2 years: low (<6%), moderate (6 to 10%), or high (>10%). To optimize care in the transition from CKD to ESRD, patients at high risk were enrolled in a case-manager based clinical program.

During the study period (4/3/2017-4/2/2018), 3696 patients met inclusion criteria. Of those, 57% (n=2097) had CKD stage 3, 38% (n=1299) had CKD stage 4, and 5% (n=204) had CKD stage 5. Mean age of the cohort was 73 years, 55% were female, and 98% were white. At study entry, 77% (n=2866) were identified as low risk of progression to kidney failure within 2 years, 7% (n=259) as moderate risk, and 16% (n=601) as high risk. By the end of 12 months, 81% (n=2654) of high-risk patients at four sites were enrolled in a clinical program to improve pre-ESRD care.

The researchers said, “A CKD registry with risk prediction can be utilized to identify patients at high risk for progressing to kidney failure and [can] allow targeted interventions to be implemented.”

AWARDS AND HONORS

During the Spring Clinical Meetings, the National Kidney Foundation honors healthcare professionals who have made significant contributions to the field of kidney disease.

SHAUL G. MASSRY DISTINGUISHED LECTURE
This lectureship was established to honor Dr. Shaul G. Massry for his scientific achievements and his contributions to the kidney health care community and to the National Kidney Foundation. The 2019 honored lecturer is Gregory Germino, MD. Dr. Germino presented the Shaul Massry Distinguished Lecture on Thursday, May 9, 2019.

DONALD W. SELDIN DISTINGUISHED AWARD
The Donald W. Seldin Award was established to recognize excellence in clinical nephrology in the tradition of one of the foremost teachers and researchers in the field. Dr. Donald W. Seldin. The 2019 Donald W. Seldin Award recipient is Jerry Yee, MD. Dr. Lee is the division head of nephrology and hypertension of the Henry Ford Hospital and chief medical officer of the Greenfield Health Systems, a wholly owned subsidiary and dialysis provider of the healthcare system. Dr. Yee is also a clinical professor of the Wayne State University School of Medicine, Detroit, Michigan.

GARABED EKNOYAN AWARD
The Garabed Eknoyan Award was created to recognize an individual who has promoted the mission of the National Kidney Foundation in making lives better for people with kidney disease through exceptional contributions to key initiatives of NKF such as the Kidney Disease Outcomes Quality Initiative (KDOQI) or clinical research in the field of kidney disease. The 2019 award recipient is Charmaine E. Lok, MD, MSc, FRCP[C]. Dr. Lok is a professor of medicine in the faculty of medicine, University of Toronto and senior scientist at the Toronto General Research Institute. She is an active researcher conducting clinical trials aimed at improving patient health outcomes and functional ability in CKD, dialysis access, and cardiovascular disease in CKD and ESRD. She supports students and trainees as a professor in the department of health policy, management and evaluation, University of Toronto and as faculty in the department of clinical epidemiology and biostatistics, and faculty of health sciences, McMaster University, Hamilton, Ontario. Dr. Lok is passionate about caring for patients and is the medical director of the multidisciplinary chronic kidney disease and hemodialysis programs at the University Health Network, Toronto General Hospital, Toronto, Canada.

DAVID M. HUME MEMORIAL AWARD
The David M. Hume Award was created in memory of one of the National Kidney Foundation’s most distinguished members. The Hume Award is the highest honor given to a distinguished scientist-clinician in the field of kidney and urologic diseases. It is bestowed upon an individual who exemplifies the high ideals of scholarship and humanitari-anism in an outstanding manner. The 2019 award recipient is Nilka Ríos Burrows, MPH.

J. MICHAEL LAZARUS LECTURE
This award was established to honor Dr. J. Michael Lazarus for his major contributions to the clinical science and care of dialysis patients, and to recognize individuals whose research has yielded novel insights related to renal replacement therapy. The 2019 award recipient is Beth Piraino, MD. Dr. Piraino received her bachelor of science from the University of Pittsburgh, then attended medical school at the Medical College of Pennsylvania, graduating magna cum laude. Her subsequent training was at the University of Pittsburgh Health Center. She is a tenured professor of medicine and associate dean of admissions and financial aid at the University of Pittsburgh School of Medicine. Her focus has been on improving the lives of those with kidney disease through patient care, teaching, and research.

EXCELLENCE IN KIDNEY TRANSPLANTATION AWARD
The Excellence in Kidney Transplantation Award was established to recognize a scientist or clinician scientist whose exceptional research has contributed novel insights in or resulted in improved access to kidney transplantation. The award embodies the dedication of the National Kidney Foundation to help people navigate the challenges of kidney disease, organ donation, and transplantation. The 2019 recipient is Matthew Cooper, MD. Dr. Cooper is a professor of surgery at Georgetown School of Medicine and the director of kidney and pancreas transplantation at the Medstar Georgetown Transplant Institute (MGTI) and the UNOS surgical director for the Pediatric Kidney Transplant program at Children’s National Medical Center.

JOEL D. KOPPLE AWARD
The Joel D. Kopple Award is an annual award honoring an individual who has made significant contributions to the field of renal nutrition. The 2019 recipient is Kathy Wilkens. For Ms. Wilkens, the primary role of the renal dietitian is to teach. Whether it is writing, speaking at events, educating peers and students, demonstrating healthy cooking techniques, developing patient education materials, or sitting down with one of her hemodialysis patients, Kat finds it rewarding to offer information that can lead others to a healthier future.

In addition to helping her patients navigate their dialysis diet, she mentors dozens of dietetic students in rotations at Northwest Kidney Centers each year and educates fellow health care professionals such as physicians, renal fellows, nurses, and social workers.

MEDICAL ADVISORY BOARD DISTINGUISHED SERVICE AWARD
This award has been established to recognize an individual for educational activities and community service in promoting the mission of the National Kidney Foundation on a local level. The 2019 recipient is Ahmed Malik, MD, JD. Dr. Malik is a nephrologist working in the Milwaukee area since 2005. He graduated from King Edward Medical College in 1984 and did his nephrology fellowship at St. Louis University. He is board certified in nephrology and internal medicine. In addition to his clinical work, he is also involved in research and teaching and has been given the Best Teacher Award by Aurora Internal Medicine residency program several times.

He is chair of medicine of Aurora St Luke’s Medical Center in Wisconsin. He has been involved in charitable work for several years and was successful in raising more than $100,000 for the Indigent Patient Endowment Fund for his medical school alumni association in 2015 when he was president of that association. He has been involved with NKF Wisconsin Kidney Early Evaluation Program (KEDP) for the last 13 years and now serves on the NKF Wisconsin Board of Directors. In addition, he holds a master’s degree in HIM and an MPH in pharmacology. He is also a licensed attorney, as he holds a JD degree from Marquette University. Dr. Malik is interested in all aspects of nephrology, with an emphasis on early evaluation and prevention of kidney disease.

CELESTE CASTILLO LEE PATIENT ENGAGEMENT AWARD
This award was established in honor of Celeste Castillo Lee, a longtime advocate for patient-centered care and empowerment. It is the highest honor given by the National Kidney Foundation to a distinguished kidney patient who exemplifies NKF’s mission and Ms. Lee’s legacy of putting patients at the center of all aspects of healthcare through their involvement with NKF and community partners. The 2019 recipient is Mary Baliker.

Ms. Baliker lives in Wisconsin where she is a graduate of the University of Wisconsin-LaCrosse. She was diagnosed with chronic kidney disease at the age of nine and was on dialysis until her transplant at seventeen. Her donor was her brother Doug. Since then she has had three additional transplants, the last of which was in 1999. As a result of this life-long experience, she cherishes life and possess a strong interest to help improve healthcare. Her illness inspired her to become a fierce healthcare advocate for her entire adult life and she is grateful for the opportunity every day.

PUBLIC SERVICE AWARD
This award was established to honor those who have dedicated their careers to public service and who have helped shape public policies or government programs that improve outcomes for kidney patients. The 2019 recipient is Nilka Ríos Burrows, MPH.

Ms. Burrows is an epidemiologist in the division of diabetes translation at the Centers for Disease Control and Prevention (CDC). She joined CDC in 1992, and its Division of Diabetes in 1997. As a member of the division’s surveillance team, she conducted public health surveillance of diabetes and its complications nationwide and worked with the Indian Health Service’s division of diabetes treatment and prevention on diabetes surveillance among Native Americans. She received awards for her work in bringing national attention to the issue of diabetes and obesity in youth.

Since 2016, Ms. Burrows has led the CDC’s Chronic Kidney Disease Initiative, collaborating with partners on surveillance, epidemiology, and cost-effectiveness studies to provide public health strategies for promoting kidney health. She manages the CKD Surveillance System and coordinates the National CKD Fact Sheet to increase awareness about kidney disease burden and prevention. For the healthy people national agenda, she has championed objectives that address CKD. She has authored or co-authored more than 80 publications, including several on racial and ethnic disparities in diabetes and kidney failure. Her professional work for CDC’s Vital Signs documented the remarkable decline in kidney failure from diabetes among Native Americans.

CAROL MATTIX AWARD FOR NEPHROLOGY NURSING
This award was established in honor of Celeste Castillo Lee, a longtime advocate for patient-centered care and empowerment. It is the highest honor given by the National Kidney Foundation to a distinguished kidney patient who exemplifies NKF’s mission and Ms. Lee’s legacy of putting patients at the center of all aspects of healthcare through their involvement with NKF and community partners. The 2019 recipient is Mary Baliker.

Ms. Baliker lives in Wisconsin where she is a graduate of the University of Wisconsin-LaCrosse. She was diagnosed with chronic kidney disease at the age of nine and was on dialysis until her transplant at seventeen. Her donor was her brother Doug. Since then she has had three additional transplants, the last of which was in 1999. As a result of this life-long experience, she cherishes life and possess a strong interest to help improve healthcare. Her illness inspired her to become a fierce healthcare advocate for her entire adult life and she is grateful for the opportunity every day.

Byrd works for Fresenius Kidney Care in Rocklin, California, as a clinical manager. She is receiving the award in recognition of her decades-long commitment to improving the lives of dialysis patients.
Only one calcimimetic lowers and maintains key sHPT lab values with IV administration you control

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 pruritic rash, urticaria, and facial 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 paresthesia, myalgias, muscle spasms, seizures, QT interval prolongation, and ventricular arrhythmia. QT Interval Prolongation and Ventricular Arrhythmia
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 (5% placebo versus 1.2% PARSABIV). In these studies, the incidence of a maximum post-baseline QTcF of > 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 congenital 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 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 receiving PARSABIV.

Seizures
Significant reductions in corrected serum calcium may lower the threshold for seizures. Patients with a history of a 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]. Patients on concomitant serum calcium in patients receiving PARSABIV and concurrent 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 (2.4) 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) and/or monitor corrected serum calcium. PARSABIV dose reduction or discontinuation of PARSABIV may be necessary [see Dosage and Administration (2.2.3) in PARSABIV full prescribing information].

Worsening Heart Failure
In clinical studies with PARSABIV, cases of hypotension, 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 1.253 patient-years of exposure had upper gastrointestinal (GI) bleeding noted at the time of death while no patient in the control groups in 3.84 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 (5.3) 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]

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 decreased*</td>
<td>10%</td>
<td>64%</td>
</tr>
<tr>
<td>Muscle spasms</td>
<td>7%</td>
<td>12%</td>
</tr>
<tr>
<td>Diarrhea</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>Hypocalcemia</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
* Asymptomatic reductions in calcium below 7.5 mg/dL or clinically significant asymptomatic reductions in corrected serum calcium between 7.5 and < 8.3 mg/dL (that required medical management)
* Symptomatic reductions in corrected serum calcium < 8.3 mg/dL
* Paresthesia includes preferred terms of paresthesia and hypesthesiа
Hypophosphatemia: 0.2% and 1% for placebo and PARSABIV, respectively.

Myalgia: 0.2% and 2% for placebo and PARSABIV, respectively.

Other adverse reactions associated with the use of PARSABIV but reported in < 5% of patients in the PARSABIV group in the two placebo-controlled clinical studies were:

- Hyperkalemia: 3% and 4% for placebo and PARSABIV, respectively.
- Hospitalization for Heart Failure: 1% and 2% for placebo and PARSABIV, respectively.
- Myalgia: 0.2% and 2% for placebo and PARSABIV, respectively.
- Hyperphosphatemia: 0.2% and 1% 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, 3.1% placebo), below 7.5 mg/dL (27% PARSABIV, 5.5% placebo), and below 8.3 mg/dL (19% 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.

**Hypophosphatemia**

In the combined placebo-controlled studies, 19% of patients treated with PARSABIV and 8.2% 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 an increase in QTc interval by 60 msec or more during treatment compared to placebo (1.9% PARSABIV, 3.7% placebo). 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 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% (71 out of 995) 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 1-800-77-AMGEN (1-800-772-6436) to discuss antibody testing.

**USE IN SPECIFIC POPULATIONS**

**Pregnancy**

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 1.6 times the human exposure for the clinical dose of 15 mg three times per week. There was no effect on sexual maturation, neurobehavioral, or reproductive function in the rat offspring. In embryo-fetal studies, when rats and rabbits were administered etelcalcetide during organogenesis, reduced fetal growth was observed at exposures 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**

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**

**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 (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/day by the intravenous route (gestation day 7 to 19), 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.

**Overdosage**

There is no clinical experience with PARSABIV overdose. Overdosage 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).

**Amgen**

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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Intensive Blood Pressure Control and Kidney Injury Markers: ACCORD Trial Subset Analysis

The SPRINT (Systolic Blood Pressure Intervention Trial) found a reduction in cardiovascular events in participants randomly assigned to a systolic blood pressure <120 mm Hg compared with those randomly assigned to standard treatment (systolic blood pressure <140 mm Hg). Those findings have increased efforts across the healthcare spectrum for aggressive blood control. However, over time, aggressive blood pressure control may result in unintended negative consequences, such as higher risk for acute and chronic kidney disease.

Recent reports have highlighted the increased risk for incident chronic kidney disease (CKD) in SPRINT participants in the intensive arm versus the standard care arm. There has also been an association between the magnitude of reduction in mean arterial pressure in the intensive arm and the risk for incident CKD. However, the significance of the type of CKD is unclear, and the reduction in cardiovascular risk outweighs the risk of CKD progression.

There are no clear findings on the optimal level of blood pressure control in patients with CKD to prevent progression to end-stage renal disease. Further, there are few data available on intensive blood pressure control and progression of kidney disease in patients with diabetes. Diabetes was an exclusion criterion in SPRINT due to the overall null results in the ACCORD (Action to Control Cardiovascular Risk in Diabetes) study, leaving open the question whether more intensive blood pressure control in patients with type 2 diabetes leads to kidney injury.

Researchers, led by Girish N. Nadkarni, MD, MPH, CPH, recently conducted a longitudinal analysis of a subgroup of ACCORD-BP participants to examine changes in estimated glomerular filtration rates (eGFR) in conjunction with four urinary biomarkers representing kidney injury: kidney injury molecule 1 (KIM-1) and interleukin 18 (IL-18), inflammation (monocyte chemoattractant protein 1 [MCP-1]), and fibrosis (human cartilage glycoprotein 39 [YKL-40]). A fifth biomarker of inflammation (monocyte chemoattractant protein) was also included. Results were reported in the American Journal of Kidney Disease [2019;73(1):31-38].

There were 529 participants in the ACCORD-BP group. Of those, 260 had been randomly assigned to the intensive blood pressure arm (systolic blood pressure target, <120 mm Hg) and 269 to the standard blood pressure arm (systolic blood pressure target, <140 mm Hg). At baseline, mean age of the overall cohort was 62 years and mean estimated glomerular filtration rate (eGFR) was 90 mL/min/1.73 m².

In the intensive arm, mean eGFR declined by 17% from baseline to 2 years (from 85.9 to 70.7 mL/min/1.73 m²) and by 9% in the standard arm (from 85.4 to 76.5 mL/min/1.73 m²). In the intensive arm versus the standard arm, the albumin-creatinine ratio was 30% lower at year 2 (12.7 vs 18.1 mg/g; P=.004).

In the intensive arm versus the standard arm, the four urinary biomarkers were unchanged or lower at year 2. All four levels trended lower in the intensive arm compared with the standard arm; this finding reached statistical significance for IL-18 (decrease of 14%; P=.04). Among patients in the intensive arm who had larger declines in eGFR, there were significant trends for a larger reduction in IL-18 (P for trend=.01) and YKL-40 levels (P for trend=.07).

Seventy-six patients in the intensive arm experienced incident CKD, defined as sustained 30% decline in eGFR and eGFR <60 mL/min/1.73 m²; among those patients, there was a mean eGFR decrease of 31% (from 8.7 to 5.9 mL/min/1.73 m²). Despite now meeting the definition for incident CKD, none of the urinary biomarker levels increased over time in that subpopulation. There were 27 patients in the standard arm who developed incident CKD; those patients had a mean eGFR decrease of 35% and one of the five biomarker levels increased (IL-18 increased by 7.1%).

Limitations to the study cited by the researchers included the small proportion of participants with baseline CKD and a single measurement of serum creatinine and thus a single eGFR value.

In conclusion, the researchers said, “Among a subset of ACCORD-BP trial participants, intensive blood pressure control was associated with reductions in eGFRs, but not with an increase in injury marker levels. These findings support that eGFR decline observed with intensive blood pressure goals in ACCORD participants may predominantly reflect hemodynamic alterations.”

**TAKEAWAY POINTS**

- Patients assigned to intensive blood pressure control in the ACCORD-BP trial experienced more rapid decline in estimated glomerular filtration rate in those meeting the definition of incident CKD.
- Researchers conducted a longitudinal analysis of a subgroup of ACCORD-BP participants to examine changes in eGFR and biomarker levels from baseline to 2 years.
- There was an association between intensive blood pressure control and reductions in eGFR; however, there was no association with an increase in injury marker levels, suggesting the decline in eGFR may predominantly reflect hemodynamic alterations.
Since the implementation of the Medicare ESRD [end-stage renal disease] Prospective Payment System (PPS), i.e., bundle payments, dialysis facilities are reimbursed at a flat rate for a bundle of ESRD-related drugs, supplies, and services per dialysis treatment. Adjustment to the base rate is made to account for patient-level case-mix and facility-level factors that are associated with higher costs related to dialysis care delivery.

Of drugs used to manage persistently elevated serum levels of parathyroid hormone (PTH), hyperparathyroidism, as of 2018 only vitamin D analogs (administered orally and intravenously) have been incorporated into the bundle. By statutory provision, the addition of oral-only drugs (phosphate binders) has been delayed until 2025.

Beginning in January 2018 with the implementation of a Transitional Drug Add-on Payment Adjustment classification, calcimimetic treatments such as oral cinacalcet and intravenous etelcalcetide, are reimbursed separately under Medicare Part B. The adjustment is scheduled to remain in effect for a minimum of 2 years. During that time, the Centers for Medicare & Medicaid Services will collect and analyze data on utilization and cost; following the analyses, the agency will determine the appropriate revisions to the bundle payment system, including calcimimetics.

According to Douglas S. Fuller, MS, and colleagues, understanding patterns of calcimimetic utilization across dialysis facilities may help align financial incentives with clinical objectives. The researchers recently conducted an analysis of cross-sectional data from DOPPS (US Dialysis Outcomes and Practice Patterns Study) from 2014. Preliminary data from 2016 were used in a sensitivity analysis. Results of the analyses were reported online in the Clinical Journal of the American Society of Nephrology [doi:10.2215/CJN.09550818].

The monthly data were used to define the distribution of cinacalcet prescription across 203 hemodialysis facilities in the United States, representing 10,521 patients. Linear mixed-effects regressions on the basis of associations with PTH levels from patient-level analyses were used to estimate the associations between three facility-level exposures (black race; age <65 years; and dialysis vintage [≥3 years]), and the prevalence of cinacalcet prescriptions, adjusting for facility- and patient-level potential confounders.

There was a steady increase in the median percentage of patients in facilities with cinacalcet prescription during 2014; the percentage increased from 22% to 24%, a difference of only 2% to 3% (slope per 30 days, 0.09%; 95% confidence interval [CI], 0.02% to 0.2%; P for trend = .01). The researchers also observed wide variability in cinacalcet prescription across facilities within each month; absolute differences between the 25th and 75th percentiles varied from 16% to 20% across months in 2014. In the sensitivity analysis of preliminary 2016 data, the estimated monthly percent-ages were slightly higher, but there were no other notable differences compared with the main analysis of 2014 data.

As the percentage of black patients in each facility increased from the lowest to the highest quartile, the mean percentage of patients with a cinacalcet prescription increased monotonically from 18% to 31%. There were similar monotonic associations with cinacalcet prescription in a facility for the percentages of patients <65 years of age and with dialysis vintage ≥3 years.

The highest levels of PTH were in patients in the quartile of facilities having the highest percentage of black patients (396 pg/mL), relative to patients in the first two quartiles. Those facilities also had the largest percentages of patients with PTH ≥600 pg/mL (21%) compared with patients at the lowest quartile. The two highest quartile facilities in this category also had the highest percentage of patients with calcium levels ≥9.5 mg/dL (12% and 15%). The lowest median PTH levels were seen in patients in the quartile of facilities with the smallest percentage of patients with dialysis vintage ≥3 years.

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The adjusted difference in prevalence of cinacalcet prescription between facilities with the highest and lowest quartiles of black patients was 7.8% (95% CI, 0.8% to 14.8%; P for trend = .03); 7.3% for the percentage of patients <65 years of age (95% CI, −0.1% to 14.7%; P for trend = .66), and 11.9% for the percentage of patients with dialysis vintage ≥3 years (95% CI, 2.4% to 21.4%; P for trend = .02). However, following further adjustment for patient-level exposure variables, the associations changed substantially, becoming much weaker or even reversing.

The lowest median PTH levels were seen in patients in the quartile of facilities with the smallest percentage of patients with dialysis vintage ≥3 years.
Some patients with end-stage renal disease on the kidney transplant waiting list are made inactive due to medical co-morbidities, incomplete testing, psychosocial issues, or financial constraints. Those who are made inactive have a higher mortality rate than those who remain on the list. Inactive patients work with their healthcare professionals, social workers, and transplant team to resolve the issues to achieve active status, providing the eligibility to obtain decreased donor organ offers. There are few data available on the implications and impact of a wait-list status change on a patient’s future chances of receiving a kidney transplant.

The Kidney Allocation System (KAS) (Organ Procurement and Transplantation Network [OPTN] policy 8.3; effective December 4, 2014), was designed to increase transplant rates in patients who are highly sensitized and to improve access to underserved populations.

Researchers, led by Sanjay Kulkarni, MD, MHCM, created a unique analysis of OPTN kidney transplant wait-list data and analyzed competing risk transplant outcomes following the implementation of KAS. The model accounts for changes in activity status. The researchers were able to examine how changes in wait-list status as well as the ability to convert from inactive to active status differ in racial/ethnic groups and how those differences factor into the probability of receiving a transplant. The model also provided status change metrics that offered a new measurement for dialysis units and transplant centers to improve quality via improved care coordination of shared patients on the inactive list.

The model was described online in JAMA Surgery [doi:10.1001/jamasurg.2019.0512].

The model included seven transitions: active to inactive status; active to death/other; inactive to active; inactive to death/other; active to living donor transplant; active to deceased donor transplant; and active to death/other. The Other transition category included listing removal for refusal of transplant, improved condition, and other reasons. The association of race/ethnicity and initial calculated panel reactive antibody (cPRA) with each transition was evaluated independently using a transition-specific Cox regression model adjusted for sex, diabetes status, dialysis status, blood type, and donor service area.

The post-KAS wait-list population in the current study included 42,558 individuals from December 4, 2014, to September 8, 2016. The median age at listing was 55 years, and 62.4% (n=26,533) were men. Diagnoses of end-stage renal disease at listing were diabetes mellitus (56.6%, n=15,568), other/unknown (28.8%, n=12,257), hypertension (21.3%, n=9,043), glomerulonephritis (11.4%, n=4,936), and graft failure (2.0%, n=854). A total of 18,417 (43.3%) individuals were white; black and Hispanic individuals accounted for 27.8% (n=11,837) and 19.5% (n=8,296), respectively, of the study population. At time of listing, 28,905 (67.9%) individuals were receiving dialysis treatments; 13,653 (32.1%) were not receiving dialysis.

On the day of listing, there were 31,643 patents with active status and 10,915 patients with inactive status (74% and 26%, respectively). In 53.1% (n=9,779) of white patients, at least one inactivity status change was observed during the first year of listing, compared with 42.3% (n=3506) of Hispanic patients, and 49.3% (n=5836) of black patients. Considering their representation on the wait-list (Hispanic patients, 19.5% [n=8,296]; black patients, 27.8% [n=11,837]), there were disproportionate numbers of Hispanic and black individuals experiencing an inactive status change.

The researchers evaluated the association of race with transition 1 (active to inactive) and transition 5 (inactive to active) separately. While there was no statistically significant interaction between cPRA and race/ethnicity, once on the inactive list, white individuals were more successful than Hispanic or black individuals at resolving issues for inactivity, resulting in wait-list activation. The differences between Hispanic and black individuals in activity status transitions were not statistically significant.

Most patients, represented in the cPRA groups of 0% or 1% to 79%, showed no statistically significant differences in probability of transplant by race/ethnicity. For patients initially listed as active, white patients had a significant advantage over black patients in cPRA categories of 80% to 90% (hazard ratio [HR], 1.8; 95% confidence interval [CI], 1.4-2.2) and ≥90% (HR, 2.36; 95% CI, 2.1-2.6). Hispanic patients had a statistically significant advantage over black patients in the cPRA category of ≥90% (HR, 2.5; 95% CI, 2.1-2.8), but not at a cPRA of 80% to 89% (HR, 1.6; 95% CI, 0.9-2.2). There were similar differences in transplant probability seen in individuals initially listed as inactive, although the effect size between races/ethnicities was less pronounced.

The authors did note several limitations to the study, including the retrospective design that made it difficult to establish robust causal inference; using a sliding scale for allocation points for patients who were highly sensitized starting at cPRA >80%; allocation priorities and geographical organ offer distribution differed in patients with a cPRA of 98%, 99%, and 100%; not accounting for additional factors associated with access to transplant, including socioeconomic status and referral rates to transplant centers; and the uncertainty regarding whether the addition of DR 0-mismatch allocation points resulted in the observed racial/ethnic disparities.

In conclusion, the researchers said, “In this study, we used a new analytic approach to OPTN data that included the association of wait-list status with transplant outcomes. For the first time to our knowledge, we are able to determine the association of post-listing status changes with the overall probability of obtaining a deceased donor kidney transplant. By including inactive patients in our analysis, we provide greater accuracy and provide new information to patients and healthcare professionals about the impact of being made inactive. We confirm that for most patients, racial/ethnic differences in obtaining a deceased donor transplant have decreased. However, barriers to transplant continue to exist in the higher cPRA groups, where higher transitions from inactive to active status and greater access to DR matching allocation points for white patients are likely contributory factors. We urge the monitoring of status changes as a quality measure for transplant centers and dialysis providers to encourage care coordination of shared patients, particularly in underserved populations.”

**Takeaway Points**

- Researchers conducted a retrospective cohort study to examine differences in changes in wait-list status and the ability to convert from inactive to active status between racial/ethnic groups.
- In the study cohort of 42,558 patients, racial disparities were reduced for most patients following implementation of the Kidney Allocation System in 2014.
- For highly sensitized patients, significant racial/ethnic differences in transplant probability remain.
Metabolic Acidosis and Risk for Cardiovascular Events Following Transplantation

Of the 135,436 kidneys transplanted between 2008 and 2015, an estimated 20% will be lost within 5 years. An additional 35,000 kidney transplants will be lost by 2025, which will result in significant morbidity, mortality, and public health costs. Patient death, primarily due to cardiovascular disease, accounts for nearly half of the failed transplanted kidneys. The other 50% are lost to rejection, disease recurrence, and tubulointerstitial fibrosis.

Kidney transplant recipients often experience metabolic acidosis. The high prevalence of metabolic acidosis in the transplant population compared with other patients with chronic kidney disease (CKD) is associated with distinct immunologic and drug-induced effects that regulate its pathogenesis following kidney transplantation.

There is no evidence that treatment of metabolic acidosis prevents cardiovascular events in patients with CKD or kidney transplant recipients. There is concern regarding sodium loading with bicarbonate. Results of the CRIC (Chronic Renal Insufficiency Cohort) study demonstrated that the risk for developing a renal end point was 3% lower per 1-mEq/L higher serum bicarbonate level (P = .01), while the risk for congestive heart failure increased by 14% for every 1-mEq/L higher serum bicarbonate level in those with bicarbonate >24 mEq/L (P = .02).

Researchers, led by Arjang Djamali, MD, conducted a single-center observational cohort study designed to assess whether metabolic acidosis is a risk factor for cardiovascular events after kidney transplantation. The study examined the association between mean serum bicarbonate (measured as total carbon dioxide [tCO2] in serum) concentration at 1 year following transplantation and the incidence of de novo ischemic, arrhythmic, or heart failure events in 2018 kidney transplant recipients. Results of the study were reported in the American Journal of Kidney Diseases [2019;73(4):476-485].

Included participants were recipients of a kidney transplant at the University of Wisconsin from January 1, 2000, to November 15, 2013, who survived at least 13.5 months without a cardiovascular event and had at least one measurement of tCO2, serum creatinine, systolic and diastolic blood pressures, and lipids during the 3-month baseline window centered at 1 year (10.5-13.5 months post-transplantation). Patients with a mean estimated glomerular filtration rate (eGFR) <15 mL/min/1.73 m² during the baseline window were excluded. Patients were divided into five groups based on mean tCO2 concentration: <20.0, 20.0 to 21.9, 22.0 to 23.9 mEq/L, 24.0 to 25.9 (reference group), and ≥26 mEq/L.

A total of 3265 kidney transplant recipients survived without a cardiovascular event until the end of the 3-month baseline window (13.5 months post-transplantation). Of those, 2128 recipients had complete data available during the baseline window and had a mean eGFR ≥15 mL/min/1.73 m² and were included in the study. Compared with excluded recipients, those included in the study were older (50.9 vs 48.5 years at the time of transplantation) and less likely to have received a prior transplant (20.0% vs 25.0%; P = .001). There were no significant differences between the two groups in age, race, sex, living/deceased donor, presence of diabetes at the time of transplantation, or delayed graft function.

Mean recipient age was 50.9 years, 40% were women, and 83% were white. Metabolic acidosis was defined as tCO2 level <24 mEq/L. 826 patients met that criterion (38.9%). Patients in the lowest category of tCO2 concentration were significantly younger and had worse kidney function and higher diastolic blood pressures. They were also more likely to have received a deceased donor kidney transplant or thymoglobulin induction and have delayed graft function. There was no difference in maintenance therapy with calcineurin inhibitors.

Diabetes was the primary cause of end-stage renal disease in 24.3% of participants and 7.1% developed new-onset diabetes following transplantation prior to the end of the baseline window. Also, before the end of the baseline window, 20.7% of recipients had an acute rejection event, and 44.9% had a history of infection other than urinary tract infection. A total of 23% of patients were receiving angiotensin-converting enzyme inhibitors or angiotensin receptor blockers during the baseline window.

During a median follow-up of 3.75 years, 384 recipients had at least one cardiovascular event. A total of 241 had an ischemic event, 137 had an arrhythmic event, and 150 had a heart failure event. There were 610 deaths; 82 were considered due to a cardiovascular event.

There was no statistically significant difference found for patients with mild acidosis (tCO2 of 22-23.9 mEq/L); however, the adjusted hazard ratio (aHR) for all cardiovascular events in patients with tCO2 levels <20 mEq/L was significantly greater than for the reference group with tCO2 levels of 24.0 to 25.9 mEq/L (aHR, 2.00; 95% confidence interval [CI], 1.29-3.10).

The risk for cardiovascular events was driven primarily by ischemic events (aHR, 2.28; 95% CI, 1.34-3.90). For every 1-mEq/L lower tCO2 level for those with tCO2 <24 mEq/L, risks for all cardiovascular events and ischemic cardiovascular events were 17% and 15% higher, respectively (aHR for all cardiovascular events, 0.83; 95% CI, 0.74-0.94 and aHR for ischemic cardiovascular events, 0.85; 95% CI, 0.74-0.99). There were no associations between metabolic acidosis and arrhythmic or heart failure events.

There was an independent association between tCO2 level <20 mEq/L, compared with tCO2 level of 24.0 to 25.9 mEq/L, and all-cause mortality (aHR, 1.43; 95% CI, 1.02-2.02). For every 1-mEq/L lower tCO2 level for those with tCO2 <24 mEq/L, there was a 17% higher risk for death (aHR, 0.83; 95% CI, 0.75-0.92).

There were some limitations to the study, including the retrospective, single-center design, lack of measurement of pH values, and lack of repeated tCO2 and covariate data.

The researchers said, “In summary, our findings indicate that metabolic acidosis is a predictor of ischemic cardiovascular events in kidney transplant recipients, independent of traditional and transplant-specific risk factors, and suggest that alkali therapy, provided as sodium ion-based alkali and/or base producing fruits and vegetables, should be considered to correct tCO2 levels to the normal range. However, this indication should be tempered because the safety and efficacy of bicarbonate therapy in kidney transplant recipients is yet to be demonstrated.”
FDA Grants Breakthrough Designation for KidneyIntelX™

The US FDA has granted the designation Breakthrough Device to RenalytixAI for its lead diagnostic KidneyIntelX™. According to a press release from RenalytixAI, this is the first such designation for an AI-enabled diagnostic tool for kidney disease announced by any company.

In an effort to curtail the estimated $114 billion annual cost of chronic and end-stage renal disease in the United States, KidneyIntelX was designed to diagnose and improve the clinical management of patients with type 2 diabetes and fast-progressing kidney disease. The device will use a combination of machine learning algorithms to assess the combination of predictive blood-based biomarkers, including sTNFR1, sTNFR2, and KIM1, and information in electronic health records to identify progressive kidney disease. KidneyIntelX is being developed in collaboration with the Mount Sinai Health System, New York, New York.

The Breakthrough Devices Program speeds up the development, assessment, and review process for certain medical devices to enable timely access to the devices for patients and healthcare providers. Sally Bowden, chief operating officer at RenalytixAI, said, “This designation is a significant advancement towards our goal of bringing to market a solution that can greatly improve the identification and treatment of patients with chronic kidney disease. We look forward to continuing to work closely with the FDA through this process, including on our data development plan, our clinical validation, and or subsequent submission for regulatory clearance.”

Erik Liun, PhD, executive vice president of Mount Sinai Innovation Partners, said, “We’re pleased RenalytixAI has received Breakthrough Designation for KidneyIntelX, providing the opportunity to work hand-in-hand with the FDA towards the goal of FDA submission. Renal disease represents an increasing healthcare crisis globally, and early detection and intervention is essential in changing the course of this disease.”

KidneyX Redesign Dialysis Award to Renal Research Institute

In a press release from Fresenius Medical Care North America, the Renal Research Institute, a division of Fresenius Medical Care North America, announced that its novel concept for “displacer-enhanced dialysis” has been selected as a winner of the KidneyX Redesign Dialysis competition. The institute plans to develop a new displacer substance that can rid the blood of protein-bound uremic toxins that are difficult to remove via hemodialysis. KidneyX (the Kidney Innovation Accelerator) is a partnership between the US Department of Health and Human Services and the American Society of Nephrology to increase innovation in the prevention, diagnosis, and treatment of kidney diseases. The Renal Research Institute is one of 15 winners of the first phase of the Redesign Dialysis competition.

Robert Kossman, MD, chief medical officer, Fresenius Medical Care North America, said, “This competition is a new opportunity to advance innovations that will hopefully improve outcomes for all patients with renal disease. This award to the RRI team further demonstrates our ongoing commitment to turning research into practical solutions and new technologies.”

There are associations between higher levels of protein-bound uremic toxins and poorer outcomes in chronic kidney disease. Using “displacer-enhanced dialysis” infuses a displacer substance into the dialysis machine’s blood tubing upstream of the artificial kidney, outside the patient’s body. The displacer binds to the same binding sites on albumin as the toxins, displaces them for the albumin molecule, allowing them to be easily removed in the artificial kidney. The goal of the Renal Research Institute’s proposal is to continue the search for ideal displacer substances that can be used routinely in chronic hemodialysis.

Analysis of Data on Hepatorenal Syndrome at International Liver Congress™

In late spring, researchers presented results of a retrospective analysis of data on hepatorenal syndrome type 1 (HRS-1) at the 2019 International Liver Congress™ of the European Association for the Study of the Liver in Vienna, Austria. HRS-1 is a rare and acute condition characterized by the development of rapid kidney failure in patients with advanced chronic liver disease.

The phase 3 REVERSE clinical trial was conducted to examine the impact of applying revised International Club of Ascites (ICA) diagnostic criteria for HRS-1 on the timing of treatment and the level of serum creatinine at time of treatment. Results of the current study continue on page 26.

Researchers in Polycystic Kidney Disease Honored

The Lillian Jean Kaplan International Prize for Advancement is the most prestigious prize in the field of polycystic kidney disease (PKD). The prize recognizes researchers whose work results in tangible achievement toward improving knowledge and treatment of PKD, and is awarded by the PDK Foundation.

In a recent press release, Andy Betts, chief executive officer of the PDK Foundation, announced that York Pei, MSc, MD, FRCP, professor of medicine at the University of Toronto and Bradley Yoder, PhD, professor and chair of the department of cell, development, and integrative biology at the University of Alabama at Birmingham Medical School, are the most recent recipients of the Kaplan Prize. Both researchers received $50,000 and the opportunity to lecture about their research at the World Congress of Nephrology in Melbourne, Australia.

Dr. Pei’s work focuses on genetic, genomic, clinical, and translational research to advance the diagnosis, prognosis, and development of novel treatment of autosomal dominant polycystic disease. Dr. Yoder’s research has focused on determining the function of the primary cilium in multiple tissues, with an interest in how loss of cilia function contributes to development of cysts in the kidney.

“It is my distinct honor to present both Dr. Pei and Dr. Yoder with the Lillian Jean Kaplan International Prize for their most significant research in the polycystic kidney field... The pioneering studies of these researchers provide great hope for the future of all PKD patients,” Mr. Betts said.
analysis were reported during a poster session in a poster titled ‘The Diagnosis of Hepatorenal Syndrome (HRS): How Much Does Use of the 2015 Revised Consensus Recommendations Affect Earlier Treatment and Serum Creatinine (SCr) at Treatment Start?’ (poster #SAT-141). The analysis was supported by Mallinckrodt.

The analysis estimated that applying revised ICA Acute Kidney Injury-HRS diagnostic criteria rather than traditional HRS-1 diagnostic criteria would result in earlier treatment by approximately 4 days, average level of serum creatinine at treatment initiation would be approximately 1 mg/dL lower on average, and 47% of patients would receive treatment prior to a further ≥1.5-fold increase in serum creatinine.

**Outset Medical Wins KidneyX Redesign Dialysis Prize**

Outset Medical has been named a winner of the KidneyX Redesign Dialysis Competition for a project featuring the Tablo™ Hemodialysis System. Outset is a commercial-stage company delivering innovative technology to the global dialysis market. The winning concept aims at coupling data from Tablo’s unique set of sensors and automation capabilities with physiologic data from the patients to deliver personalized dialysis treatments, with an eye toward improving patient outcomes.

The US Department of Health and Human Services and the American Society of Nephrology have partnered to create the KidneyX Redesign Dialysis Competition to support innovative strategies for the management of kidney disease. Outset is one of 15 winners selected for the award.

In a press release, Michael Aragon, MD, chief medical officer at Outset Medical, said, “Dialysis technology has changed little in 30 years and continues to rely on a cookie-cutter approach to treating patients. Other disease areas such as cancer, heart failure, and diabetes have rapidly moved towards delivering more personalized treatment based on the underlying physiology of the patient. In dialysis, we have intimate contact with the same patient’s blood for over 600 hours a year while inducing significant, controlled physical and chemical changes. We need to use these data to tailor our approach and deliver a better patient experience and improved clinical outcomes.”

Leslie Trigg, Outset’s chief executive officer, added, “We are very appreciative of the recognition and the opportunity to partner with the KidneyX program to help bring more innovation to the renal space. While we are proud of our technology development, we are just getting started. The opportunity to transform dialysis care through software, sensors, and predictive data analytics is vast, and achievable.”
News Briefs

Fresenius Medical North America Organizational Changes

Following a merger with NxStage Medical, Inc., Fresenius Medical Care North America has announced some organizational changes. Jeff Burbank, former NxStage founder and chief executive officer, will serve as chief technology officer of Fresenius. Joe Turk, former president at NxStage, will assume the role of president of home and critical care therapies at Fresenius. Both men will report to Bill Valle, Fresenius chief executive officer. “I’m thrilled that we are bringing these talented groups together under Jeff and Joe’s leadership to ensure we continue to seamlessly integrate the incredible experience and groundbreaking technology from the NxStage team directly into Fresenius Medical Care North America. Under their leadership, we will centralize our focus on home therapies that are giving life back to our patients with kidney failure by offering more freedom, control, and better health,” Mr. Valle said in a press release.

ANNA Launches Podcast in Celebration of 50th Anniversary

2019 marks the 50th anniversary of the American Nephrology Nursing Association (ANNA). The association is marking the anniversary with a multilayered tribute to the nephrology nurses who have had a crucial part in advances in nephrology treatments, patient care, and healthcare legislation. The tribute includes ANNA’s 50th Anniversary Podcast Series, a 50th anniversary issue of Nephrology Nursing Journal, and a video titled Nephrology Nursing: The Career of a Lifetime. Tamara Kear, PhD, RN, CMS, CNN, president of ANNA, said, “Nurses have the knowledge, ability, and tools to innovate and advocate, now more than ever.”

According to a press release from ANNA, the podcast series documents ways “nephrology nurses have been leaders and innovators, working with inventors, physicians, and patients to pave the way for the specialty to evolve into the life-saving science it is today.” Beth Ulrich, EdD, RN, FACHE, FAAN, described the series as an oral recounting of ANNA, nephrology nursing, and patient care. The podcast includes interviews with nephrology nurse leaders. “The interviews capture what nursing was like as a profession from the 1960s to the present,” Dr. Ulrich said. “The podcast also shows the tremendous impact of specialty organizations like ANNA on the lives of patients and nurses.” The series is available on iTunes, Google Play-Music, Spotify, Stitcher, Tunein, Spreaker, and other podcast delivery services.

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Conservative Kidney Management Recommendations for Patients with CKD

Clinical Journal of the American Society of Nephrology. doi.org/10.2215/CJN.10510917

For patients with estimated glomerular filtration rate category 5 chronic kidney disease (CKD) who are deemed unlikely to benefit from dialysis and/or who choose a nondialysis option, conservative kidney management is increasingly accepted as an appropriate treatment option. However, according to Sara N. Davison, MD, MSc, and colleagues, there is no clear consensus on the optimal model for delivery of care. A set of recommendations specific to conservative kidney management has been developed as part of the development of a conservative kidney management pathway that is currently being evaluated. The recommendations are designed to manage the complications and common symptoms of CKD, and focus on the values and preferences of the patient. The guidelines seek to optimize comfort and quality of life for this patient population.

This review provides explanations for the suggested interventions to support the shared decision-making process among healthcare professionals, patients, and family members. Generally, the recommendations emphasize the reservation of function (cognitive, physical, and renal) and address symptom burden. The guidelines also take into account the possibility that management priorities may change over time. Other key elements of conservative management should be used in conjunction with the new recommendations, including clear communication and shared decision making, advance care planning, and psychosocial support.

The researchers said, “Although there are limitations to the existing evidence specific to conservative kidney management, these recommendations are intended as a starting point toward reaching consensus and generating further evidence.”

Patients and Nephrologists Rate Smartphone-Based Self-Care Applications


Patient self-care is an important element in management of chronic kidney disease (CKD), particularly related to medication and dietary adherence, self-monitoring of blood pressure, and daily physical activity. There are data that suggest the benefits of incorporation of smartphone-based applications designed to support self-care in chronic disease and CKD.

Karandeep Singh, MD, MS, and colleagues recently conducted an analysis of smartphone applications that target patients with CKD. The researchers conducted a search of the US Apple App Store (iOS) and Google Play Store (Android) using the terms kidney disease, renal, dialysis, and kidney transplant. The first 50 applications for each search term on each application store were considered in the current analysis. The applications were evaluated using a previously described framework for assessment of mobile health applications. Applications were evaluated on their types of patient engagement, quality, usability, and safety.

Engagement and quality were assessed by both a patient and a nephrologist, usability was assessed by a patient, and safety was assessed by a nephrologist. In total, the evaluations were conducted by two patients with CKD and three nephrologists.

The search identified 174 unique applications on the Android platform and 168 unique applications on iOS. Following exclusion of applications not related to kidney disease, those that were not patient facing, and those that were last updated prior to 2014, the current analysis included 12 Android-only applications, 11 iOS-only applications, and five dual-platform applications. Patient and nephrologist application quality ratings, assessed by the net promoter score, were not correlated (r=0.36; P=.06). There was no correlation between consumer ratings on the application stores and patient ratings of application quality (r=0.03; P=.18).

“Only a small subset of CKD applications was highly rated by both patients and nephrologists. Patients’ impressions of application quality are not directly linked to consumer applications ratings or nephrologist impressions,” the researchers concluded.

Peripheral Nerve Function in Patients with CKD

Nephrology Dialysis Transplantation. 2019;34(4):625-632

Poor mobility is a common complication of chronic kidney disease due, in part, to alterations in peripheral nerve functions. Ranjani N. Moorthi, MD, and colleagues recently conducted an analysis designed to test the hypothesis that early CKD is associated with altered sensory, motor, and autonomic nerve function.

The cohort included participants in the Health, Aging and Body Composition who had kidney function measures in year 3 (1999-2000) and nerve function measurements at year 4 (2000-2001) (n=2290). The researchers compared sensory (vibration threshold, monofilament insensitivity to light, and standard touch), motor (compound motor action potentials [CMAPs], nerve conduction velocities [NCVs]), and autonomic (heart rate response and recovery after a 400-meter walk test), nerve function and participant characteristics across cystatin C- and creatinine-based estimated glomerular filtration rate categorized as ≤60 mL/min/1.73 m2 (CKD) and >60 mL/min/1.73 m2 (non-CKD). Logistic regression adjusted for covariates was used to examine the association between CKD and nerve function.

Those with CKD (n=476) were older (77 vs 75 years; P<.05) and had a higher prevalence of diabetes (20.6% vs 13.1%; P<.001) than those without CKD. There were associations between CKD and higher odds for vibration detection threshold (odds ratio [OR], 1.7; 95% confidence interval [CI], 1.1-2.7) and light touch insensitivity (OR, 1.4; 95% CI, 1.1-1.7). There were no significant differences in CMAPs and NCVs between
patients with CKD and patients without CKD. Patients with CKD had higher odds of abnormal heart rate response (OR, 1.6; 95% CI, 1.1-2.2) and poor heart rate recovery (OR, 1.6; 95% CI, 1.1-2.0) in adjusted analyses.

In conclusion, the researchers said, “CKD is associated with changes in sensory and autonomic nerve function, even after adjustment for demographics and comorbidities, including diabetes. Longitudinal studies in CKD are needed to determine the contribution of nerve impairments to clinically important outcomes.”

**Appropriateness of Antibiotic Prescribing in Patients with CKD**

*Nephrology Dialysis Transplantation. 2019;34(4):642-649*

Patients with chronic kidney disease (CKD) treated in the primary care setting are frequently prescribed excessive doses of antibiotics relative to their kidney function, according to Justin X G Zhu and colleagues. The researchers recently conducted a retrospective propensity score-match cross-sectional study to assess whether nephrology comanagement is associated with improved prescribing patterns in primary care.

The study examined the appropriateness of antibiotic prescriptions by primary care physicians to residents of Ontario ≥66 years of age with CKD stages 4 and 5 (defined as estimated glomerular filtration rate <30 mL/min/1.73 m² not receiving dialysis therapy). The study period was from April 1, 2003, to March 31, 2014. Comanagement was defined as having at least one outpatient visit with a nephrologist within the year prior to the date of the antibiotic prescription. The study compared the rate of appropriately dosed antibiotics in primary care between patients who were comanaged by a nephrologist (n=3937) and those who were not comanaged (n=329,713 patient-years of follow-up). The total cohort included 72,856 individuals. At baseline, those with overt hypothyroidism (n=704) and those with subclinical hypothyroidism (n=3356) had an average –4.07 mL/min/1.73 m² and –2.40 mL/min/1.73 m² lower eGFR, respectively, compared with euthyroid subjects (n=66,542). In (subclinical) hyperthyroidism individuals (n=2254), average eGFR was 5.01 mL/min/1.73 m² higher. Compared with individuals with normal thyroid function, eGFR did not decline more rapidly in those with low thyroid function during 329,713 patient-years of follow-up.

In conclusion, the researchers said, “Low thyroid function is not associated with a deterioration of renal function. The cross-sectional association may be explained by renal dysfunction causing thyroid hormone alterations.”

**No Association between Low Thyroid Function and Decline in Renal Function**

*Nephrology Dialysis Transplantation. 2019;34(4):650-659*

Thyroid hormone dysfunction is a common complication of chronic kidney disease (CKD). There are few data on whether this dysfunction is a cause or consequence of CKD. Christiaan L. Meuwese, MD, PhD, and colleagues conducted a study designed to examine the effect of thyroid hormone alterations on renal function in cross-sectional and longitudinal analyses in individuals from all adult age groups.

The study utilized participant data from 16 independent cohorts with measured thyroid stimulating hormone, free thyroxine levels, and creatinine levels available. Thyroid hormone status was defined using clinical cut-off values. For this IPD meta-analysis, baseline estimated glomerular filtration rate (eGFR) and change in eGFR during follow-up were computed by fitting linear regression models and linear mixed models in each cohort separately. Random effects models were used to pool effect estimates.

The total cohort included 72,856 individuals. At baseline, those with overt hypothyroidism (n=704) and those with subclinical hypothyroidism (n=3356) had an average –4.07 mL/min/1.73 m² and –2.40 mL/min/1.73 m² lower eGFR, respectively, compared with euthyroid subjects (n=66,542). In (subclinical) hyperthyroidism individuals (n=2254), average eGFR was 5.01 mL/min/1.73 m² higher. Compared with individuals with normal thyroid function, eGFR did not decline more rapidly in those with low thyroid function during 329,713 patient-years of follow-up.

In conclusion, the researchers said, “Low thyroid function is not associated with a deterioration of renal function. The cross-sectional association may be explained by renal dysfunction causing thyroid hormone alterations.”

**DIABETIC KIDNEY DISEASE**

**Uric Acid and Diabetic Complications**

*Nephrology Dialysis Transplantation. 2019;34(4):659-666*

Researchers, led by Sascha Pilemann-Lyberg, MD, PhD, conducted a cross-sectional study to assess the association between plasma uric acid and the presence of diabetic complications including diabetic nephropathy and cardiovascular risk factors. Study participants had type 1 diabetes (n=676).

Participants were recruited from the Steno Diabetes Center in Copenhagen, Denmark. The study compared participants with uric acid within the three lowest sex-specific quartiles with those with levels in the highest quartile. Unadjusted and adjusted linear regression analyses were conducted. Adjustments included sex, age, diabetes duration, body mass index, high-density lipoprotein cholesterol, smoking, hemoglobin A1c, 24-hour pulse pressure, urinary albumin excretion rate (UAER), estimated glomerular filtration rate (eGFR), and treatment with renin-angiotensin-aldosterone system blockers.

Of the 676 patients, 55% (n=372) were men, mean age was 55 years, and eGFR was 82 mL/min/1.73 m². Median uric acid was 0.30 mmol/L. In unadjusted analyses, there was an association between uric acid in the upper sex-specific quartile and lower eGFR,
Abstract Roundup

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higher UAER and carotid-femoral pulse wave velocity, and lower 24-hour and daytime diastolic blood pressure (P < 0.001). There was also an association between uric acid in the upper sex-specific quartile and higher night-time systolic blood pressure and the presence of cardiovascular disease in unadjusted analyses (P < 0.001); however, the significance was lost following adjustment (P = 0.17).

Across the retinopathy groups, uric acid was higher in unadjusted analyses; but not after adjustment. Compared with patients with slow decline in eGFR, those with accelerated decline in eGFR (≥3 mL/min/1.73 m² per year) had significantly higher uric acid at baseline in unadjusted analysis (P = 0.006); significance was lost following adjustment.

“In type 1 diabetes patients, higher uric acid was associated with lower kidney function and other diabetic complications. The association between higher uric acid and lower eGFR and lower diastolic blood pressure was independent of traditional risk factors,” the researchers said.

DIALYSIS

Cardiac Safety of SSRIs in Patients Receiving Hemodialysis


Patients on maintenance dialysis therapy may be at risk for adverse cardiac events of drug-induced QT prolongation due to the substantial cardiovascular disease burden of end-stage renal disease and the high level of polypharmacy, in addition to exposure to electrolyte shifts during dialysis. Previous data have shown that among selective serotonin reuptake inhibitors (SSRIs), citalopram and escitalopram prolong the QT interval to the greatest extent. However, according to Magdalene M. Assimon, PharmD, MS, and colleagues, there are few data on the relative cardiac safety of SSRIs among patients on hemodialysis.

The researchers conducted a retrospective cohort study to compare the 1-year risk of sudden cardiac death among patients on hemodialysis who initiated SSRIs with a higher potential for prolonging the QT interval (citalopram and escitalopram) versus the risk among hemodialysis patients who initiated SSRIs with a lower QT-prolonging potential (fluoxetine, fluvoxamine, paroxetine, sertraline). Adjusted hazard ratios were estimated using inverse probability of treatment weighted survival models. Non-sudden cardiac death was treated as a competing event.

The study group initiating SSRIs with higher QT-prolonging potential included 30,932 patients; the group initiating SSRIs with lower QT-prolonging potential included 34,722 patients. Those initiating an SRI with higher QT prolonging potential at were increased risk of sudden cardiac death compared with those initiating an SRI with a lower QT-prolonging potential (adjusted hazard ratios, 1.18; 95% confidence interval 1.05-1.31). The association was more pronounced among elderly patients, women, patients with conduction disorders, and those treated with other non-SSRI QT-prolonging medications.

“A heterogeneous QT-prolonging potential of SSRIs may differentially affect cardiac outcomes in the hemodialysis population,” the researchers said.

Researchers Develop Summary Score to Aid Interpretation of KDQOL-36 Survey


The Kidney Disease Quality of Life 36-item short form survey (KDQOL-36) is used to measure patient-reported outcomes for patients with end-stage renal disease on dialysis. In an effort to aid interpretation of the survey results, John D. Peipert, PhD, and colleagues utilized data on 58,851 dialysis patients who participated in the Medical Education Institute (MEI) KDQOL Complete program and 44,947 patients from the US Renal Data System (USRDS) to develop the KDQOL-36 Summary Score (KSS) for kidney-targeted KDQOL-36 scales.

The scales of interest were Burdens of Kidney Disease (BKD), Symptoms and Problems of Kidney Disease (SPKD), and Effects of Kidney Disease (EKD) Data from MEI and USRDS were used to calculate normative values for the Short Form-12 Health Survey’s Physical Component Summary (PCS) and Mental Component Summary (MCS), and the KDQOL-36 BKD, SPKD, and EKD scales for the dialysis population in the United States. A bifactor confirmatory factor analysis fit the data well, supporting the KSS. Mean dialysis normative scores were PCS=37.8 and MCS=50.9; and KSS=73.0, BKD=52.8, SPKD=79.0, and EKD=74.1 (0-100 possible score).

“The KSS is a reliable summary of the KDQOL-36. The United States KDQOL-36 normative facilitate interpretation and incorporation of patient-related outcomes measures into kidney disease care,” the researchers said.

PEDiatric END-STAGE Renal disease

Hemodiafiltration versus Hemodialysis in Children


Children undergoing dialysis often experience hypertension and cardiovascular disease. Previous studies in adults have shown that hemodiafiltration (HDF) may reduce cardiovascular mortality; however, there are few data on the effects of HDF in children.

Rukshana Shroff, MD, FRCPCH, PhD, and colleagues conducted a nonrandomized observational study. The HDF, Heart and Height Study compared outcomes of conventional hemodialysis versus postdilution online HDF in children. The primary outcomes of interest were annualized changes in carotid intima-media thickness (cIMT) standard deviation (SD) score and height SD score.

The study enrolled 190 children from 28 centers; of those, 78 were receiving hemodialysis and 72 were on HDF. Follow-up was 1 year. The groups were comparable in terms of age, dialysis vintage, access type, dialysis frequency, blood flow, and residual renal function. At follow-up, there was significant increase in the cIMT score in the group on HDF; the score remained static in the group on hemodialysis. On propensity score analysis, there was an association between hemodialysis and a +0.47 higher annualized cIMT SD score compared with HDF. Height SD score increased in the HDF group but remained static in the hemodialysis group. There was an increase in mean arterial pressure SD score in the hemodialysis group but not in the HDF group.

Factors associated with higher cIMT and mean arterial pressure SD scores were hemodialysis group, higher ultrafiltration rate, and higher β2-microglobulin. Children in the HDF group had lower β2-microglobulin, parathyroid hormone, and high-sensitivity C-reactive protein at 1 year, as well as fewer headaches, dizziness, or cramps, and shorter postdialysis recovery time.

In conclusion, the researchers said, “HDF is associated with a lack of progression in vascular measures versus progression with hemodialysis, as well as an increase in height not seen in the hemodialysis cohort. Patient-related outcomes improved among children on HDF correlating with improved blood pressure control and clearances. Confirmation through randomized trials is required.”
Controversy over Commercial Insurance

Earlier this year the California Assembly passed AB 290, a bill with the stated purpose of “preventing dialysis companies from increasing their already excessive corporate profits through a scheme to bankroll patients’ health care premiums,” according to the official website of California Assembly member Jim Wood.

The bill, which is now under consideration by the California Senate, would require the identity of dialysis patients whose insurance premiums are paid by a financially interested provider to be disclosed to their health insurance company. The insurance company is required to accept the commercial insurance premiums and reimburse the patient’s dialysis claims at the Medicare rate, which is normally significantly lower than the commercial rate. Collecting high premiums and reimbursing claims at lower rates is a good deal for the insurance company.

In my years billing for dialysis facilities, I have had little interaction with dialysis programs large enough to have massive corporate profits. The facilities served by Sceptre Management are independent free-standing or hospital-based dialysis programs that fall under the category of small or medium dialysis organizations, some as small as five patients. In a small dialysis facility, the reimbursement from government payers is often at or below the cost of providing treatment. Thus, even one patient with a commercial policy that pays more than the Medicare allowed amount can make a big difference in the financial viability of the entire dialysis program.

The revenue a dialysis facility generates can seem like a large amount of money if we disregard the costs of providing treatment, including supplies, medications, water systems, dialysis machines, labor, and more. In 2017, a renal industry association report found the cost of a dialysis treatment in a small free standing dialysis facility was approximately $240. In comparison, Medicare’s 2017 Base Rate for a dialysis treatment was $231.55.

To illustrate the difference commercial payers can make in a dialysis facility, let’s look at the revenue for two facilities: one that receives all reimbursements at the Medicare rate and one where just over 5% of the patients have commercial coverage with premiums that are paid by charitable premium assistance. Both facilities have 35 patients, and each patient receives an average of 12 treatments per month for a total of 420 treatments per month. To keep the revenue in perspective, assuming our example facilities spend $240 per treatment, it would cost $100,800 to provide 420 dialysis treatments (see Table).

In this example, two patients are the difference between losing money each month and having a small profit to put back into the program. Collecting 100% of the Medicare allowed amount does not always cover all the costs associated with a patient’s dialysis treatments. The reimbursement received from commercial payers, when above the Medicare rate, can be the difference that allows a small, independent dialysis program to remain independent and continue providing dialysis treatments.

**ADMINISTRATOR INSIGHT**

I spoke with the administrator of a small dialysis program to discuss what it means to their program when they receive reimbursement from commercial policies that pay more than the Medicare allowed amount. She explained that in her area there is a profound shortage of dialysis technicians, so they have an abnormally high number of RNs on staff; resulting in extraordinarily high labor costs. Her facility would find it difficult to pay bills on time, make upgrades to the program, or save money for emergencies such as equipment failures if there were no patients whose insurance reimbursed above the Medicare rate. She candidly explained that without reimbursement from commercial payers, her program would find it difficult to keep the doors open.

Sarah Tolson is the director of operations for Sceptre Management Solutions, Inc., which specializes in billing for outpatient ESRD facilities, nephrology practices, and vascular access. Your questions are welcome and she can be reached at stolson@sceptremanagement.com, 801.775.8010, or via Sceptre’s website: www.sceptremanagement.com.

<table>
<thead>
<tr>
<th>Facility 1</th>
<th>Facility 2</th>
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<tr>
<td>Number of Medicare patients</td>
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<td>Number of commercial patients</td>
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<td><strong>Total Medicare treatments</strong></td>
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<td><strong>Total commercial treatments</strong></td>
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<td>Medicare allowed reimbursement ([231.55*420])</td>
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<td><strong>Total Medicare collectable</strong></td>
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<td>Commercial payment ($500 per treatment)</td>
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<td><strong>Total payments</strong></td>
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<td>Cost of providing treatments ($240 X 420 treatments)</td>
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<tr>
<td>Difference between expenses and revenue</td>
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The PRISMAX control unit is intended for:
Continuous Renal Replacement Therapy (CRRT) for patients weighing 20 kilograms or more with acute renal failure and/or fluid overload.
Therapeutic Plasma Exchange Therapy (TPE) for patients with diseases where removal of plasma components is indicated.
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