Nephrology Times

Practical News, Trends, and Analysis

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Correcting Potassium in Hypokalemia to Improve Outcomes

Chronic kidney disease (CKD) is a public health concern worldwide. The prevalence of kidney failure requiring renal replacement therapy (RRT) is increasing, with an expectation of doubling of the numbers in this decade.

The numbers are expected to increase substantially in Asia. In 2016, the estimated number of patients receiving RRT in Thailand was 346 per million, representing a tripling from the previous decade. The modality of choice for RRT in Thailand is peritoneal dialysis, and the number of patients receiving peritoneal dialysis has increased 10-fold over the past 10 years.

Hypokalemia, serum potassium level below 3.5 mEq/L, is a frequent complication of peritoneal dialysis. In results of PDOPPS (Peritoneal Dialysis Outcomes and Practice Patterns Study), there is wide variation in the prevalence of hypokalemia in patients receiving peritoneal dialysis among participating countries (from 3% to 47%).

Hypokalemia is a common electrolyte abnormality in that patient population and had been associated with increased risks of peritonitis and death. It is unknown whether correction of hypokalemia improves those outcomes. Previous studies have suggested that low dietary potassium, as opposed to increased potassium excretion, is the primary contributing factor to hypokalemia in maintenance peritoneal dialysis.

continued on page 5

Ultraprocessed Food Consumption and CKD Risk

Ultraprocessed foods and beverages are processed industrially and contain little to no intact foods; they are composed primarily of ingredients extracted from foods and include nonculinary substances and artificial additives meant to enhance shelf life and palatability. Ultraprocessed foods are high in added sugar, refined carbohydrates, saturated and trans fats, sodium, and they contain low amounts of fiber, protein, and micronutrients.

Consumption of ultraprocessed foods is on the rise in the United States and worldwide. Previous studies have examined the link between consumption of ultraprocessed foods and cardiovascular diseases, all-cause mortality, and cancers.

continued on page 4

Racial Disparities in Risk of Hospitalized AKI Among Patients With CKD

Compared with White Americans, Black Americans face a disproportionately higher risk of kidney failure. This disparity may be due to a combination of clinical, socioeconomic, and genetic risk factors. There have been multiple studies examining contributors to racial disparities in chronic kidney disease (CKD), including kidney failure. However, there are few data available regarding racial variations in acute kidney injury (AKI).

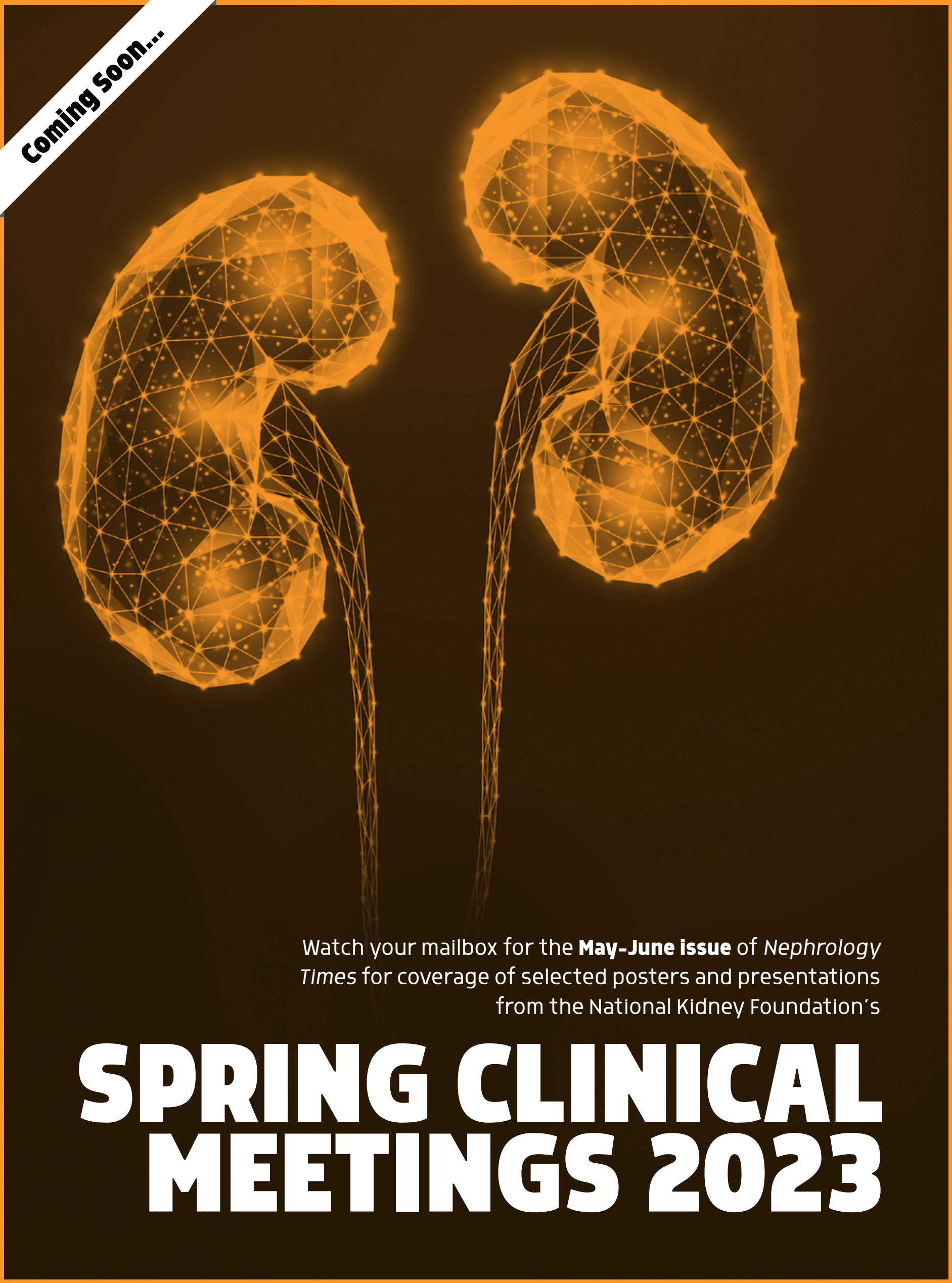
Results of previous studies have suggested that the risk of AKI is higher among Black Americans than among White Americans. However, according to **Anthony N. Muiru, MD, MPH,** and colleagues, those results were limited by inclusion of patients with diabetes or trauma or those undergoing procedures such as percutaneous coronary intervention or knee surgery.

Dr. Muiru et al conducted a prospective cohort study to examine the association of race with hospitalized AKI following adjustment for clinical, socioeconomic, and genetic risk factors among Black and White Americans with CKD. Results were reported in the *American Journal of Kidney Diseases* [2022;80(5):610-618].

The analysis utilized data from the CRIC (Chronic Renal Insufficiency Cohort) Study to estimate rates of hospitalized AKI, defined by changes in serum creatinine level. The cohort included self-identified Black and White participants with CKD enrolled in the CRIC Study from July 1, 2013, to December 31, 2017.

continued on page 14

Coming Soon...



Watch your mailbox for the **May–June issue** of *Nephrology Times* for coverage of selected posters and presentations from the National Kidney Foundation's

SPRING CLINICAL MEETINGS 2023

Effectiveness of Combined RAS and SGLT2 Inhibitor Therapy in Patients With CKD

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Studies point to under-utilization of renin-angiotensin system (RAS) blockade in patients with chronic kidney disease (CKD) despite strong evidence favoring their use for both renal and cardiac protection. Indeed, only a fraction (approximately 30%-40%) of patients with CKD who should be receiving treatment are treated with a RAS blocker based on real-world evidence.[1,2] Concerns about acute kidney injury, hyperkalemia, and cough seem to be limiting factors.

Multimodal therapy approaches such as RAS blockers and sodium-glucose cotransporter-2 (SGLT2) inhibitors, glucagon-like peptide 1 receptor agonists (GLP1RAs), and nonsteroidal mineralocorticoid receptor antagonists (nsMRA) are increasingly suggested in guidelines as "pillars" in slowing CKD progression and providing cardioprotection in patients with CKD and type 2 diabetes.[3] In patients with non-diabetic CKD, the use of both RAS blockade and SGLT2 inhibition is emerging as a mainstay of treatment. Still, if one modality, namely RAS blockade, is being underutilized, it is reasonable to ask what is the likelihood that a strategy using multiple agents will be adopted? Indeed, data support limited uptake of newer agents.[1,4,5]

Fifty years ago, Archie Cochrane, widely considered the father of evidence-based medicine (EBM), proposed the term *effectiveness* as a measure of "a particular medical action in altering the natural history of a particular disease for the better."[6] Cochrane emphasized the importance of randomized controlled trials and summarizing of trial data from multiple studies in the form of systematic reviews and/or meta-analysis. Beyond this, a basic tenet in EBM is to express benefits of treatment in ways that are more easily understood.[7]

An elegant and well-done study, published recently by Priya Vart and colleagues[8] in the *Clinical Journal of the American Society of Nephrology,* adopts the Cochrane framework of summarizing evidence from well-designed trials to estimate the cumulative effect of combination therapy with angiotensin-converting enzyme inhibitors (ACE)/angiotensin receptor blockers (ARBs) and SGLT2 inhibitors compared with no treatment in effecting "extra years free from the disease or death" in patients with albuminuric CKD without diabetes. The point being that this latter term "of extra years" is more accessible than describing benefit in statistical terms such as "a reduction in relative risk."

Vart and colleagues calculated the event-free survival related to combination therapy with ACE inhibitors/ARBs and SGLT2 inhibitors and then calculated the estimated event-free survival for patients not treated with ACE inhibitors/ARBs and SGLT2 inhibitors. In their modelling the primary end point was a composite of a sustained doubling of serum creatinine, kidney failure (defined as a sustained estimated glomerular filtration rate ≤15 mL/min/1.73 m^2, initiation of dialysis for at least 30 days, or kidney transplantation), or all-cause mortality.

The purported benefits of combination therapy in the Vart analysis are impressive: an absolute risk benefit when treated with the combination of ACE inhibitor/ARB and SGLT2 inhibitor of 17%–29% over 3 years for the primary composite end point; number needed to treat of four to six to prevent one primary composite end point.

Vart et al arrive at an easily understood conclusion: "A patient of age 50 years with albuminuric CKD without diabetes, when treated with a combination of ACE inhibitors/ARBs and SGLT2 inhibitors, may experience about 7 additional years free of kidney failure and death compared with a person not treated with these agents."

There are, of course, limitations to the Vart analysis. Foremost is the assumption that the effects of RAS inhibition and SGLT2i therapy are additive (between 120% and 50%). Second, that the effect is long-lasting and assumes compliance with the therapies (between 50% and100%). These limitations are acknowledged by the authors.

The bottom line is that in addition to the primary trial data, say from the DAPA-CKD study where tremendous benefit in cardio-renal protection as demonstrated in nondiabetic CKD patients,[9] a modeled analysis like the one by Vart and colleagues underlines the benefit of combining RAS blockade and SGLT2i therapy in real terms in nondiabetic CKD patients; such an analysis in type 2 diabetes mellitus with CKD is likely to demonstrate similar results.

Combination therapy with a RAS blocker and an SGLT2 inhibitor should be a top priority in managing nondiabetic CKD. ■

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Ultraprocessed Food Consumption

continued from page 1

There are few available data on the impact of consumption of ultraprocessed food on renal health.

Shutong Du, MHS, and colleagues conducted a prospective cohort study designed to examine the association between ultraprocessed food consumption and incident chronic kidney disease (CKD). Results of the study were reported in the *American Journal of Kidney Diseases* [2022;80(5):589-598].

The study included 14,769 adults without CKD at baseline in the ARIC (Atherosclerosis Risk in Communities) study. The study exposure was consumption of ultraprocessed foods (servings per day), calculated using dietary data collected via a food frequency questionnaire at visit 1 and visit 3.

The primary outcome of interest was incident CKD, defined as estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2, accompanied by ≥25% decline in eGFR, CKD-related hospitalization or death, or kidney failure requiring renal replacement therapy.

The association between consumption of ultraprocessed foods and CKD was assessed using multivariable-adjusted Cox proportional hazards models. The shape of the association was examined using restricted cubic splines.

Of the 14,769 patients included in the current analysis, 55.1% were female and 25.2% were Black. Mean age was 54.1 years and mean body mass index (BMI) was 27.6 kg/m^2. More than two-fifths had an education level higher than a high school diploma (44.4%) and never smoked tobacco (41.5%). More than half never drank alcohol (56.7%).

Participants were stratified into quartiles based on mean energy-adjusted ultraprocessed food consumption. In quartile 4, mean energy-adjusted ultraprocessed food consumption was 8.4 servings per day, compared with 3.6 servings per day in quartile 1. Participants in the highest quartile of ultraprocessed foods were younger, more likely to be White and former smokers, and more likely to have obesity and lower levels of physical activity. Those who consumed more ultraprocessed foods also had lower overall diet quality.

There were associations between ultraprocessed food consumption and lower intake of protein, cholesterol, fiber, and micronutrients, including niacin, vitamin A, vitamin B_6, vitamin B_{12}, calcium, phosphorus, magnesium, and potassium, and a higher intake of fat (total, saturated, monounsaturated, and polyunsaturated). Those in the highest quartile had lower consumption of fruits and vegetables, and higher consumption of sugar-sweetened beverages. The food groups that contributed the most to consumption of ultraprocessed foods were sugar-sweetened beverages (27%), margarine (18%), bakery goods (15%), and ultraprocessed meats (11%).

The follow-up period was a median of 24 years. During the follow-up period, there were 4859 cases (34.0%) of incident CKD. Among those in the highest quartile of ultraprocessed food consumption the incidence rate of incident CKD was 12% higher (16.5; 95% CI, 15.6-17.4 per 1000 person-years) compared with those in the lowest quartile (14.7; 95% CI, 13.9-15.5 per 1000 person-years). There was an association between higher intake of ultraprocessed foods and a higher risk of incident CKD; results were consistent across different models.

In model 1, adjusting for age, sex, race-center, and total energy intake, those in the highest quartile had a 27% higher risk of incident CKD compared with those in the lowest quartile (hazard ratio [HR], 1.27; 95% CI, 1.17-1.37). Results were similar in the main model (model 2) that was further adjusted for education level, smoking status, and physical activity (HR, 1.24; 95% CI, 1.15-1.35 for quartile 4 vs quartile 1). Following additional adjustment for potential mediators (model 3), results were attenuated, but the association between ultraprocessed food consumption and incident CKD remained statistically significant (HR, 1.16; 95% CI, 1.07-1.26 for quartile 4 vs quartile 1).

There was a significant association between each additional serving of ultraprocessed food consumed per day and a 5% higher risk of incident CKD, using the composite definition of CKD (model 2 HR, 1.05; 95% CI, 1.04-1.07; $P<.001$), as well as the visit-based definition of CKD (model 2 HR, 1.05; 95% CI, 1.03-1.07; $P<.001$).

There was a significant association between replacing one serving per day of ultraprocessed food with minimally processed food and a 6% lower risk of incident CKD (HR, 0.94; 95% CI, 0.93-0.96; $P<.001$). There was also an association between higher intake of unprocessed or minimally processed foods and a lower risk of CKD. In the main model, those in the highest quartile of minimally processed food intake had a 10% lower risk of incident CKD compared with those in the lowest quartile (model 2 HR, 0.90; 95% CI, 0.83-0.98 for quartile 4 vs quartile 1; $P=.003$).

In citing limitations to the study findings, the researchers included the use of self-reported dietary data that are prone to measurement error and recall bias, use of a food frequency questionnaire that was not specifically designed to collect data on consumption of ultraprocessed foods, and the observational design that may have resulted in findings of reverse causality.

In summary, the authors said, "In this large prospective cohort of middle-aged adults, higher ultraprocessed food consumption was associated with a higher risk of incident CKD. This association was independent of CKD risk factors, was not entirely explained by potential mediating health conditions and diet quality, and was consistent across subgroups of the study population by sex, race, BMI, diabetes status, and hypertension status. Given the rise of ultraprocessed foods in the global food supply, our study provides further support to avoid ultraprocessed foods and to replace ultraprocessed foods with minimally processed or unprocessed foods. These findings should be confirmed in other settings and other populations, and further studies should explore the specific mechanisms by which ultraprocessed foods may be harmful to the kidneys." ■

TAKEAWAY POINTS

- Researchers reported results of a prospective cohort study designed to examine the impact of consumption of ultraprocessed foods on the risk of incident chronic kidney disease (CKD).
- There was an independent association between higher consumption of ultraprocessed foods and a higher risk of incident CKD in a general population.
- The association remained even after adjustment for known CKD risk factors and across subgroups by sex, race, body mass index, and diabetes and hypertension status.

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Correcting Potassium in Hypokalemia

continued from page 1

There are no data evaluating whether correction of hypokalemia through potassium supplementation would mitigate the risk of peritonitis. **Watthikorn Pichitporn, MD,** and colleagues conducted a multicenter, open-label, prospective, randomized controlled trial to examine the efficacy and safety of protocol-based potassium treatment over 12 months for reducing peritonitis in peritoneal dialysis patients with hypokalemia. Results were reported in the *American Journal of Kidney Diseases* [2022;80(5):580-588].

The study cohort included adults ≥18 years of age receiving peritoneal dialysis with hypokalemia, defined as one of two of these criteria in the previous 6 months: (1) spot serum potassium values below 3.5 mEq/L on at least three measurements or (2) an average serum potassium value below 3.5 mEq/L. Exclusion criteria were peritonitis within 3 months, receiving hybrid RRT, Child class C liver cirrhosis, chronic infection, cancer, or gastrointestinal disease. Randomization was stratified according to center and residual urine output (≤100 or >100 ml/day).

The study interventions were random assignment to either protocol-based potassium supplementation (titratable dose of oral potassium chloride to maintain serum potassium of 4-5 mEq/L) or conventional potassium supplementation (reactive supplementation when serum potassium is <3.5 mEq/L) over 52 weeks. Intention-to-treat analyses using Cox proportional hazards regression were used to compare treatment groups.

The primary outcome of interest was the time from randomization to the first episode of peritonitis (any organism). Secondary outcomes included all-cause mortality, cardiovascular mortality, hospitalization, and conversion to hemodialysis.

Screening occurred between January 2020 and May 2021. A total of 809 patients were screened; of those, 208 were eligible and 167 underwent 1:1 randomization. Following randomization, seven participants in the intervention group did not complete the study. Median study follow-up was 401 days. The two groups were similar in follow-up time.

The two groups were balanced in baseline characteristics. The mean time-averaged serum potassium concentrations at baseline were similar in the intervention and control groups (3.32 and 3.35 mEq/L, respectively). During the study period, the average serum potassium level in the intervention group increased to 4.04 mEq/L at the first 4 weeks and remained at levels ranging from 4.23 to 4.45 mEq/L. In the control group, the average serum potassium level ranged from 3.47 to 3.74 mEq/L.

Further, in the protocol-based treatment group, serum potassium was achieved at target ranges and was significantly higher than with conventional treatment throughout the study period. Time-averaged serum potassium level in the intervention group was 3.97 mEq/L throughout the study period, compared with 3.47 mEq/L in the control group ($P<.001$).

Thirteen participants in the intervention group experienced peritonitis (13 episodes) compared with 24 participants in the control group (25 episodes) in the follow-up period. Median time to the first episode of peritonitis was significantly longer in the intervention group than in the control group (233 days vs 133 days, respectively; $P=.03$). The proportion of participants without peritonitis was significantly greater in the intervention group than in the control group (29% vs 15%, respectively; $P=.03$). There was no statistically significant difference between the two groups in the overall rate of peritonitis.

The intervention group had a significantly lower hazard of peritonitis (hazard ratio, 0.47; 95% CI, 0.24-0.93) compared with the control group. There were no significant differences in hazards between the two groups for any of the secondary outcomes.

Mean prescribed potassium supplement dosages were 25 mEq/d in the intervention group and 12 mEq/d in the control group. A total of 69 participants in the intervention group (81%) received potassium supplementation throughout the entire study period; the remainder had potassium temporarily withheld due to hyperkalemia.

Oral potassium supplements were generally well tolerated in both groups. Three participants in the intervention group were withdrawn from the study due to diarrhea. Hyperkalemia (defined as serum potassium level >6 mEq/L) occurred in participants in the intervention group only, with an incidence of 4% (3/85, one episode per participant). All episodes of hyperkalemia were asymptomatic and had no associated characteristic electrocardiogram changes.

Limitations to the study findings cited by the authors included calculating the sample size assuming no competing event; the open-label design that may have introduced observer and performance biases; not measuring potassium in urine, peritoneal dialysis effluent, and diet; and difficulty in follow-up with some participants due to the study being conducted during the COVID-19 pandemic.

In conclusion, the researchers said, "Protocol-based oral potassium supplementation to maintain serum potassium concentration in the range of 4-5 mEq/L appears to be safe and may reduce the risk of peritonitis in hypokalemic peritoneal dialysis patients compared with reactive potassium supplementation when serum potassium falls below 3.5 mEq/L." ■

TAKEAWAY POINTS

- Patients on peritoneal dialysis may experience hypokalemia, an electrolyte abnormality that is associated with increased risk of peritonitis and death.
- Researchers conducted a study to examine whether correction of hypokalemia via protocol-based potassium supplementation or conventional potassium supplementation would improve those outcomes.
- During the mean study follow-up period, serum potassium levels in the protocol-treated group increased to 4.86 mEq/L compared with 3.57 mEq/L in the group treated conventionally.

Conference Coverage

Orlando, Florida | November 3-6, 2022

KIDNEY WEEK 2022

The American Society of Nephrology Kidney Week 2022 included presentations and posters highlighting the latest findings in kidney health research, as well as sessions on advances in the care of patients with kidney and related disorders.

This is part two of our coverage of Kidney Week 2022.

Acceptable Benefit-Risk Profile of Tolvaptan in Number Needed to Harm Analysis

Autosomal dominant polycystic kidney disease (ADPKD) is the most prevalent monogenic kidney disease. ADPKD is associated with a risk for progression to loss of kidney function and kidney failure. Tolvaptan has been approved to slow decline in kidney function in adults with rapidly progressing ADPKD.

The FDA Risk Evaluation and Mitigation Strategy program closely monitors the potential risk of liver injury in patients treated with tolvaptan. **Sasikiran Nunna, PhD,** Otsuka Pharmaceutical Development & Commercialization, Inc, and colleagues conducted a study to examine the safety profile of tolvaptan related to liver function using the number needed to harm (NNH) approach. Results were reported during a poster session at the American Society of Nephrology Kidney Week 2022 in a poster titled *Number Needed to Harm (NNH) Analysis of Tolvaptan in Patients With Autosomal Dominant Polycystic Kidney Disease (ADPKD).*

The analysis utilized individual patient-level data from the TEMPO 3:4 trial to assess abnormalities in liver function, and serious alanine aminotransferase (ALT) or aspartate aminotransferase (AST) elevation adverse events over 12 and 36 months of treatment. Abnormalities in liver function were defined as ALT >3 times and >5 times the normal range. The reciprocal of the difference in the proportion of patients experiencing a given outcome between tolvaptan and placebo was used to calculate NNH.

The cohort included 961 patients in the tolvaptan arm and 483 in the placebo arm. The NNHs for ALT >3 times the upper level of normal were 56.19 (95% CI, 33.60-171.33) over 12 months and 39.81 (95%CI, 25.59-89.57) over 24 months. For every 100 patients treated with tolvaptan rather than placebo, only 1.78 and 2.51 additional patients would have ALT >3 times the upper level of normal over 12 and 24 months, respectively.

There were no statistically significant differences between the two study arms in the proportion of patients with ALT >5 times the upper level of normal or serious ALT or AST elevation in either time period. The results suggest that for every 100 patients treated with tolvaptan rather than placebo, fewer than one additional patient would experience ALT >5 times the upper level of normal or serious ALT or AST elevation over 12 or 24 months.

"The large NNH values help further characterize the safety profile of tolvaptan by demonstrating an acceptable benefit -risk profile," the researchers said.

Source: Nunna S, Betts Kam Kumar RK, Nie X, Fernandes A. Number needed to harm (NNH) analysis of tolvaptan in patients with autosomal dominant polycystic kidney disease (ADPKD). TH-P0411. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 3, 2022; Orlando, Florida. Support was provided by Otsuka Pharmaceutical Development & Commercialization, Inc.

There were no statistically significant differences between the two study arms in the proportion of patients with ALT >5 times the upper level of normal or serious ALT or AST elevation in either time period.

Disparities in Access to Genetic Testing Among Patients With Kidney Disease

Compared with White Americans, Black Americans are nearly four times as likely to develop kidney failure. Over the past 10 years, there have been significant advances in the diagnosis and management of patients with genetic kidney disease. According to researchers at the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio, there are few data available on whether there are disparities in access to genetic testing between racial groups.

Chloe Borden and colleagues conducted a retrospective review of patients referred to the Cleveland Clinic Renal Genetics Clinic from January 2019 to March 2022. Results of the review were reported during a poster session at the American Society of Nephrology Kidney Week 2022 in a poster titled *African American Kidney Disease Patients Experience Reduced Access to Genetic Testing Compared With White Patients.*

The researchers collected data on patient demographics, clinical characteristics, insurance coverage, referring providers, diagnostic modality, and diagnostic yield. The review included data on 309 patients from 299 pedigrees; 118 were male (38.2%) and 191 were female (61.8%), and mean age was 35.1 years. Forty-nine were Black, 232 were White, 24 were neither White nor Black, and four patients declined to provide race.

Black patients were significantly more likely to have progressed to end-stage renal disease at the time of referral compared with White patients (odds ratio [OR], 3.7; P=.003). Black patients were also more likely to be covered by Medicaid compared with White patients (OR, 1.4) and less likely to have private insurance (OR, 0.3). Nonadherence was also more prevalent among Black patients.

There were no differences in referring providers, family history, diagnostic yield, Medicare coverage, estimated glomerular filtration rate at first visit, and age at first visit among the groups.

In conclusion, the researchers said, "This study suggested inequitable access to genetic testing amongst African American kidney disease patients. As personalized genetic health care becomes increasingly prevalent, steps will need to be taken to ensure equitable access for all persons."

Source: Borden C, Tan XY, Wang X. African American kidney disease patients experience reduced access to genetic testing compared with White patients. SA-P0535. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 5, 2022; Orlando, Florida.

Associations Between AKI and Cardiovascular Outcomes

Studies have demonstrated associations between acute kidney injury (AKI) during hospitalization and increased risk of cardiovascular events. However, according to **Ian McCoy, MD,** of the University of California San Francisco, and colleagues, the associations may be confounded by variations in prehospitalization clinical characteristics, including rate of decline in kidney function and proteinuria level prior to hospitalization.

The researchers conducted an analysis of findings from the CRIC (Chronic Renal Insufficiency Cohort) study to examine associations between AKI and subsequent cardiovascular outcomes. Results were reported during a poster session at the American Society of Nephrology Kidney Week 2022 in a poster titled *Pre-Hospitalization Characteristics Confound AKI Associations With Cardiovascular Outcomes: Findings From the CRIC Study.*

The analysis included data on 1630 participants hospitalized from 2013 to 2019 in the CRIC study who survived until the first posthospitalization study visit. The cardiovascualr events of interest were time to first hospitalization for heart failure and time to first atherosclerotic event (ASCVD: myocardial infarction, ischemic stroke, or peripheral arterial disease). Following adjustment for demographics and family history of coronary disease, cause-specific hazard models were used to assess AKI-outcome associations before and after adjusting for prehospitalization variables (estimated glomerular filtration rate [eGFR], eGFR slope, proteinuria, blood pressure, and antihypertensive medication use).

A total of 1317 patients did not experience AKI during their hospitalization; 313 did experience AKI during hospitalization.

Compared with the group without AKI, those with AKI had worse kidney function prehospitalization (eGFR 44 mL/min/1.73 m^2 vs 50 mL/min/1.73 m^2) as well as faster chronic loss of kidney function prior to the hospitalization (eGFR slope -0.68 mL/min/1.73 m^2 per year vs -0.43 mL/min/1.73 m^2 per year), and more proteinuria prehospitalization (urine protein creatinine ratio 0.24 g/g vs 0.15 g/g). Patients in the AKI group also had higher prehospitalization systolic blood pressure (130 mm Hg vs 127 mm Hg), despite more antihypertensive medications (P<.001 for all comparisons).

Following adjustment for pre-AKI variables, the associations between AKI and heart failure and ASCVD were attenuated and did not reach statistical significance.

In summary, the researchers said, "Prehospitalization variables including eGFR slope and proteinuria confound associations between AKI and cardiovascualr outcomes."

Source: McCoy I, Hsu JY, Zhang X, et al. Pre-hospitalization characteristics confound AKI association with cardiovascular outcomes: findings from the CRIC study. TH-P0057. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 3, 2022; Orlando, Florida.

Fluid Balance in Patients With COVID-19 and AKI

In patients with acute kidney injury (AKI) related to severe COVID-19 infection, the optimal amount of hydration has not been established. **Pranav Sharma, MD,** and colleagues at Robert Wood Johnson University Hospital, New Brunswick, New Jersey, conducted a retrospective chart review and analysis to examine the impact of fluid management strategy on outcomes in patients with AKI and respiratory failure associated with COVID-19.

Results were reported during a poster session at the American Society of Nephrology Kidney Week 2022. The poster was titled *A Retrospective Analysis of Fluid Balance in Patients With AKI and Respiratory Failure Due to COVID-19*.

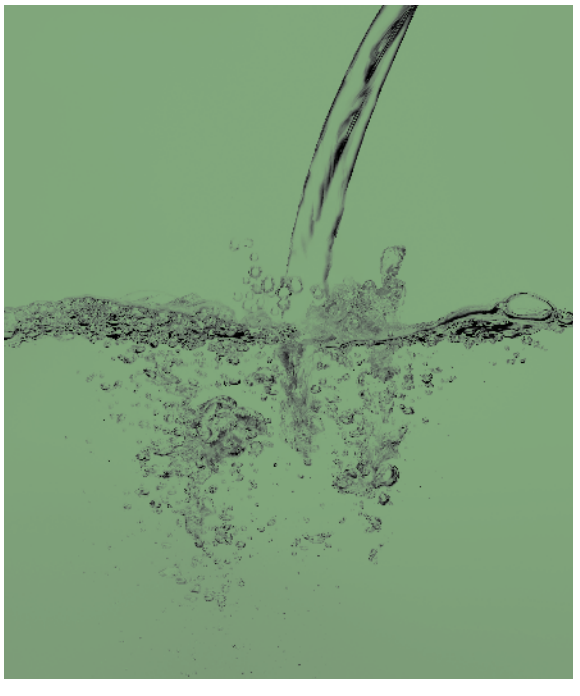
The chart review included patients with hypoxia due to COVID-19 and AKI stage 2 or greater. The primary outcome of interest was the difference in net fluid balance between patients who were successfully weaned to lower levels of oxygen support and discharged compared with patients who died or remained dependent on ventilator therapy.

The analysis included 58 cases. Of those, 41 died, three remained ventilator-dependent, and 14 were discharged without the need for supplemental oxygen. There was a difference in net fluid balance between the groups (-10,065 cc vs +7,908 cc; $P<.001$) and in daily fluid balance (-367 cc/day vs 515 cc/day; $P<.001$).

There was a substantially lower fluid balance in patients who survived with minimal requirement for supplemental oxygen. Patients who maintained a positive fluid balance were significantly more likely to die or become ventilator-dependent (odds ratio, 40.7; 95% CI, 5.3-312.9). There was no reduction in the likelihood of recovery from AKI or an increase in the need for renal replacement therapy with a strategy of fluid restriction.

In conclusion, the authors said, "In our cohort, patients with COVID-19 and AKI who survived with minimal or no oxygen requirements tended to have negative fluid balance in contrast to those who died or remained ventilator-dependent. A fluid restrictive strategy with judicious volume removal using diuretics or dialysis may lead to improved outcomes in COVID-19 patients with AKI."

Source: Sharma P, Bhagat AM, Madu C, Lebowitz J, Saro-Nunez L, Khalil SI. A retrospective analysis of fluid balance in patients with AKI and respiratory failure due to COVID-19. TH-P0078. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 3, 2022; Orlando, Florida.



Longer-Term Results With HIF-PHi for Post-Kidney-Transplant Anemia

Masatomo Ogata, MD, and colleagues previously reported results of a study examining the short-term efficacy of hypoxia-inducible factor prolyl hydroxylase inhibitors (HIF-PHi) for the treatment of post-kidney-transplant anemia. During a poster session at the American Society of Nephrology Kidney Week 2022, they presented results of re-analyzation of HIF-PHi for post-transplant anemia in the context of longer follow-up using a different class of HIF-PHi.

The poster was titled *Hypoxia-Inducible Factor Prolyl Hydroxylase Inhibitors for Treatment of Post Kidney Transplant Anemia.*

The current analysis included nine kidney transplant recipients at Marianna University School of Medicine, Kawasaki, Japan. In erythropoiesis-stimulating agent (ESA)-naïve patients, the indication of HIF-PHi was hemoglobin level below 11.0 g/dL; among patients treated with an ESA, the indication was hemoglobin level below 13.0 g/dL. Either roxadustat or enarodustat was used according to the recommended dose adjustments to achieve target hemoglobin levels between 11.0 and 13.0 g/dL.

Patients were monitored for anemia-related parameters, including hemoglobin, total iron-binding capacity, and ferritin levels, in addition to low-density lipoprotein (LDL) cholesterol up to 14 months. Adverse events of interest were thromboembolic events and malignancy.

Of the nine kidney transplant recipients, six were prescribed roxadustat and three were prescribed enarodustat. Mean estimated glomerular filtration rate in the total cohort was 25.6 mL/min/1.73 m^2. Most of the transplant recipients showed an increase or maintained their hemoglobin levels from baseline; two kept their hemoglobin levels below the target range.

A few of the transplant recipients treated with roxadustat showed rapid increase and decrease in hemoglobin and ferritin levels, respectively, despite being prescribed the recommended initial dose. Only those in the roxadustat group had a drop in LDL cholesterol levels. There were no adverse events reported during the observation period.

"Based on the recommended dose of HIF-PHi, treatment with roxadustat resulted in a more rapid increase in hemoglobin levels along with a stronger improvement in iron utilization as compared to that seen in treatment with enarodustat," the researchers said. "For posttransplant anemia, HIF-PHi would be safe and useful in clinical use."

Source: Ogata M, Miyauchi T, Murata M, et al. Hypoxia-inducible factor prolyl hydroxylase inhibitors for treatment of post kidney transplant anemia. FR-P0832. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 4, 2022; Orlando, Florida.

Blood Pressure Control in Young Patients at Elevated Cardiovascular Risk

The benefits of physical activity include reduction in the risk of cardiovascular disease, maintenance of an appropriate weight, and potentially lowering systolic blood pressure. **Divya Seth, MD,** and colleagues in the Division of Nephrology at the University of California San Francisco conducted a parallel arm crossover design trial to assess whether children and young adults with hypertension, diabetes, and/or chronic kidney disease (CKD) could improve blood pressure control via randomized assignment to a pedometer compared with usual care.

Results of the trial were reported during a poster session at the American Society of Nephrology Kidney Week 2022. The poster was titled *Improving Blood Pressure Control in Young Patients at Elevated Cardiovascular Risk: A Pilot Study.*

Participants at a single center were randomized 2:1 to the intervention group or the control group. Step count was measured using a Fitbit Flex 2 in combination with bimonthly study team feedback. After 6 months, participants in the control group were crossed over to the intervention group.

The primary outcome of interest was change in systolic blood pressure. Secondary outcomes included weight and average weekly step count. Outcomes were tracked every 3 months for 1 year. Mixed models were used to compare outcomes in the two groups.

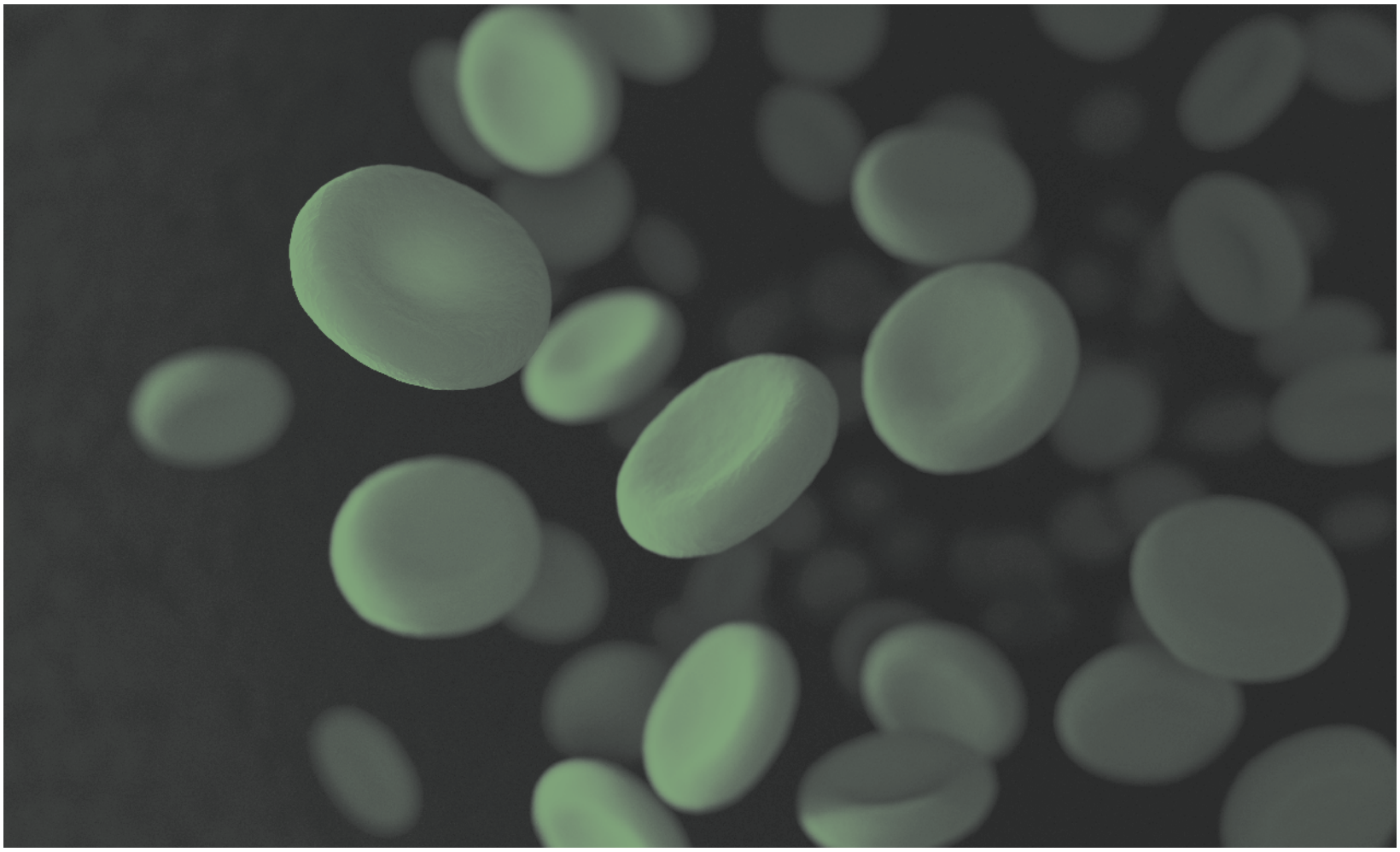
The total cohort included 63 participants. Of those, 57% were male, 48% were Hispanic, and 13% were Black. Mean age was 18 years and mean body mass index z-score was 1.5.

In comparison of intervention to control, there was no significant change in step count when provider feedback was coupled with a self-monitored pedometer. There was no change in weight over time.

At week 39, following adjustment for age, sex, baseline systolic blood pressure, and weight, the intervention arm showed a decline in systolic blood pressure compared with the control arm. The change was not sustained at week 52.

"Pilot results suggest that self-monitored pedometer use, even with provider feedback, may not result in sustained improvement in blood pressure, daily step count, or weight," the authors said. "Augmented interventions or alternative strategies to mitigate risk are needed."

Source: Seth D, Bicki A, Sadiq S, Ku E. Improving blood pressure control in young patients at elevated cardiovascular risk: a pilot study. FR-P0435. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 4, 2022; Orlando, Florida.



Mortality in Patients With Anemia of CKD

Among patients with chronic kidney disease (CKD), the most common causes of death are cardiovascular etiologies, including diabetes mellitus. **Ajay K. Singh, MBBS, FRCP, MBA,** and colleagues conducted a post-hoc analysis of adjudicated causes of death in patients with anemia both with and without diabetes mellitus in the ASCEND-ND trial. The analysis was designed to examine the safety of daprodustat, a hypoxia-inducible factor prolyl hydroxylase inhibitor, for the treatment of anemia of CKD in patients not on dialysis.

Results of the analysis were reported during a poster session at the American Society of Nephrology Kidney Week 2022. The poster was titled *Causes of Death in Patients With Anemia of CKD (With/Without Diabetes Mellitus) in the ASCEND-ND trial.*

The ASCEND-ND trial (NCT02876835) was a global, randomized, open-label, phase 3 cardiovascuair outcome trial. Trial participants received daily oral daprodustat or subcutaneous darbepoetin alfa. Trial outcomes were centrally adjudicated. Kaplan-Meier methods were used to analyze survival data for the intent-to-treat population (diabetes mellitus vs non-diabetes mellitus).

A total of 3872 patients were randomized (diabetes mellitus n=2194; non-diabetes mellitus n=1678). The two treatment arms were generally balanced in baseline characteristics. Patients with diabetes were older, had greater body mass index, higher systolic blood pressure, and more cardiovascular disease and use of cardiovascular medication compared with the patients without diabetes.

All-cause mortality was significantly higher among patients with diabetes compared with those without diabetes (hazard ratio [HR], 1.87; 95% CI, 1.57-2.23). The association did not differ by treatment (HR, 1.87 [daprodustat] vs 1.86 [darbepoetin alfa]; *P*=.96). Independent of diabetes mellitus status, infection and cardiovascuair mortality accounted for approximately 30% of deaths.

"In patients with anemia of CKD not on dialysis, the overall death rate was higher in diabetes mellitus patients, but cause of death was similar regardless of diabetes mellitus status; infection in patients with or without diabetes mellitus was the most frequent cause of death," the researchers said.

Source: Singh AK, Aarup M. Claggett B, et al. Causes of death in patents with anemia of CKD (with/without diabetes mellitus) in the ASCEND-ND trial. TH-P0685. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 3, 2022; Orlando, Florida.

Risk of Malignancy in Kidney Transplant Recipients With Glomerulonephritis

Recipients of kidney transplants with glomerulonephritis (GN) as their native disease who are exposed to significant amounts of pretransplant immunosuppression may face increased risk for the development of posttransplant malignancy. **David Massicotte-Azarniouch, MD,** and colleagues conducted a study of kidney transplant recipients who received pretransplant immunosuppression for the treatment of GN.

Results of the single-center, retrospective study were reported during a poster session at the American Society of Nephrology Kidney Week 2022. The poster was titled *Malignancy Risk in Kidney Transplant Recipients Exposed to Immunosuppression Pretransplant for the Treatment of Glomerulonephritis.*

The study cohort included adult and pediatric kidney transplant recipients at the University of North Carolina Hospitals from January 2005 until May 2020. Patients with GN as their native kidney disease who were treated with immunosuppression prior to the transplant (n=184) were compared with a control cohort of nondiabetic kidney transplants who did not receive pretransplant immunosuppression (n=579).

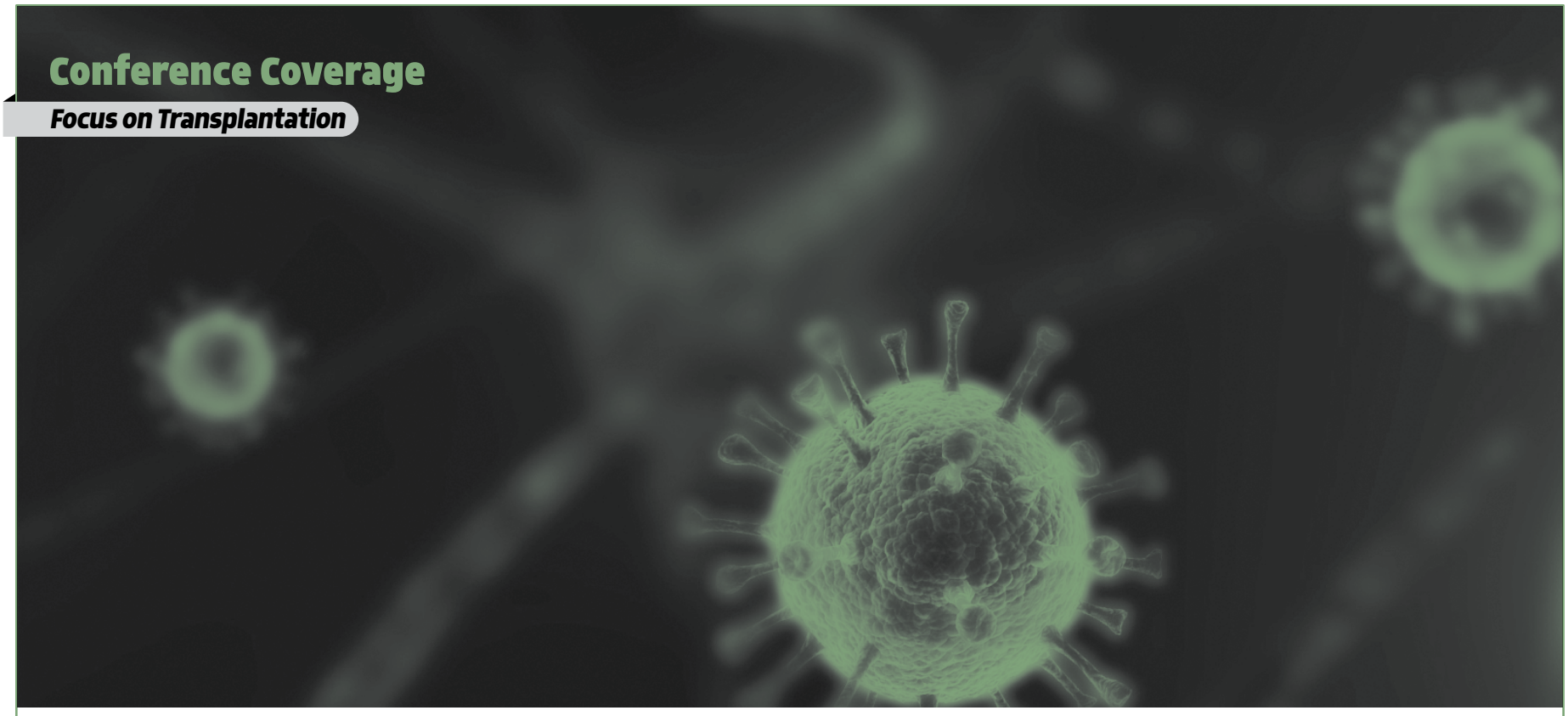
Hazard ratios with 95% CIs for the first occurrence of solid or hematologic malignancy, nonmelanoma skin cancer (NMSC), and posttransplant lymphoproliferative disorder (PTLD) were calculated.

During median follow-up of 5.7 years, there was an association between pretransplant immunosuppression for GN and significantly increased risk for malignancy compared with controls: 13.0% versus 9.7%, respectively (adjusted HR [aHR], 1.82; 95% CI, 1.10-3.00). There were no significant associations between pretransplant immunosuppression for GN and NMSC (10.3% vs 11.4%, respectively; aHR, 1.09; 95% CI, 0.64-1.83) or PTLD (3.3% vs 3.1%, respectively; aHR, 1.02; 95% CI, 0.40-2.61).

Among those receiving cyclophosphamide or rituximab pretransplant, the risk for malignancy was significantly increased (HR, 2.59; 95% CI, 1.48-4.55 and HR, 3.82; 95% CI, 1.69-8.65, respectively), particularly among those who received both cyclophosphamide and rituximab. There was no increased risk among those who received calcineurin inhibitors or mycophenolate.

In conclusion, the researchers said, "The use of pretransplant immunosuppression for treatment of GN, in particular cyclophosphamide or rituximab, is associated with increased risk for development of solid or hematologic malignancy posttransplant."

Source: Massicotte-Azarniouch D, Detwiler RK, Hu Y, et al. Malignancy risk in kidney transplant recipients exposed to immunosuppression pre-transplant for the treatment of glomerulonephritis. FR-P0809. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 4, 2022; Orlando, Florida.



Outcomes Among Kidney Transplant Recipients in the Omicron Wave

During the first 3 months of 2022, the most prevalent SARS-CoV-2 variant in Portugal was the Omicron variant. The Omicron variant is associated with greater transmissibility and less severe disease in immunocompetent patients. However, less is known about the clinical characteristics of the variant in immunosuppressed patients such as kidney transplant recipients.

João Filipe Bernardo, MD, and colleagues at the Centro Hospitalar Universitario Lisboa Norte EPE, Lisboa, Portugal, conducted a single-center retrospective cohort study to characterize and compare the clinical characteristics of kidney transplant recipients infected during the SARS-CoV-2 Omicron and Delta waves. Results were reported during a poster session at the American Society of Nephrology Kidney Week 2022 in a poster titled *COVID-19 Outcomes in Kidney Transplant During the Period of Omicron Predominance*.

The study included clinical outcomes among kidney transplant recipients with COVID-19 infection throughout epidemic waves: June to November 2021, Delta predominant wave (DPW) and January to March 2022, Omicron predominant wave (OPW). Electronic clinical records were utilized for data collection. Continuous variables were compared using Student's *t* tests and categorical variables were compared using Chi-square tests.

The incidence of SARS-CoV-2 infection among kidney transplant recipients was significantly higher during the OPW than during the DPW (10.7% vs 3.7%, respectively; $P<.001$). Most patients had received a booster of COVID-19 vaccine at the time of diagnosis (DPW 88.8% vs OPW 91.6%). Hospitalization rates were lower during OPW (20.8% OPW vs 44.0% DPW, $P=.024$). During OPW, patients had less need for invasive ventilation (OPW 4.1% vs DPW 24%, $P=.003$), lower rates of admission to the intensive care unit (ICU) (OPW 4.1% vs DPW 24%, $P=.003$), and lower rates of mortality (OPW 5.6% vs DPW 24.0%, $P=.009$).

Among the hospitalized patients, the rates of respiratory failure were similar in both waves (OPW 81.9% vs DPW 81.8%). The percentage of lung parenchyma involvement as determined by computed tomography was also similar in the two waves (parenchyma involvement >50%: OPW 53.4% vs DPW 63.5%). There was a higher prevalence of acute kidney graft injury at hospital admission during the OPW (OPW 53.3% vs DPW 18.2%).

"Omicron variant was associated [with] higher infection rates but less severe respiratory disease, lower admission to the ICU, and lower mortality rates than Delta SARS-CoV-2 in kidney transplant recipients," the authors said. "Nonetheless, severe pulmonary involvement occurred in a few cases and mortality sems to be higher than in the general population. Thus, preventive strategies of Omicron variant infection in kidney transplant recipients should go beyond vaccination."

Source: Bernardo JF, Gonçalves S, Santos, NL, et al. COVID-19 outcomes in kidney transplant during the period of Omicron predominance. TH-P0947. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 3, 2022; Orlando, Florida.

Response to COVID-19 Vaccine in CKD and Kidney Transplant Recipients

Among patients with chronic kidney disease (CKD) and recipients of kidney transplantation, immune response to vaccination may be less robust than among the general population.

During a poster session at the American Society of Nephrology Kidney Week 2022, **Thananda Trakarnvanich, MD,** of the Medicine Vajira Hospital, Bangkok, Thailand, reported results of a prospective observation study designed to estimate the immunogenicity of humoral and cellular responses to two SARS-CoV-2 vaccines in different patient groups with CKD compared with a control group. The poster was titled *Antibody Response After COVID-19 Vaccination in CKD and Kidney Transplant Recipients*.

Secondary outcomes of interest were adverse events following vaccination and the incidence and severity of COVID-19 breakthrough infection.

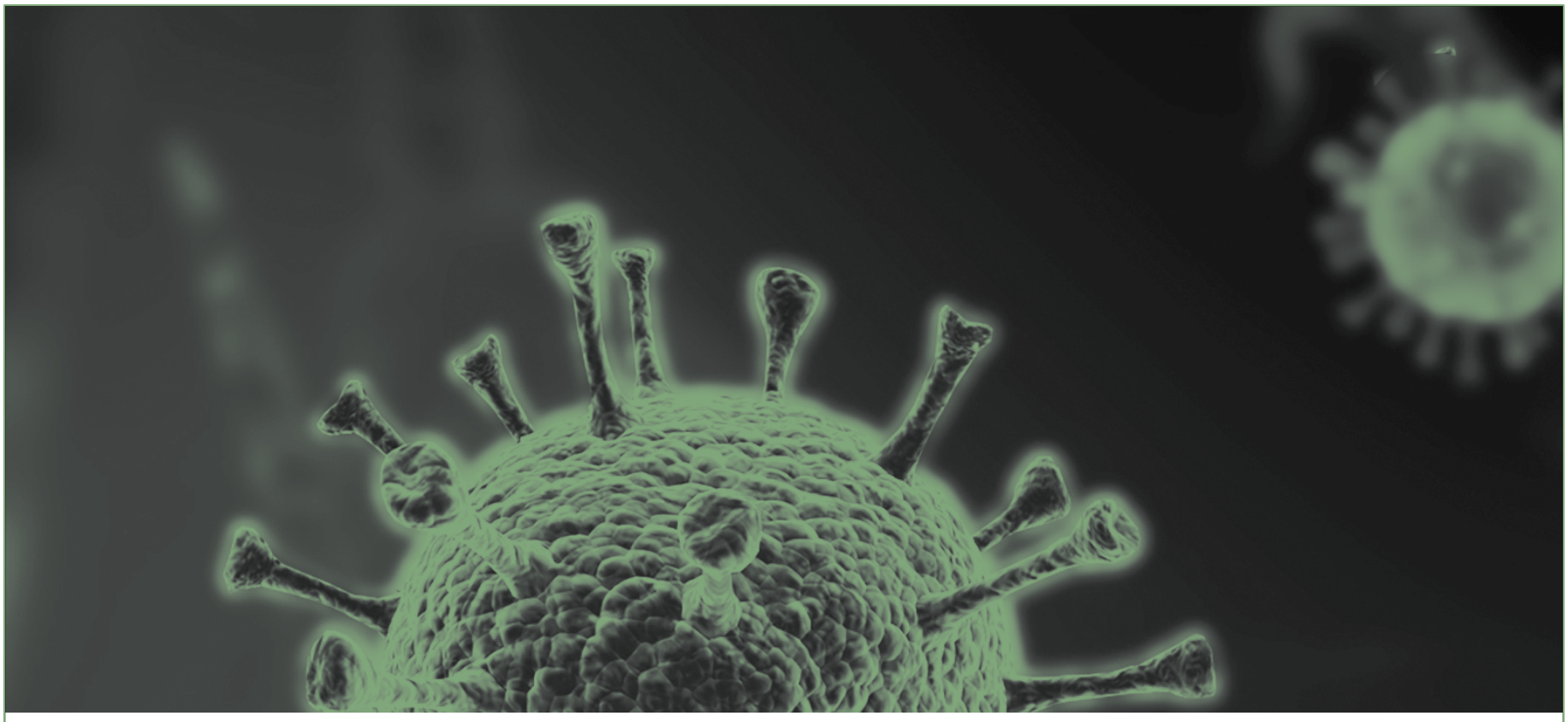
A total of 212 patients received ChAdOx1 nCoV-19 (89.62%) or inactivated vaccines (10.38%). The antibody response against the S protein was analyzed before the first injection (T0), before the second injection (T1), and 12 weeks after the second injection (T2).

At T2, seroconversion occurred in 92.31% of controls and in 100% of patients with CKD, 42.86% of kidney transplant recipients, 80.18% of those on hemodialysis, and 0% of patients on continuous ambulatory peritoneal dialysis who received the ChAdOx1 nCoV-19 vaccine.

Neutralizing antibody levels were above the protective level at T2 in each group. Kidney transplant recipients had the lowest neutralizing antibody and IFNγ. There were associations between blood groups O and vaccine type and good immunological responses. In the total cohort, 6.6% (n=14) had breakthrough COVID-19 infection after the first dose of the vaccine.

"Immunity in patients with CKD and hemodialysis after vaccination was strong and comparable to that of healthy controls. Our study suggests that a single dose of the vaccine is not efficacious and delays may result in breakthrough infection. Some blood group and type of vaccine can affect the immune response."

Source: Trakarnvanich T. Antibody response after COVID-19 vaccination in CKD and kidney transplant patients. TH-P0929. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 3, 2022; Orlando, Florida.



Response to SARS-CoV-2 Vaccine Among Immunocompromised Patients

Results of previous studies have demonstrated an association between immune status and severity of SARS-CoV-2 infection. However, there are few data available on specific immunosuppressive medications and COVID-19 severity. Immunocompromised individuals are at increased risk of mortality and morbidity, making vaccination against COVID-19 essential in that patient population. Previous research has suggested that there is correlation between elevated IgG levels following vaccination and host viral neutralization.

In conjunction with the American Society of Nephrology Kidney Week 2022, **Olusola Sogbein, MD,** and colleagues at the University of Texas Medical Branch at Galveston, Texas, reported data indicating that induction and maintenance immunosuppression therapy in kidney transplant recipients affects responsiveness to SARS-CoV-2 vaccination. The report was titled *Kidney Transplant Patient Immunological Hyporesponsiveness to SARS-CoV-2 Vaccination.*

The retrospective analysis included 48 kidney transplant recipients at the center who received two doses of the SARS-CoV-2 mRNA type vaccine between January and March 2021. The patients underwent kidney transplantation between 1983 and 2020. Immunological responsiveness to the vaccine was evaluated by measuring SARS-CoV-2 spike antigen-specific IgG levels 30 days following vaccination.

After the second vaccine dose, 35% of the cohort showed detectable peak COVID IgG levels; 65% showed no response. Among the nonresponders, 62% were predominantly heavily immunocompromised, on either high dose mycophenolate (at least 720 mg twice daily) in addition to standard calcineurin inhibitor/sirolimus plus or minus prednisone, or had received high dose thymoglobulin (≥6 mg/kg) within 1 year of vaccination.

These findings contrast with published reports of more than 95% immunological responsiveness or viral neutralization following the second vaccination dose among immunocompetent patients.

"Induction therapy with anti-thymocyte globulin and maintenance immunosuppression with mycophenolate serve as the cornerstone of transplantation management," the authors said. "However, their utilization impacts B cell proliferation, which is hypothesized to reduce antibody production and the effectiveness of the SARS-CoV-2 vaccine in transplant patients. This finding supports the need for a third or possible fourth booster dose to achieve a sustained and effective response in combination with ongoing immunological surveillance post-vaccination among transplant patients."

Source: Sogbein O, Rizvi A, Mujtaba MA, Kueht M, Gamilla-Crudo AKN, Hussain SA. Kidney transplant patient immunological hyporesponsiveness to SARS-CoV-2 vaccination. PUB321. Abstract published in conjunction with the American Society of Nephrology Kidney Week 2022; November 3-6, 2022; Orlando, Florida.

Monoclonal Antibodies for Kidney Transplant Recipients With COVID-19

The mainstay of treatment for patients with COVID-19 at high risk for mortality is monoclonal antibodies. **Yorg Al Azzi, MD,** and colleagues at Montefiore Medical Center, Bronx, New York, conducted a review to examine the center's experience with monoclonal antibodies in kidney transplant recipients with COVID-19.

Results of the review were reported during a poster session at the American Society of Nephrology Kidney Week 2022. The poster was titled *Treatment With Monoclonal Antibodies Is Safe and Effective for Kidney Transplant Recipients With COVID-19.*

The review included 93 kidney transplant recipients with COVID-19 who received treatment with monoclonal antibodies. The monoclonal antibody infusion was the one active against the variant that was circulating during the period of interest. Of the 93 patients, 39 received either bamlanivimab or casirivimab/imdevimab, 41 received sotrovimab, and 13 received bebtelovimab. All 93 patients were on standard immunosuppression with tacrolimus and prednisone, and 88% were on mycophenolate prior to the diagnosis of COVID-19, which was subsequently reduced or held for at least 2 weeks.

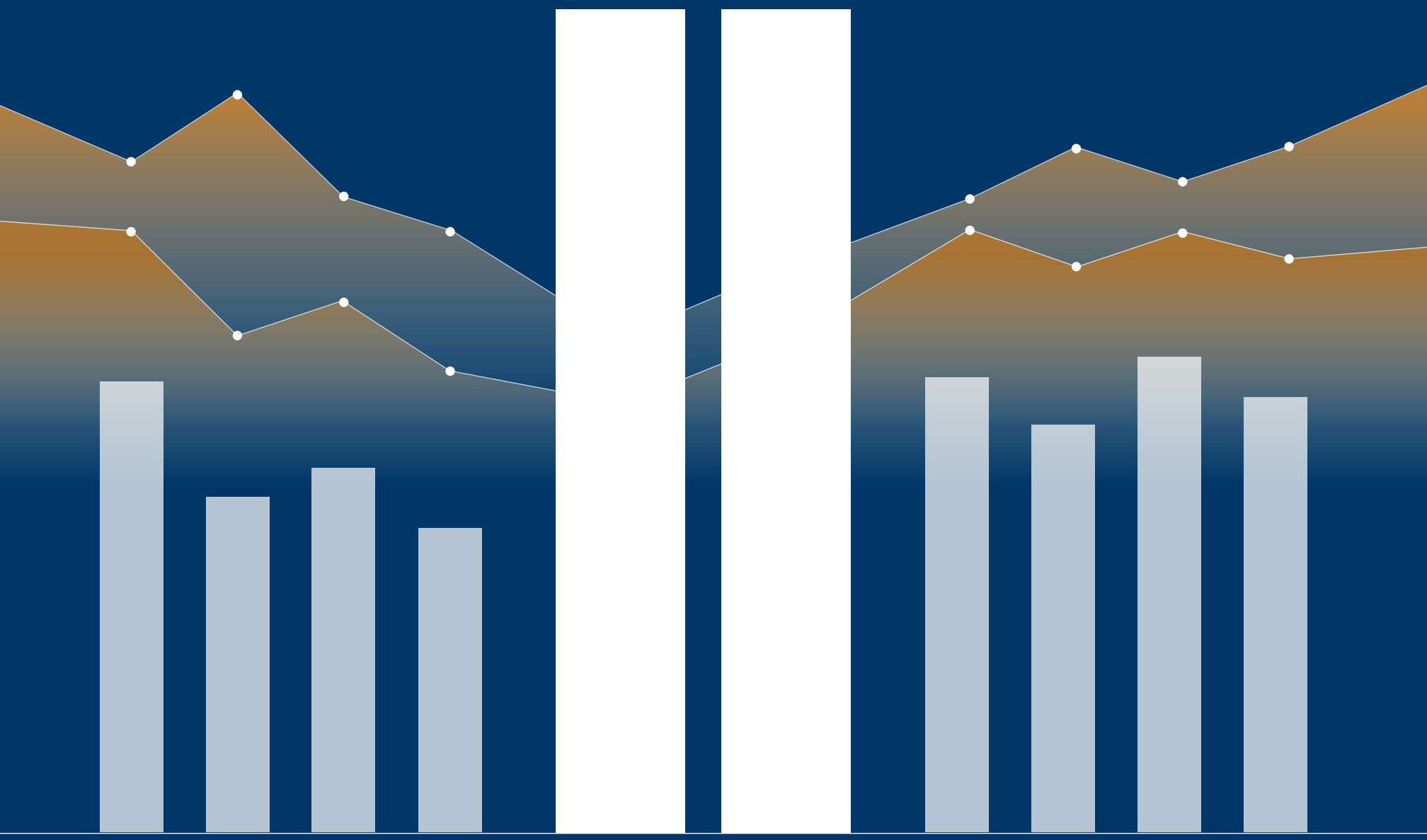
Median age of the cohort was 54 years, 44% were male, 42% were Hispanic, and 36% were Black. Overall, 76% had received a deceased donor kidney transplant, 94% had a history of hypertension, 47% had a history of diabetes mellitus, and 18% had coronary artery disease. All 93 patients had mild symptoms without initial hypoxia requiring supplemental oxygen; five of the 93 patients were admitted to the hospital.

Thirty-three patients were unvaccinated at the time of the COVID-19 diagnosis. The remining 60 patients had received at least two doses of COVID vaccine at the time of the COVID-19 diagnosis; of those, 27 received a third dose.

One patient who was rehospitalized with severe COVID-19 died. There was no allograft loss. Following monoclonal antibody treatment, the rate of reinfection was 6.5%. There were no serious adverse events related to the monoclonal antibody infusion.

In conclusion, the authors said, "Our experience suggests that monoclonal antibodies are a safe therapeutic to reduce the need for COVID-19 related hospitalization in this high-risk kidney transplant population, while one-third of those were unvaccinated at the time of COVID-19 diagnosis."

Source: Al Azzi Y, Pynadath CT, Ajaimy M, Liriano-Ward Le, Kapoor S, Akalin E. Treatment with monoclonal antibodies is safe and effective for kidney transplant recipients with COVID-19. TH-P0944. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 3, 2022; Orlando, Florida.



Common Genetic Variants and Decline in Glomerular Filtration Rate

Overall, the prevalence of chronic kidney disease (CKD) among adults in the United States is approximately 15%. In younger individuals, the prevalence is comparatively lower: approximately6% among those 18 to 44 years of age; approximately12% among those 45 to 64 years of age; and approximately 38% for those ≥65 years of age.

Progression of CKD is associated with a decline in glomerular filtration rate (GFR). Recent data suggest that even mild reductions in estimated GFR (eGFR) are associated with adverse long-term outcomes. There are few data available on predictors and correlates of early eGFR decline in adults at low risk for kidney disease (young and middle-aged adults with a low comorbidity burden).

CKD tends to cluster within families. According to **Farrukh M. Koraishy, MD,** and colleagues, most individual polymorphisms explain a small proportion of risk. The limited potency of individual polymorphisms has led to the development of polygenic risk scores (PRS) that aggregate the estimated effects of numerous single nucleotide polymorphisms (SNPs) into a single genetic risk score.

The researchers conducted a study among responders enrolled in the World Trade Center (WTC) Health Program to test the hypotheses that a PRS based on data from a large genome-wide association study of rapid decline in eGFR would be associated with early decline in eGFR, even following adjustment for traditional risk factors associated with CKD progression. Decline in eGFR was defined in separate analyses: (1) clinical (>–1.0 mL/min/1.73 m^2 per year) and (2) empirical (lower most quartile of eGFR slopes).

A secondary outcome of interest was the association between PRS and individual differences in baseline eGFR, CKD stage, and trajectories of eGFR. Results of the study were reported online in *BMC Nephrology* [doi.org/10.1186/s12882-022-02967-5].

The WTC Health and Wellness Program is a prospective study providing annual health monitoring visits for individuals who responded to the terrorist attacks of September 11, 2001. The current study included WTC responders with genotyping data and three or more eGFR values available.

Measures of serum creatinine were gathered from blood samples collected between 2016 and 2020 during annual visits. The study observation period was ~4 years for individual responders, beginning in 2016 and ending in 2020. None of the study participants had end-stage renal disease (ESRD).

The study cohort included 1601 adult participants of European ancestry. Average baseline age was 54.12 years and 93% were male. More than 90% had a high school or college education. Mean calculated body mass index was 30.96 kg/m^2; 50% were obese. Common comorbidities were hypertension (23%), diabetes (7%), and cardiovascular disease (1%). Mean baseline eGFR was 86.23 mL/min/1.73 m^2 and mean final eGFR was 83.57 mL/min/1.73 m^2. Mean rate of decline in eGFR was 0.75 mL/min/1.73 m^2 per year. The study cohort had no patients with baseline CKD stages 4 and 5.

Based on the categorization of patients by clinical cut-off for rates of annual change, 553 (34.5%) had a decline in eGFR, while 1048 had stable eGFR. Mean rate of eGFR decline in those with a decline in eGFR was 1.47 mL/min/1.73 m^2 per year; for those with stable eGFR, mean rate of decline was 0.38 mL/min/1.73 m^2 per year.

Based on empirical categorization, the mean rates of eGFR change were –1.62, +0.11, and –0.75 mL/min/1.73 m^2 for the lower, upper, and middle two quartiles, respectively. Compared with the reference group, patients with decline in eGFR were more likely to have diabetes.

Before and after adjustment for covariates, the PRS for GFR decline was a significant predictor of eGFR at baseline. After excluding female patients from sensitivity analyses and including only participants 45 to 65 years of age, results were similar. Other covariates associated with lower baseline eGFR were age, diabetes, and cardiovascular disease.

There was also a significant association between the PRS and more advanced baseline CKD stage, both prior to and following adjustment for covariates. Following exclusion of females and including only participants 45 to 65 years of age, results were similar. Age, diabetes, and cardiovascular disease were also associated with higher baseline CKD stage.

There was no significant association between the PRS for GFR decline and eGFR slopes in the full sample among males or those 45 to 65 years of age. There was an association between older age at baseline and a more rapid decline in eGFR.

There was significant association between the PRS and decline in eGFR, relative to no eGFR decline as defined by the clinical categories, both prior to and following adjustment for covariates in the overall cohort, following exclusion of females and those 45 to 65 years of age. There was an association between diabetes and a higher risk of eGFR decline.

In a secondary analysis, PRS was more strongly associated with a rapid decline in eGFR compared with those showing no eGFR decline. There was also a significant association between the PRS and the lower quartile of eGFR change over time, relative to the middle quartiles; there was no significant association between the PRS and the upper eGFR quartile. Older ager was significantly associated with a lower risk of being in the upper quartile, and cardiovascular disease with a higher risk of being in the lower quartile, relative to the middle quartiles.

There was a significant association between the polygenic risk score and decline in estimated glomerular filtration rate (eGFR), relative to no eGFR decline as defined by the clinical categories, both prior to and following adjustment for covariates in the overall cohort, following exclusion of females and those 45 to 65 years of age.

The authors cited some limitations to the study, including the observational design that precludes establishing causality, the inability to determine the association of the PRS with the hard renal outcomes of doubling of serum creatinine levels or ESRD, comorbid conditions being self-reported, and limiting the study to predominantly Americans of European ancestry.

In conclusion, the researchers said, "We report that genetic markers in the aggregate are associated with decline in eGFR among middle-aged, relatively healthy individuals even after accounting for traditional risk factors of CKD progression. Our findings will need to be validated in larger multi-ethnic cohorts with longer follow-up periods to provide insight into the potential associations with advanced kidney disease." ■

TAKEAWAY POINTS

- Researchers reported results of a study testing the hypothesis that a polygenic risk score would be associated with decline in estimated glomerular filtration rate (eGFR) in adults at low risk.
- The study cohort was drawn from the World Trade Center Health Program that provides annual health monitoring visits for individuals who responded to the attacks on September 11, 2001.
- There were significant associations between polygenic risk score and lower baseline eGFR, higher chronic kidney disease stage, and decline in eGFR relative to stable eGFR.

Racial Disparities

continued from page 1

The study exposure was self-reported race (Black or White). The outcome of interest was hospitalized AKI, defined as a ≥50% increase in serum creatinine from nadir to peak. The analyses included multivariate Cox regression models. Adjustments included age and sex, as well as prehospitalization clinical risk factors and socioeconomic status (insurance status and education level). In a subset of participants with genotype data, the analysis also adjusted for apolipoprotein L1 gene (*APOL1*) high-risk status and sickle cell trait.

Of the 2720 CRIC participants in the main analysis, 47% (n=1266) self-identified as Black and 53% (n=1454) self-identified as White. Compared with the White participants, Black participants were younger; less likely to have graduated from high school; and more likely to have diabetes, dyslipidemia, higher blood pressure, higher body mass index, and a greater amount of proteinuria. The two groups were similar in insurance status: 95% of Black participants had health insurance compared with 96% of White participants.

During follow-up, there were 205 AKI hospitalizations among the Black participants and 208 among the White participants. Median time between identification of baseline characteristics and development of an episode of AKI was 1.78 years. Most of the AKI events were stage 1: 55% of AKI events among Black participants and 59% among White participants. Stage 2 and 3 AKI accounted for 24% and 20% among Black participants, respectively, and among 14% and 27% among White participants, respectively.

Among the Black participants, the incidence of first AKI hospitalization was 6.3 (95% CI, 5.5-7.2) per 100 person years; among White participants, the incidence was 5.3 (95% CI, 4.6-6.1) per 100 person-years. The differences in rates of AKI hospitalization were similar in magnitude to the difference in rates of all hospitalizations among Black versus White participants. The two groups were comparable in the potential reasons for hospitalizations.

In the unadjusted Cox regression model, there was a modest increase in the risk of incident AKI among Black participants compared with White participants (hazard ratio [HR], 1.22; 95% CI, 1.01-1.48). Following adjustment for demographic factors, the increased risk among Black participants remained (adjusted HR [aHR], 1.24; 95% CI, 1.02-1.51). The risk was attenuated and no longer statistically significant after further adjustment for prehospitalization risk factors (aHR, 1.02; 95% CI, 0.83-1.25). Results were not materially changed after further adjustment for socioeconomic factors (aHR, 1.05; 95% CI, 0.85-1.29). Results were also similar when the analyses used the race-free 2021 CKD-Epidemiology Collaboration estimated glomerular filtration rate equation.

In the subset of Black participants with *APOL1* and sickle cell trait data (n=499), 18% (n=89) had high-risk *APOL1* status and 16% (n=79) had sickle cell trait. Among participants with high-risk *APOL1* status, 12% (n=11) had at least one episode of AKI. Among those with sickle cell trait, 18% (n=14) had at least one AKI episode.

There was no significant association between Black race and AKI in an unadjusted Cox regression model limited to the subset of participants with genetic data (HR, 1.10; 95% CI, 0.82-1.48). Following adjustment for demographic factors, there was no significant association between Black race and AKI (aHR, 1.12; 95% CI, 0.83-1.52). After further adjustment for prehospitalization clinical risk factors, there was no material change in results (aHR, 0.94; 95% CI, 0.69-1.29). There was also no significant association between Black race and AKI in the model adjusted for sickle cell trait (aHR, 0.88; 95% CI, 0.63-1.22).

Including only hospitalized AKI in the analysis and not considering community-acquired AKI was cited by the authors as a limitation to the study findings. Other limitations were the lack of biopsies to better define the etiology of AKI, the small sample size of the subset with genetic data, not accounting the inpatient risk factors for AKI, the inability to account for the severity of clinical risk factors, and the cohort being limited to research volunteers who may not be fully representative of all patients with CKD.

In conclusion, the researchers said, "Our study suggests that racial disparities in AKI incidence are modest and can be explained by differences in AKI clinical risk factors. Targeted screening and aggressive management of prehospitalization clinical risk factors may reduce the incidence of AKI." ■

TAKEAWAY POINTS

- Researchers reported results of a prospective cohort study designed to examine potential racial disparities in the risk of acute kidney injury (AKI) among patients with chronic kidney disease.
- The incidence rate of AKI hospitalization was 6.3 per 100 person-years among Black participants compared with 5.3 per 100 person-years among White participants.
- In unadjusted Cox regression analysis, there was a modest increased risk of incident among Black participants compared with White participants. The risk was attenuated and no longer significant following adjustment for prehospitalization clinical risk factors.

ASHP Midyear Clinical Meeting

Complications and Mortality Risk of CVC-Related Bloodstream Infections

Patients with kidney failure receiving maintenance hemodialysis with central venous catheters (CVCs) are at increased risk of catheter-related bloodstream infections (CRBSIs). CRBSI is a preventable complication in CVC-dependent hemodialysis and is associated with high rates of morbidity and mortality from long-term complications.

Researchers at CorMedix Inc. conducted a retrospective propensity score-matched analysis of 2013-2018 linked data to examine the incremental real-world clinical burden of CRBSIs in both inpatient and outpatient settings among patients with CVC-dependent hemodialysis. Results were reported during a poster session at the 2022 American Society of Health-System Pharmacists Midyear Clinical Meeting & Exhibition in a poster titled *Mortality Risk and Long-Term Complications Associated With Catheter-Related Bloodstream Infections (CRBSIs).*

The analysis linked data from the United States Renal Data System, CROWNWeb, and Medicare claims. Eligible study participants had kidney failure and initiated CVC hemodialysis during 2014-2017 and had at least 1 year pre-index CVC hemodialysis and at least 1 year CVC hemodialysis follow-up. Post CVC insertion date, patients with occurrence or no occurrence of CRBSI (CRBSI/no CRBSI) were identified on index date/assigned index date in inpatient or outpatient settings, respectively.

The study outcomes of interest were incidence and 1-year post-CRBSI incremental rates of stroke, myocardial infarction (MI), heart failure (HF), peripheral vascular disease (PVD), and dysrhythmia. Secondary outcomes included mortality within 1 year of CRSI index/assigned index date.

Patient demographics were described using frequencies and proportions for categorical variables and mean and standard deviations for continuous variables. Cramer's V and Wilcoxon tests were used to compare differences in baseline characteristics between CRSBI and no CRSBI patients. Associations between CRSBI and mortality and long-term complications were assessed using Cox proportional hazards models.

Of the 51,161 CVC hemodialysis patients analyzed, nearly 33% developed a CRBSI. Median time to CRBSI was 107 days. Eighty-one percent (n=13,559) were diagnosed in inpatient settings and 19% (n=3254) were diagnosed in outpatient settings. CRSBI developed in 33% (n=4804) of cases within 30 days and in 47% (n=6922) within 90 days of CVC insertions in unmatched patients.

CRBSI occurrence was associated with high rates of cardiovascular events, including dysrhythmia, HF, MI, PVD, and stroke. Overall, the 1-year mortality rate among patients with CRBSI was 36%. Mortality rates among CRBSI patients at 30 days were nearly five times greater than among patients who did not develop CRBSI. At 90 days post CVC insertion, the mortality rates were nearly four times greater among patients with CRBSI.

In conclusion, the researchers said, "The high magnitude of morbidity and mortality burden associated with CRBSIs underscores the importance of early intervention to prevent CRBSIs among kidney failure patients with CVC hemodialysis."

Source: Massey K, Rajagopalan K, Seyedin R. Mortality risk and long-term complications associated with catheter-related bloodstream infections (CRBIs). Poster presented at the American Society of Health-System Pharmacists Midyear Clinical Meeting & Exhibition; December 4-8, 2022; Las Vegas, Nevada. Funding for the analysis was provided by CorMedix Inc.

Pegloticase + Immunomodulator Cotherapy for Uncontrolled Gout

Patients with chronic hyperuricemia commonly develop gout, a painful inflammatory arthritis. Gout has been associated with metabolic comorbidities, cardiovascular disease, renal dysfunction, lower quality of life (QoL), and increased risk of mortality. Gout-related disease burden and rates of comorbidities are higher in patients with uncontrolled or refractory gout, as are more severe chronic kidney disease (CKD) and highly impacted QoL. There are limited options for the treatment of patients with uncontrolled gout.

Pegloticase has been shown to lower serum urate in patients with uncontrolled gout; however, due to development of antidrug antibody in some patients, the durability of the effect can be limited. Previous studies have demonstrated an increase in treatment response rates with the coadministration of pegloticase with an immunomodulating agent. In a systematic review, the rate of response in patients treated with pegloticase + immunomodulator was 83% compared with 42% for patients treated with pegloticase monotherapy. A recent randomized, controlled trial of pegloticase + methotrexate (MTX) found a 71% response rate during month 6, compared with 38% for pegloticase + placebo.

Aaron Broadwell, MD, and colleagues conducted a retrospective study designed to examine use of pegloticase-immunomodulation cotherapy at two community rheumatology practices where immunomodulating therapy is routinely coprescribed in patients with uncontrolled gout undergoing pegloticase treatment. Results were reported in *Rheumatology and Therapy* [doi.org/10.1007/s40744-022-00492-3]. The study examined treatment response rates, effect on kidney function, and safety signals.

Data from medical records were extracted and deidentified by an independent party. Parameters of interest were patient demographics, gout characteristics, treatment parameters, and the proportion of patients considered to be pegloticase responders, defined as ≥12 pegloticase infusions received and serum urate <6 mg/dL just prior to infusion 12. Change in kidney function was assessed using estimated glomerular filtration rate (eGFR) prior to therapy and at last infusion. Changes in continuous variables over time were statistically examined using two-tailed, paired Student's *t* tests. Statistical significance was defined as $P<.05$.

The analyses included 34 patients with uncontrolled gout. Most (79%, n=27) were male and White (74%, n=25). Mean age was 62.4 years. The most frequently reported comorbidities were hypertension (76%), obesity (71%), osteoarthritis (68%), chronic kidney disease (CKD, 47%), and cardiovascular disease (35%). Average baseline eGFR was 65.4 mL/min/1.73 m^2; 41% of the cohort had eGFR <60 mL/min/1.73 m^2. None of the 34 patients were on dialysis or had received a kidney transplant.

Average duration of gout was 14.7 years and mean serum urate before initiation of pegloticase exposure was 9.1 mg/dL. Subcutaneous (subQ) tophi were noted in 91% of patients, and all had signs of severe gout, including chronic pain, frequent gout flares, and/or bone erosions on radiography. Of the 34 patients, 91% (n=31) had documented oral urate-lowering therapy (ULT) use prior to initiation of pegloticase; 28 had a history of allopurinol use. Of the three patients without oral ULT use, one was not on an oral ULT use at first rheumatology office visit and two reported allopurinol intolerance.

Over a mean study period of 28.5 weeks, a total of 498 pegloticase doses were administered (14.6 infusions/patient). Immunomodulator use included subQ MTX (20 patients [59%], 10-25 mg/week), oral MTX (9 patients [26%], 7.5-20 mg/week), oral mycophenolate mofetil (MMF; 3 patients [9%], 1000 mg/day), and oral azathioprine (AZA; 2 patients [6%], 100 mg/day). In 32 patients (94%) immunomodulation cotherapy was initiated 5.3 weeks prior to the first pegloticase infusion. In the remaining two patients, immunomodulation (both subQ MTX) and pegloticase were initiated on the same day.

At the time of data collection, 32% (n=11) of the patients remained on therapy, 50% (n=17) had met treatment goals and discontinued therapy, and 18% (n=6) had prematurely discontinued therapy. Of the 11 patients who remained on therapy, six had not yet reached infusion 12 and were excluded from the responder analyses. Reasons for discontinuation of therapy included loss of follow-up (n=2), urate-lowering efficacy loss (n=1), patient choice (n=1), COVID concerns (n=1), and adverse event (n=1, unrelated stroke). Analyses of responder rates included 28 patients.

Twenty-five of the 28 patients in the responder analyses (89%) met treatment response criteria. On average, serum urate fell to 1.0 mg/dL following the first infusion of pegloticase, remaining approximately 1 mg/dL for the remainder of therapy. Of the 17 patients who met treatment goals and discontinued pegloticase, 88% (n=15) had tophi before beginning therapy. Of those 15, 87% (n=13) no longer had visible tophi following discontinuation of pegloticase.

Response rates for individual immunomodulators were 100% for MMF, 93% for subQ MTX, 89% for oral MTX, and 50% for AZA. Of the three patients who were considered nonresponders, one met treatment goals after three pegloticase infusions and discontinued therapy, one had a serum urate of 11.3 mg/dL prior to infusion 12 but remained on therapy due to ongoing clinical improvement, and one self-discontinued AZA 2 weeks prior to infusion 5 (serum urate rise after infusion 6 followed by pegloticase discontinuation).

Over the course of therapy, mean eGFR among pegloticase + immunomodulation cotreated patients improved from 65.4 mL/min/1.73 m^2 at baseline to 75.7 mL/min/1.73 m^2 ($P=.001$, n=34) at the time of the last infusion. Mean change over pretherapy values was +10.3 mL/min/1.73 m^2 at the last infusion of pegloticase.

In addition, kidney disease remained stable or improved in 29 patients (85%), with CKD progression of one stage or less in the remaining five patients: one patient moved from stage 1 to stage 2, two moved from stage 2 to stage 3a, and two moved from stage 3a to stage 3b.

No new safety concerns were identified. Twenty patients (59%) experienced one or more adverse events during the therapy period. The most common adverse event was acute gout flare, seen in 19 patients. There were no infusion reactions or infections. As a precaution, clinical laboratory values were monitored in all patients, including liver function tests; no new laboratory abnormalities emerged.

Limitations to the study cited by the authors included the possibility of selection bias and the small sample size.

In conclusion, the researchers said. "This case series highlights experiences with pegloticase plus immunomodulation cotherapy in a real-world clinical setting, further supporting the use of immunomodulators to increase pegloticase treatment response rates. Importantly, several different immunomodulation agents may be effective for increasing treatment response rates and seem well tolerated by patients with uncontrolled gout. However, further study is needed, particularly with AZA and MMF." ■

TAKEAWAY POINTS

- Researchers reported results of a retrospective study designed to examine outcomes and adverse events in patients with uncontrolled gout treated with pegloticase + immunomodulation therapy at two community rheumatology practices.
- The overall response rate was 89%; response rates varied among different immunomodulators.
- No new safety concerns were identified, and no infusion reactions or infections were noted.

Cancer and Cancer-Related Mortality in CKD

The estimated worldwide prevalence of chronic kidney disease (CKD) is 11% to 13%. Compared with the general population, patients with CKD may face an increased risk of cancer, possibly related to heightened inflammation and immune dysfunction. According to **Abhijat Kitchlu, MD, MSc, FRCPC,** and colleagues, there are few clinical data available on increased cancer risk among patients with CKD.

The researchers utilized data from a population-based cohort of individuals with serum creatinine measurements, along with linked registries of dialysis and kidney transplant registries, to examine the overall and site-specific cancer incidence and cancer-specific mortality across the spectrum of CKD. Results were reported in the *American Journal of Kidney Diseases* [2022;80(4):436-448].

The study included all patients ≥18 years of age with data on serum creatinine level in the provincewide Ontario Laboratory Information System or registration in the Canadian Organ Replacement Register as maintenance dialysis or kidney transplant recipients between April 1, 2007, and October 31, 2016. Patients with prior cancer diagnoses (10 years prior to the index date) and non-Ontario residents were excluded. Ontario residents receive single-payer publicly funded health care under the Ontario Health Insurance Plan.

Patients were categorized as of the first date they had two assessments of estimated glomerular filtration rate (eGFR) or were registered as receiving maintenance dialysis or having received a kidney transplant. Patients were further categorized based on eGFR: ≥60, 45 to 59, 30 to 44, 15 to 29, and <15 mL/min/1.73 m^2. The latter four categories meet Kidney Disease: Improving Global Outcomes criteria for CKD G3a, G3b, G4, and G5, respectively.

The outcomes of interest were overall and site-specific cancer incidence and mortality. Fine and Gray subdistribution hazard models were used in the data analyses.

A total of 5,882,388 individuals had data on eGFR; of those, 7.4% (n=439,554) had CKD G3a to G5; there were 29,809 patients on maintenance dialysis and 4951 who had received a kidney transplant, for a total follow-up of 29,938,374 person-years.

Median age of the cohort was 60 years and 57% were women. Those with CKD G3 to G5 and those on maintenance dialysis were older than those with eGFR ≥60 mL/min/1.73 m^2 and those who had received a kidney transplant. The comorbidity burden was greater among those with CKD G4 to G5 and those receiving kidney replacement therapy (maintenance dialysis or transplant), with a higher Charlson index and more frequent emergency department visits and hospitalizations.

During a median follow-up of 5.33 years, there were 325,895 cancer diagnoses. The overall 1-year cumulative incidences of all cancer diagnoses in patients with eGFR ≥60 mL/min/1.73 m^2; those with CKD G3a, G3b, G4, or G5; patients receiving dialysis; and transplant recipients were 9.0% (95% CI, 8.6%-9.3%), 15.3% (95% CI, 14.4%-16.3%), 13.7% (95% CI, 13.5%-14.0%), 11.5% (95% CI, 11.1%-11.9%), 10.8% (95% CI, 9,5%-12.3%), 11.5% (95% CI, 11.0%-12.1%), and 13.2% (95% CI, 11.6%-14.8%), respectively.

The malignancies with the highest cumulative incidences in patients with eGFR ≥60 mL/min/1.73 m^2 were prostate (2.6%), breast (2.5%), lung (1.2%), and colorectal (1.0%) cancers and non-Hodgkin lymphoma (o.4%). In individuals with CKD G4 and G5, dialysis patients, and transplant recipients, kidney cancers were among the top five most frequent cancers. In transplant recipients, kidney cancers were the third most common after breast cancer and lung cancer. Kidney cancers were the fourth most common among patients on dialysis.

Compared with patients with eGFR ≥60 mL/min/1.73 m^2, adjusted hazard ratios (aHRs) for all cancer diagnoses among patients with CKD G3a, G3b, G4 or G5, patients on maintenance dialysis, and transplant recipients were 1.08 (95% CI, 1.07-1.10), 0.99 (95% CI, 0.97-.01), 0.85 (95% CI, 0.81-0.88), 0.81 (95% CI, 0.73-0.90), 1.01 (95% CI, 0.96-1.07), and 1.25 (95% CI, 1.12-1.39), respectively.

Cancers with increased risk among patients with kidney disease included bladder cancer (in CKD G3a-G4), kidney cancer, and multiple myeloma. The risks of kidney cancers and diagnoses of multiple myeloma increased with worsening eGFR. There was a lower hazard of breast and prostate cancer among patients with kidney disease.

A total of 72,143 deaths were attributed to cancer. There was an increased risk of cancer-specific mortality among patients with CKD G3a, G3b, and G4, and transplant recipients (aHRs, 1.27 [95% CI, 1.23-1.32], 1.29 [95% CI, 1.24-1.35], 1.25 [95% CI, 1.18-1.33], and 1.48 [95% CI, 1.18-1.87], respectively). There were no increased risks for cancer-specific mortality among patients with CKD G5 and those receiving dialysis.

Across all of the study categories, bladder and kidney cancer risk became progressively greater. With the exception of those with CKD G5, mortality related to multiple myeloma also increased in all groups. Compared with participants with eGFR ≥60 mL/min/1.73 m^2, the incidences of breast, colorectal, and prostate cancer diageneses were lower in most categories of kidney disease. Cancer-specific mortality was greater in CKD G3a and G3b and similar in other categories.

Compared with those with eGFR ≥60 mL/min/1.73 m^2, the proportion of stage 4 cancers at the time of diagnosis was higher among those in all categories of kidney disease. In all kidney function categories, the median cancer stage at diagnosis was 2. There was no association between time from dialysis initiation or time since transplant and increased risk of cancer among those on dialysis and transplant recipients.

In patients with CKD G3a to G5, cardiovascular-related mortality exceeded cancer-related mortality. In those with eGFR ≥60 mL/min/1.73 m^2 and in kidney transplant recipients, cancer and cardiovascular mortality were comparable.

Citing limitations to the study, the researchers noted the possibility of residual confounding related to measured covariates or due to missing cancer factors such as family history or smoking, the possibility that death certificates may have misclassified cause of death, and the inability to generalize the findings to other jurisdictions.

In conclusion, the authors said, "In a population-wide cohort of patients across the spectrum of kidney disease, we found that incident cancer affected as many as 15% of patients with CKD. However, cancer risk did not consistently vary with CKD severity. Specific cancers including kidney and bladder cancers and multiple myeloma were more frequent in patients with kidney disease. Overall cancer mortality rates were significantly higher in those with moderate to severe CKD and in kidney transplant recipients relative to patients with eGFR ≥60 mL/min/1.73 m^2. Efforts to improve cancer treatment strategies in this population are needed, particularly for urologic cancers and multiple myeloma." ■

TAKEAWAY POINTS

- Researchers reported results of a population-based cohort study designed to examine cancer incidence and mortality across the spectrum of chronic kidney disease (CKD).
- Cancer risk was increased in mild to moderate CKD and among recipients of kidney transplant, but not in patients with advanced kidney disease.
- Cancer-related mortality was significantly higher among patients with kidney disease, particularly urologic cancers and multiple myeloma.

AKF Launches Patient Access Initiative

The American Kidney Fund (AKF) recently announced the launch of the Patient Access Initiative, a program designed to examine and address the ongoing health care access issues experienced by people with kidney diseases, including rare kidney diseases, and their caregivers.

In a press release from AKF, **LaVarne A. Burton,** president and CEO, said, "We know that a significant number of kidney disease patients have challenges accessing the proper care necessary to appropriately treat their chronic kidney disease, including kidney failure. We need to closely examine these obstacles, which can lead to life-threatening gaps in care, and develop actionable solutions so that we can slow the progression of kidney disease. Our new Patient Access Initiative represents a critical step toward addressing the crisis in kidney disease in America."

AKF will host an in-person Patient Access Summit in 2023 as part of a multiyear effort. The summit will seek to identify existing obstacles and challenges to patient access to innovative and effective treatments; gather insights on the challenges presented to patients as they navigate public and private insurance coverage; highlight resources to provide patients and caregivers with information on access to innovative treatments; increase recognition of challenges associated with racial, ethnic, and socioeconomic factors that impact a patient's ability to access and afford innovative treatments; create strategies for improving provider education about treatment innovations; and develop public policy solutions to help patients access innovative and effective treatments.

The program will be led by a steering committee that includes public policy experts, advocacy professionals, industry stakeholders, health care providers, and patients.

PKD Foundation Names Centers of Excellence

The Polycystic Kidney Disease (PKD) Foundation has announced the formation of the PKD Foundation Centers of Excellence (COE). The PKD Foundation is the only organization in the United States dedicated solely to finding treatments and a cure for PKD by advancing education, advocacy, support, and awareness. The foundation's work is based on the belief that the best way to provide care for patients with autosomal dominant polycystic disease (ADPKD) is through patient-focused, comprehensive care with the coordination and support of a patient navigation team.

According to a press release from the foundation, after an extensive review process, a COE Advisory Group that included clinicians and patient stakeholders identified 28 research institutions nationwide to receive recognition as ADPKD Centers of Excellence. The Advisory Group also recommended an additional 15 institutions as a PKDF Partner Clinic.

Chris Rusconi, PhD, interim CEO and chief research officer of the PKD Foundation, said, "Congratulation to these nephrology practices on their Centers of Excellence and Partner Clinic recognition. We're looking forward to working closely with them to help those affected by ADPKD to find better care, maintain and improve their quality of life, and plan for the future. Creating a brighter future for the PKD community has always been our goal. The organizations who've received our COE and Partner Clinic designations are doing incredible work to bring a patient-centered approach to ADPKD care. With comprehensive teams of experts in nephrology, radiology, hepatology, genetics, pain, and patient navigator services collaborating, we'll ensure better patient outcomes as we move closer to our vision of ending PKD."

The 28 COEs provide a coordination of care for patients with ADPKD and their families and caregivers to eliminate barriers to timely care, facilitate flow through the health system and interactions with clinical research, and serve as the first point of contact for patients and families with ADPKD. The Partner Clinics consist of at least one experienced ADPKD nephrologist who offers a defined plan for patients and follow-up to optimize clinical management.

Interwell Health's Managed Services

Interwell Health has announced a new program aimed at helping nephrology practices with value-based kidney care agreements designed to improve outcomes while lowering the total cost of care. The program, Managed Services, is available to Interwell Health network members and offers support with auditing, financing and refinancing, contract negotiations, and group purchasing.

In a recent press release, **David Arrieta,** vice president of physician solutions at Interwell Health, said, "As a change in practice patterns is often necessary to achieve success in value-based care, we must provide all the support physicians, and their administrative staff, need along their value-based care journey. This new suite of offerings will help providers in our network effectively optimize their practice operations with the ultimate goal of delivering great patient care at lower cost."

Services included in the new program include practice review to identify opportunities to adjust practice operations, productivity measures, and tactical recommendations; debt cost insights to identify areas for cost reduction including current and future debt instruments; expense control to analyze expense reductions in all facets of practice operations; and payer analytics to maximize current payer contractual relationships.

George Hart, MD, chief medical officer of Interwell Health, said, "As physicians, our focus is always on helping patients become healthier, yet it is often frustrating for practices to balance all the business decisions when you must function in both a fee-for-service and value-based world. By providing these extensive managed services, we are helping ensure that our practice partners thrive as they make this transition from volume to value."

The Interwell Health network currently includes more than 1600 physician partners.

AOPO Foundation Announced

In a recent press release the Association of Organ Procurement Organizations (AOPO) announced the formation of the AOPO Foundation. The Foundation is a 501(c)3 organization dedicated to administering research in the field of organ donation and transplantation, and will expand the work of AOPO's Organ Donation Research Collaboration. The emphasis of the new Foundation's work will be on bringing new knowledge and innovation to the organ donation community, with

continued on page 18

MAJOR MEETINGS 2023

National Kidney Foundation Spring Clinical Meetings 2023
April 11-15, 2023
Austin, Texas
www.kidney.org/spring-clinical

American Nephrology Nurses Association 2023 National Symposium
May 7-10, 2023
Palm Springs, California
www.annanurse.org/events/national

American Transplant Congress 2023
June 3-7, 2023
San Diego, California
https://atcmeeting.org/faqs

American Society of Nephrology Kidney Week 2023
November 2-5, 2023
Philadelphia, Pennsylvania
www.asn-online.org/education/kidneyweek

continued from page 17

a focus on organ procurement organization (OPO) advancement.

The Foundation's Board of Directors, who are eligible to serve two consecutive 2-year terms, began their first term on January 1, 2023. They are working to develop Foundation bylaws, budget, and strategic plan. The board includes nine members selected by the AOPO Board of Directors. Eight of the members are from AOPO member OPOs and one is not affiliated with AOPO or its member organizations.

Barry Massa, president of AOPO and executive director of the LifeCenter Organ Donor Network, said, "With more research going into organ donation and transplantation, we will discover more effective technologies and processes, which will lead to more organs donated and ultimately more lives saved."

Results of Global Survey on Management of Lupus

GSK announced results of a survey of rheumatologists, nephrologists, and internal medicine specialists designed to examine approaches to preventing organ damage, a potential outcome among individuals living with systemic lupus erythematosus (SLE). SLE is the most common form of lupus and impacts millions of patients worldwide and amounts to billions of dollars in health care costs. Organ damage is a key determinant of poor long-term prognosis in SLE, and delays in care can be critical in managing patients.

Nearly one-third of the health care professionals responding to the survey reported that during the pandemic patients experienced more flares, a risk factor for organ damage. More than two-thirds said they typically wait more than a year after diagnosis to discuss the potential for organ damage with patients. Eighty percent said that the current standard of care regimen can reduce the risk of long-term organ damage for most patients.

Mike Donnelly, vice president of communications at the Lupus Foundation of America and secretariat of the World Lupus Federation, said, "Some of these findings echo what we know about the experiences of people with lupus and organ damage. These important conversations are happening between people with lupus and their doctors, but more action is needed and should be happening at diagnosis if we are going to truly reduce the burden of organ damage on people with lupus and their families."

Roger A. Levy, MD, GSK global medical expert, immunology and specialty medicine, said, "Lupus can be better managed with early diagnosis and expert medical care, but organ damage affects many people living with lupus within 5 years of diagnosis. The survey results highlight that, as we emerge from the pandemic, there are critical opportunities to drive proactive conversations about organ damage risk and how to align the short- and long-term treatment goals. We are committed to ongoing research and scientific exchange on a proactive approach to lupus care."

NFK Patient Engagement Award Recipient

The National Kidney Foundation (NKF) announced that kidney patient advocate **Maria Elena Grijalva** will receive the Celeste Castillo Lee Patient Engagement Award at the 2023 Spring Clinical Meetings in Austin, Texas. The award honors the work of longtime patient advocate Celeste Castillo Lee by recognizing the efforts of advocates who work on behalf of others.

In a recent press release, **Sylvia Rosas, MD, MSCE,** president of the NKF, said, "I first met Maria at the 2020 Congressional briefing and was impressed by her dedication to raise awareness of kidney disease in her community, particularly in individuals of Native American and Hispanic backgrounds. She gives so much to others with kidney disease. It is dedicated volunteers like Maria and their relentless work to improve the lives of people facing kidney disease that provides us the inspiration to continue to do our work."

Positive Topline Results in ORIGIN Trial Announced

In early January, Vera Therapeutics, Inc. announced that the ORIGIN clinical trial met its primary end point. Vera Therapeutics is a late-stage biotechnology company that focuses on the development and commercialization of treatments for patients with serious immunological disease. ORIGIN is a phase 2b trial of atacicept in patients with immunoglobulin A nephropathy (IgAN).

According to a press release from Vera Therapeutics, atacicept is a potential best-in-class, disease modifying dual inhibitor of the cytokines B lymphocyte stimulator and a proliferation-inducing ligand. ORIGIN is a multinational, randomized, double-blind, placebo-controlled trial (n=116) designed to evaluate the efficacy and safety of atacicept in the patients with IgAN who have persistent proteinuria and are at high risk of disease progression despite therapy with angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers.

Jonathan Barratt, PhD, FRCP, said, "IgAN is a serious and progressive autoimmune disease of the kidney, can severely impact quality of life as up to half of patients develop end-stage kidney disease, requiring dialysis or kidney transplant within 20 years of diagnosis. The positive topline results for the ORIGIN clinical trial demonstrate atacicept's ability to reduce Gd-IGA1, the source of this disease, which in turn lead to clinically meaningful reductions in proteinuria at an early, 24-week time point, and is strongly supportive of a long-term benefit on kidney function. A 30% reduction in proteinuria at 9 months has shown clear association with slowing of kidney function decline in patients with IgAN, and atacicept—having shown this in the ORIGIN trial—is a promising potential therapy for chronic treatment of IgAN."

The trial's primary end point analysis, change in proteinuria as evaluated by urine protein creatinine ratio at week 24 of the pooled 75/150 mg dose groups, achieved statistical significance and showed a 31% mean reduction versus baseline (P=.037 vs placebo). Statistical significance was also achieved in the individual 150 mg dose group, with a 33% mean reduction in proteinuria versus baseline (P=.047 vs placebo) and the all-atacicept group versus placebo.

Living Donor Support Act Passed in New York State

New York Governor Kathy Hochul signed the New York State Living Donor Support Act (SB S1594/A 146A) into law. The law provides direct reimbursements of up to $10,000 to living organ donors for expenses associated with organ donation not covered by insurance. The law is the first of its kind in the United States.

In a recent press release, **LaVarne A. Burton,** president and CEO of the American Kidney Fund (AKF), said, "The New York State Living Donor Support Act sets a nationwide precedent for removing the financial obstacles that are in the way of living organ donors who are considering taking this altruistic action. In New York, there are currently over 8000 people on the waiting list for an organ transplant and more than 7000 (87%) are waiting for a kidney. AKF is grateful to Sen. Gustavo Rivera and Assemblymember Richard Gottfried for working on this bill and their commitment to saving New Yorkers' lives through living organ donation."

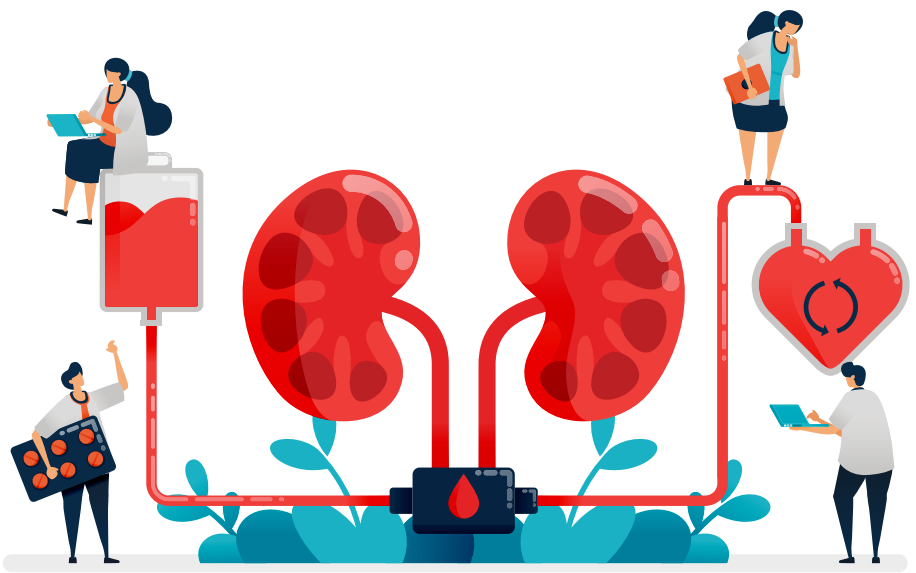
New York is the first state to provide direct reimbursement to donors for expenses associated with donation, including lost wages (including demonstrated lost non-employment income) or the economic value of sick or vacation days expended; travel and lodging, child care and elder care expenses; and costs of medications and care associated with the living donation surgery. Both the organ donor and the recipient must be residents of New York state to be eligible for reimbursement. ■

Sarah Tolson

Simple Tips for Maximizing Dialysis Facility Reimbursement

Since the beginning of the pandemic, dialysis facilities have been battling with increasing labor and supply costs, with very few options for increasing revenue. In many dialysis facilities, traditional Medicare is the majority payer and the 2023 ESRD PPS base rate in many cases is not sufficient reimbursement to cover the costs of dialysis treatment. There are a few things that a dialysis facility can do to reduce lost reimbursement and solidify the revenue cycle.

A thorough insurance verification is the foundation to ensuring optimal reimbursement for dialysis treatments. This entails more than simply verifying that a patient has active insurance coverage. The biggest questions to answer are which insurance company should pay for the treatments, how much should you expect, and what do you need to do to get the reimbursement as quickly as possible.



WHICH PAYER SHOULD BE BILLED FIRST?

When determining the insurance company that should reimburse patient treatments, important things to consider include what type of plan(s) does the patient have—employer group health plan, Medicare Advantage Plan, Medicaid Managed Care, or maybe a plan from the health insurance exchange? Does the patient have traditional Medicare? What are the original effective dates of that policy? Depending on the plan type, there are different rules for determining who the primary payer is and who the secondary payer is. By figuring out which payer should be primary, you are eliminating delays in reimbursement due to submitting to the wrong payer first as well as reducing the risk for overpayments caused by the wrong payer paying as primary.

HOW MUCH REIMBURSEMENT SHOULD BE EXPECTED?

Knowing whether the dialysis program is in-network or contracted with the insurance plan is critical. Many insurance plans have different benefit levels for in- and out-of-network providers, which has a significant impact on the amount of reimbursement the dialysis program can expect to receive. Occasionally when a dialysis program is out of network, there is a possibility of obtaining a single case agreement with the insurance company to cover the dialysis treatments. While single case agreements often reimburse at a higher rate, there are typically more administrative barriers to obtaining reimbursement.

In the event the dialysis program is contracted with the insurance company, the contract should detail how much reimbursement can be expected, based on the patient's plan type. If no contract is in place, many insurance companies can tell you the anticipated reimbursement amount for dialysis based on the codes that will be used for billing and the patient's plan type. It is also important to determine any out-of-pocket amounts the patient may be assessed. For patients whose primary insurance will likely assign coinsurances and deductibles to the patient, efforts should be made to assist the patient in obtaining secondary insurance coverage to cover any amounts the primary insurance passes on to the patient. The anticipated reimbursement amount should be recorded and communicated to the billing staff to ensure that is what is collected.

WHAT ARE THE REQUIREMENTS FOR OBTAINING REIMBURSEMENT?

Knowledge of the plan type is key to knowing the requirements for obtaining reimbursement. Medicare Advantage Plans commonly require dialysis claims to meet the same requirements set forth by traditional Medicare and Medicaid Managed Care plans that look for the same billing requirements as traditional Medicaid.

Many insurance companies require an authorization for reimbursement of dialysis services. In the event the patient's insurance plan requires an authorization, having a solid system in place for obtaining, tracking, and communicating information pertinent to the authorization with those billing for dialysis is just as important as obtaining the authorization. There have been many times in my career where insurance companies deny claims stating no authorization was on file, and I have successfully obtained reimbursement by disputing the denial with the name of the representative, date of the phone call, and reference number of the phone call where the authorization was obtained. Had I not recorded and kept organized records regarding authorizations, I would have struggled to win those disputes. ■

Sarah Tolson is the director of operations for Sceptre Management Solutions, Inc., a company specializing in billing for outpatient ESRD dialysis programs, nephrology practices, and interventional nephrology. Your questions are welcome, and she can be reached at stolson@sceptremanagement.com, 801.775.8010, or via Sceptre's website, www.sceptremanagement.com.

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