Nephrology Times

Practical News, Trends, and Analysis

May/June 2022

VOLUME 14, NUMBER 4

Symptoms and Impacts of ADPKD on Adolescent Patients

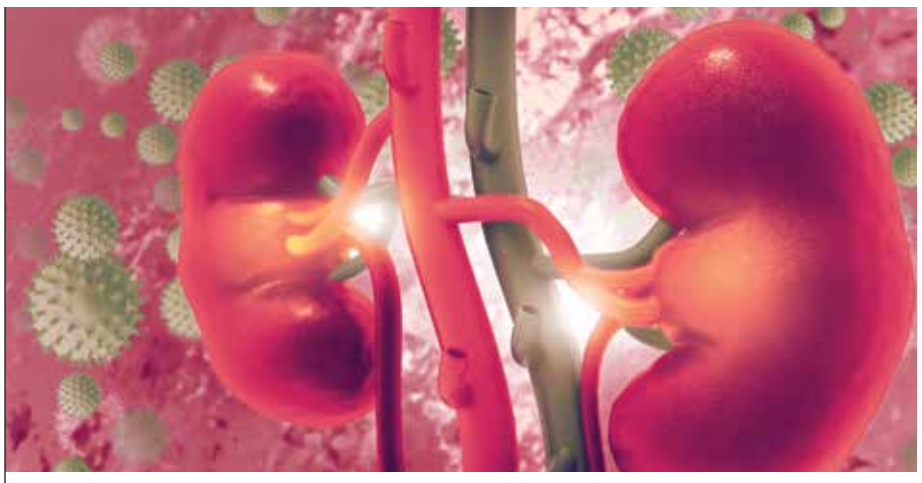
The most common inherited kidney disorder is autosomal dominant polycystic kidney disease (ADPKD), a progressive, systemic disease characterized by the formation and growth of renal cysts, enlargement of the kidneys, destruction of renal parenchyma, and reduced kidney function, progressing to kidney failure. There are also impacts on other organs including the liver, heart, connective tissue, gastrointestinal system, and cerebral vasculature.

The prevalence of ADPKD is estimated to be 3.96 per 10,000 population. In the United States, the average age of diagnosis is approximately 30 years. The disease presents across a clinical spectrum beginning as early as in utero or infancy, and progresses slowly with a long latency period. Most symptoms do not appear until the third or fourth decade of life; children and adolescents are typically asymptomatic.

There are few data available on ADPKD symptoms and disease impacts in adolescents. Early clinical manifestations of ADPKD in the pediatric population include urinary concentrating defects, gross hematuria, abdominal pain, and hypertension. Treatment includes control of hypertension, management of complications related to cyst growth (abdominal pain, urinary tract infections), and dietary restrictions.

Dorothee Oberdhan, MS, and

continued on page 9



Kidney Function Recovery in COVID-19–Related AKI

Of patients hospitalized with COVID-19, 17% to 46% experience acute kidney injury (AKI); of those patients, 14% to 20% are treated with kidney replacement therapy (KRT). Critically ill patients with COVID-19-related AKI who were treated with dialysis had high rates of mortality. Dialysis requires intense resource use and patients on long-term dialysis experience adverse impacts on their quality of life as well as adverse clinical outcomes.

At present, there are no widely accepted tools for prediction of kidney recovery from AKI associated with COVID-19, particularly among patients with COVID-19-related AKI treated with KRT (AKI-KRT). In previous studies, mortality as a competing outcome has been difficult to account for; studies have also been limited by variation in patterns of recovery and lack of detailed data on clinical status at the time of AKI or initiation of KRT.

continued on page 7

Disparities in CKD Prevalence in a Universal Healthcare Coverage Setting

Patients with chronic kidney disease (CKD) commonly progress to kidney failure and the need for renal replacement therapy. There are strong and well-documented associations between health-impeding social determinants of health (i.e., social risks) and the incidence, prevalence, and progression of CKD. There are also substantial disparities in racial and socioeconomic factors that characterize CKD.

Poverty fuels social risks and combines and interacts with clinical and biological factors, resulting in poor health outcomes, including CKD. In the general population in the United States, particularly among low-income individuals, inadequate access to healthcare is a social risk affecting health outcomes. In 2017, 7.4% of the total US population, including 16.2% of those living below the federal poverty level, delayed or missed necessary medical care due to cost. There are associations between poor outcomes in CKD and being underinsured or uninsured.

In some medical conditions, racial and socioeconomic disparities seem to be mitigated with universal healthcare coverage. However, in CKD, racial disparities often persist despite universal access to care. According to **Jenna M. Norton, PhD, MPH,** and colleagues, socioeconomic disparities in CKD remain in settings with universal

continued on page 8

Print-only Content

Print-only Content

Print-only Content

Print-only Content

Reimagining the Nephrologist's Role in Treating Gout

Brad Marder, MD
Medical Director at
Horizon Therapeutics

For patients with gout, call in the... nephrologist? It might sound unconventional, but nephrologists can and should play a key role in the diagnosis and treatment of gout, a systemic and inflammatory disease that be a significant health burden on patients with chronic kidney disease (CKD).

Prior to my current role as medical director at Horizon Therapeutics, I was a practicing nephrologist focused on patients with CKD and kidney transplants for nearly two decades. During my tenure, I was surprised to discover the strong correlation between CKD and gout. In fact, studies have shown that more than 25% of patients with moderate-to-severe CKD also suffer from gout. It might be more common in practice than many nephrologists realize.

THE IMPORTANCE OF UNDERSTANDING AND MANAGING GOUT

For the majority of patients with gout, the condition can be controlled with oral urate-lowering and anti-inflammatory medications. But for some, painful symptoms and elevated uric acid levels continue; this is referred to as uncontrolled gout.

This excess of retained uric acid is highly associated with decreased kidney function, as damaged kidneys are less effective at removing uric acid from the circulation. These elevated levels of serum uric acid can then form crystals, which can be found in nearly any tissue of the body. In patients with CKD who have had kidney transplants, gout may be even more common and more severe due to the side effects of commonly used immunosuppression medications that can elevate serum uric acid levels further. The risk of comorbidities is also much higher for these patients, with a higher prevalence of heart disease and stroke, diabetes, depression, and more, leading to increased morbidity and mortality.

In addition to poor health outcomes, there is often a significant impact on quality of life in patients with coexisting CKD and gout. The physical toll of their disease can cause them to miss out on life's important moments, like family events, and may hamper their ability to live an active, healthy lifestyle due to disabling recurrent flares that, when left undertreated, can lead to permanent joint damage.

It's crucial for nephrologists to take an active role in the early diagnosis and treatment of gout, paying particular attention to monitor patients' symptoms and uric acid levels to prevent their disease from progressing.

REIMAGINING OUR ROLE AS NEPHROLOGISTS

It's crucial for nephrologists to take an active role in the early diagnosis and treatment of gout, paying particular attention to monitor patients' symptoms and uric acid levels to prevent their disease from progressing. Nephrologists are often focused on CKD and other comorbidities (e.g., cardiovascular disease, metabolic bone disorder, and anemia), but they can also help prevent poor health outcomes, including hospitalization and mortality, in their patients due to uncontrolled gout.

At the start of my career, I didn't know how painful and damaging gout could be for my patients, nor did I understand the role I could play in helping to address the disease. It wasn't my specialty, so I focused more on other aspects of their care. But the more involved I became in managing my patients' gout, the more I became aware how impactful my care could be for this condition that is so frequently overlooked with potentially devastating consequences.

It is critical that patients who have CKD and gout be treated for both conditions, and so I urge my fellow nephrologists to embrace this opportunity to help their patients with gout to improve their quality of life and overall health outcomes.

Brad Marder, MD, is the medical director of nephrology in medical affairs at Horizon Therapeutics. Dr. Marder has devoted his career to both patient care and groundbreaking research. Since completing a nephrology fellowship at Icahn School of Medicine at Mount Sinai in New York City, he has served as the director of clinical research and the principal investigator in multiple clinical trials on treatments for kidney transplant patients and those with chronic kidney disease.

Kidney Function Recovery

continued from page 1

AKI associated with COVID-19, while occurring via multiple possible mechanisms, has less heterogeneity regarding timing and underlying cause. **Caroline M. Hsu, MD,** and colleagues conducted a multicenter cohort study to examine the association of severity of AKI with kidney function at the time of hospital discharge. Using baseline characteristics and measures of clinical status at the time of initiation of dialysis among those with AKI-KRT, the researchers examined clinical factors that may predict kidney recovery. Results were reported in the *American Journal of Kidney Diseases* [2022; 79(3):404-416].

The analysis utilized data from STOP-COVID (Study of the Treatment and Outcomes in Critically Ill Patients with COVID-19), a multicenter cohort study that enrolled consecutive adult patients ≥18 years of age with laboratory-confirmed COVID-19 who were admitted to intensive care units (ICUs) at 68 hospitals across the United States. Patients admitted to an ICU between March 1 and June 22, 2020, were included.

Exposures were demographics, baseline medical status (history of diabetes mellitus, estimated glomerular filtration rate [eGFR] using the CKD-EPI equation with a race coefficient), initial modality of dialysis (continuous KRT [CKRT], intermittent hemodialysis, or peritoneal dialysis), markers of severity of illness on KRT day (serum albumin, arterial pH, 24-hour urine output, maximum number of vasopressors or inotropes received that day), and occurrence of a major cardiac event on or preceding day 1 of KRT.

Patients were followed until hospital discharge or death. Kidney recovery was defined as independence from dialysis at discharge. Among survivors discharged with kidney recovery, serum creatinine at the time of discharge was used to calculate discharge eGFR, which was then compared with baseline eGFR in a series of descriptive analyses.

Of the 5154 patients enrolled in STOP-COVID, 741 had incomplete data and 192 were receiving maintenance dialysis at admission; the remaining 4221 patients were included in the current analysis. Of those, 63% (n=2681) were male, mean age was 61 years, and 26% (n=1085) had a baseline eGFR of ≤60 mL/min/1.73 m^2.

A total of 2361 patients (56%) developed AKI within the first 14 days after admission to the ICU. Of those, 527 (12%) had stage 1 AKI, 468 (11%) had stage 2 AKI, 490 (12%) had stage 3 without KRT AKI, and 876 (21%) received KRT. There was an association between more severe AKI and greater mortality: among those with no AKI, AKI stage 1, AKI stage 2, AKI stage 3 without dialysis, and AKI-KRT, 26%, 44%, 60%, 73%, and 67% died, respectively. Among the patients with AKI-KRT, 11% were discharged dependent on dialysis. Of the patients with other stages of AKI, discharge with dialysis occurred in less than 0.5%.

Among the patients who survived to discharge, there was an association between more severe AKI and a higher likelihood of nonrecovery of kidney function at discharge. There was also an association between more severe AKI and higher serum creatinine at discharge. Percentages of those with a discharge Scr ≥1.5 times their baseline Scr or were continuing to receive KRT at discharge among those with no AKI, AKI stage 1, AKI stage 2, AKI stage 3 without dialysis, and AKI-KRT were 1%, 7%, 11%, 41%, and 52%, respectively.

OUTCOMES IN THE AKI-KRT SUBCOHORT

In the subcohort with AKI-KRT (n=876), mean age was 61 years, 71.5% (n=626) were male, 41.3% (n=362) were Black, and 20.2% (n=177) were Hispanic or Latino. Forty-one percent (n=362) had baseline eGFR ≤60 mL/min/1.73 m^2. The most common dialysis modality at initiation of KRT was CKRT (76.4%, n=590). Most patients required at least one vasopressor/isotope on the day of initiation of KRT (75.9%, n=665). In 521 patients (59.5%), urine output was <500 mL/day and <50 mL/day in 149 patients (17.0%) on day 1 of KRT.

Median serum albumin was 2.5 g/dL, and median arterial pH was 7.27. Prior to initiation of KRT, 32.8% of the patients (n=287) had received steroids, 17.1% (n=155) received tocilizumab, and 6.2% (n=54) received remdesivir. Median time elapsed from admission to the ICU to day 1 of KRT was 3 days.

In the AKI-KRT subcohort, 67% (n=588) died, 11% (n=95) were discharged alive and were continuing to receive dialysis at discharge, and 22% (n=193) had recovery of kidney function by the time of discharge. In multinomial logistic regression models, there were associations between both lower baseline kidney function and lower urine output on day 1 of KRT and nonrecovery of kidney function.

The odds of nonrecovery approximately doubled with each more severe baseline eGFR category, with odds ratios of 2.09 (95% confidence interval [CI], 1.09-4.04), 4.27 (95%CI, 1.99-9.17), and 8.69 (95% CI, 3.07-24.55) for patients with eGFR of 31-60, 16-30, and ≤15 mL/min/1.73 m^2, respectively, compared with patients with eGFR >60 mL/min/1.73 m^2. Compared with patients with urine output ≥500 mL/day, urine output 50-499 mL/day (oliguria) was associated with a 2.10-fold increased odds of nonrecovery (95% CI, 1.14-3.88). Urine output <50 mL/day was associated with a 4.2-fold increased odds of nonrecovery (95% CI, 1.72-9.39).

Limitations to the findings cited by the authors included only collecting data on Scr and KRT for the first 14 days following admission to the ICU and on hospital discharge, lack of postdischarge data, and the challenge associated with addressing death as a competing outcome.

In summary, the researchers said, "In this large cohort study of critically ill patients with COVID-19, decreased eGFR, and oliguria at the time of dialysis initiation were each significantly associated with a lower likelihood of kidney recover. The magnitude of the associations presented here may assist prognostication of long-term dialysis treatment, which carries implications for patients' physical health and quality of life." ■

TAKEAWAY POINTS

- Results of a multicenter cohort study to examine clinical factors associated with kidney recovery in critically ill patients with COVID-19-related AKI who were treated with dialysis.
- The odds of nonrecovery of kidney function were greater for patients with lower eGFR at baseline.
- There was also an association between oliguria at the time of kidney replacement therapy initiation and nonrecovery of kidney function.

Disparities in CKD Prevalence

continued from page 1

healthcare coverage, including the United Kingdom, Denmark, and Australia.

The researchers conducted a cross-sectional study to examine the role of healthcare access in racial and socioeconomic disparities in CKD and the extent to which socioeconomic factors and race are associated with CKD in the context of universal healthcare coverage. The study was designed to test the hypothesis that CKD prevalence would be elevated in beneficiaries of Black versus White race, lower versus higher rank (as a proxy for socioeconomic status and social class), lower-income versus higher-income areas, and unmarried versus married status. Results were reported in *Kidney Medicine* [2022;4(1):1-10].

The study utilized data from the Military Health System (MHS) Data Repository (MDR) via the Comparative Effectiveness and Provider Induced Demand Collaboration project. The MDR includes data for all in-patient and outpatient visits for the approximately 9.5 million MHS beneficiaries who receive care paid for by the military's TRICARE Health plan.

The study sample included all patients 18 to 64 years of age who received healthcare through the MHS between October 2, 2105, and September 30, 2018, including active-duty military personnel and their dependents, retired military personnel and their dependents, and dependent survivors. Beneficiaries ≥65 years of age were excluded because Medicare, rather than TRICARE, is the primary payer for that age group.

The primary outcome of interest was CKD, defined by the presence of an *International Classification of Diseases, Tenth Revision* code for CKD and/or a validated laboratory value-based electronic phenotype. Comparisons of CKD prevalence by the predictors of interest (race, sponsor's rank, median household income by sponsor's zip code, and marital status) were examined using multivariable logistic regression after controlling for confounders (age, sex, active-duty status, sponsor's service branch, and depression) and mediators (hypertension, diabetes, HIV, and body mass index [BMI]).

The study population included 3,330,893 MHS beneficiaries. Mean age was 33 years and mean BMI was 28 kg/m^2. Of the total population, 55% were White (n=1,827,435), 15% were Black (n=493,390), 10% were other race (n=314,683), 5% were Asian American and Pacific Islander (n=149,828), and 0.6% were American Indian and Alaska Native (n=21,461) beneficiaries; 16% of the population had missing or unknown race data. Fifty-two percent of the population was active duty, 36% were dependents, and 12% were retired.

Of the total study population, 3.32% (n=105,504) had CKD. Compared with those without CKD, those with CKD were on average older, less likely to be active duty, more likely to be retired, morel likely to be Black, more likely to be senior enlisted or a senior officer, and more likely to be married. Those with CKD also had a higher average BMI and were more likely to have hypertension, diabetes, and depression than those without CKD. Nearly all of those with CKD (99%) had one measure of estimated glomerular filtration rate in the MDR; only 50% had a measure of proteinuria.

Following adjustment for confounders, Black beneficiaries had 1.67 times higher odds of prevalent CKD compared with their White counterparts (odds ratio [OR], 1.67; 95% confidence interval [CI], 1.65-1.70). Following adjustment for suspected mediators, the association was partially but not totally mitigated (OR, 1.30; 95% CI, 1.28-1.32). CKD prevalence was lower in single versus married beneficiaries (OR, 0.77; 95% CI, 0.76-0.79).

Compared with very high median household income quintile, the high quintile had 1.40 (95% CI, 1.36-1.44) times greater odds of CKD, the medium quintile had 1.98 (95% CI, 1.94-2.02) times greater odds of CKD, the low quintile had 2.76 (95% CI, 2.70-2.82) times greater odds of CKD, and the very low quintile had 2.58 (95% CI, 2.52-2.64) times greater odds of CKD. Following further adjustment for suspected mediators, the magnitude of the association was attenuated but remained significant for all income levels. The prevalence of CKD was increased among those with a lower rank and those with a lower media household income in a nearly dose-response fashion (P<.0001).

In sensitivity analyses, the overall pattern of increased prevalence of CKD among Black beneficiaries, beneficiaries of lower rank, and beneficiaries living in lower-income areas remained consistent.

Limitations to the analysis cited by the authors included the cross-sectional design, the lack of data for laboratory tests conducted outside the MHS, and the use of a specific definition of CKD that may have led to an underestimation of CKD prevalence. Further, the accuracy of zip code-level median household income data may have been limited by the transient nature of the MHS population.

In conclusion, the researchers said, "Despite the universal healthcare coverage provided through the MHS, racial and socioeconomic CKD disparities exist in this population. Our findings are consistent with racial and socioeconomic CKD disparities identified in other domestic and international settings that provide universal healthcare coverage., Genetic differences may partially account for the racial differences in CKD in insured populations. However, the existence of disparities by rank and zip code-level median household income suggests that socioeconomic status, social class, and associated social risks may increase the risk for CKD despite access to universal healthcare coverage. Therefore, access to healthcare coverage alone may not be sufficient, and broader interventions to address social risk factors may be necessary to significantly mitigate racial and socioeconomic CKD disparities." ■

TAKEAWAY POINTS

- Researchers conducted a cross-sectional study to examine racial and socioeconomic disparities in the prevalence of CKD in a large, diverse population with universal healthcare coverage.
- CKD prevalence was higher among Black beneficiaries compared with White beneficiaries and lower in single versus married beneficiaries.
- Among those with a lower military rank and those with a lower median household income, CKD prevalence was increased in a nearly dose-response fashion.

Nephrology Times
Practical News, Trends, and Analysis

PUBLISHER
AMC Media Group

NEPHROLOGY TIMES STAFF

EDITORIAL

MANAGING EDITOR
Victoria Socha

DIGITAL PROJECTS MANAGER
Chris Gedikli

ART DIRECTOR
Ari Mihos

ASSISTANT ART DIRECTOR
John Salesi

ADVERTISING

ACCOUNT MANAGER

Jen Callow
jcallow@amcmediagroup.com

Recruitment advertising orders can be sent to:

DIRECTOR, RECRUITMENT CLASSIFIEDS

Lauren Morgan
lmorgan@amcmediagroup.com

Visit us at www.nephtimes.com

AMC MEDIA GROUP

630 Madison Avenue
Manalapan, NJ 07726

Nephrology Times (ISSN 1940-5960) is published monthly by AMC Media Group, at 630 Madison Avenue, Manalapan, NJ 07726. Printed in the U.S.A.
 Subscription information and orders: Physicians who are listed with AMA/AOA as having a primary or secondary specialty related to nephrology within the US are eligible for a free subscription. If you are not currently receiving the publication, send an email with your name, address, and specialty to Victoria Socha at: tsocha@amcmediagroup.com. For customer service on your free subscription, please call 732.490.5530. Annual subscription rates: US: $99 individual, $200 institution.

Postmaster: Send address change to: ***Nephrology Times,*** 630 Madison Avenue, 2nd Floor, Manalapan, NJ 07726.

continued from page 1

colleagues conducted an observational, qualitative study to examine the burden of disease in adolescents with ADPKD, including symptoms, impact on daily life, and emotional and social issues and concerns. Results of the study were reported online in *Kidney Medicine* [doi:10.1016/j.xkme.2022.100415].

Eligible participants were 12 to 17 years of age with a diagnosis of ADPKD or under the care of a physician for suspected ADPKD. Semi-structured interviews were conducted in 13 countries in Asia, Europe, North America, and South America to assess personal experiences with symptoms and physical, social, and emotional impacts of ADPKD. The interviews were transcribed and coded to identify conceptual themes.

A total of 33 adolescents in the 13 countries participated in the interviews. Mean age of the participants was 14.6 years, 42.4% were female, and 90.9% indicated a family history of ADPKD.

SYMPTOMS

Pain and urinary issues were the most frequently reported symptom. Twenty-one participants (63.6%) reported some type of pain attributed to ADPKD. Nine of the participants (27.3%) reported an ache, hurt, or pain in the back, and six (18.2%) reported kidney pain. Others described pain as discomfort, dull pain, or a feeling of pressure or heavy kidneys. One participants said, "I was just sitting and I felt the pain."

Most of the pain was described as mild to moderate; five patients reported intense pain due to rupture of a cyst or infection. One said, "They [kidneys] hurt so bad I could not get out of bed." Pain frequency ranged from seldom (1 or 2 episodes in a 6-month period) to daily. The duration of most pain episodes was short, lasting from seconds to minutes; however, some episodes lasted 15 minutes or more. Three participants (9.1%) reported headaches they attributed to ADPKD-related hypertension.

Ten participants (30.3%) reported a symptom of fullness, described as feeling full quickly when eating, not feeling hungry at all, or feeling full despite not having eaten in a long time. Approximately half of the participants reporting fullness experienced the feeling daily or several times a week.

Some type of urinary symptom was reported by 17 participants (51.5%); the most common was urinary urgency (n=10; 30.3%). Some participants reported experiencing urinary urgency on a daily basis. Three (9.1%) said it interrupted their sleep, with awakenings ranging from one or two to more than five times per night.

DISEASE IMPACTS

Seven participants (21.2%) reported no impact of ADPKD on their daily life. Ten (30.3%) said that, based on advice from their doctor or because they experienced pain or discomfort during physical activity, they avoided sports. In addition, six participants (18.2%) said they had missed school because of ADPKD. Some also said they felt uncomfortable at school due to the need to urinate frequently. Seven participants (21.2%) said they were bothered or impacted by dietary limitations, particularly the need for reduced salt intake and increased water intake.

Social impacts were also mentioned. Six participants (18.2%) reported not being able or willing to engage in some activities with friends; reasons included the desire to keep their condition secret, avoid being teased, or avoid the feeling of being different. One participant said, "You can't really talk about it with anybody."

Most of the participants said they had adapted to living with a progressive, chronic disease. Some said they wanted to see themselves as normal and did not want to think about having the disease. Some participants reported feeling nervous, frustrated, sad, or worried about the disease and their future. Many were feared deterioration in their kidney health and the resulting consequences. Seven said they were concerned about having children due to the hereditary risk for ADPKD.

In general, the participants did not experience emotional concerns on a daily basis. Some said that receiving medical checkups or other medical care sparked their feelings of worry or concern about their disease.

Five participants in the United Kingdom participated in cognitive debriefing interviews (London, Manchester, and Huddersfield). Mean age was 13.6 years, 40% were female, all were White, and 80% indicated a family history of ADPKD. The interviews confirmed the concepts gathered in the concept elicitation interviews, including those related to pain, tiredness, urinary frequency and urgency, as well as impacts of daily activities and emotional impacts.

Limitations to the study included the small sample size, the possibility of selection bias, and the inability to conduct focus groups with participants due to a lack of parental or guardian consent.

In summary, the authors said, "Adolescents with ADPKD exhibit a wide diversity of symptoms and disease impacts. Contrary to common perception, a substantial proportion of adolescents with ADPKD experience pain and urinary symptoms, as well as social and emotional impacts. Overall, the experience of the disease and its symptoms was very similar to that of adult patients, indicating that the impact of ADPKD is felt earlier than commonly throught to be the case, especially in adolescents with rapidly progressing disease. These qualitative findings provide a foundation for further research and may help the medical community to better address the health and emotional needs of adolescents with ADPKD, who have a lifetime of challenges ahead of them." ■

The study was funded by Otsuka Pharmaceutical Development & Commercialization, Inc.

TAKEAWAY POINTS

- Researchers reported results of an observational, qualitative study to examine the symptoms and disease impacts in adolescents with autosomal dominant polycystic kidney disease (ADPKD).
- Sixty-four percent of participants reported symptoms that included pain, abnormal feelings of fullness, and urinary frequency and urgency.
- Disease impacts reported included avoiding sports and physical activity, missing school and social activities, and feeling worried, sad, or frustrated about the disease.

CONFERENCE COVERAGE KIDNEY WEEK 2021

Roxadustat for Anemia in CKD in Patients Treated for ≥3 Years

Roxadustat is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor that is in development in the United States for chronic treatment of anemia with chronic kidney disease (CKD). During a virtual poster session at ASN Kidney Week 2021, **Chuan-Ming Hao, MD, PhD,** and colleagues reported the results of pooled post hoc analysis of outcomes in patients with dialysis-dependent CKD (DD-CKD) who were treated with roxadustat for ≥3 years. The poster was titled *Efficacy and Safety of Roxadustat in Patients with Anemia of Dialysis-Dependent CKD (DD-CKD) Treated Continuously for ≥3 Years.*

There were three phase 3 DD-CKD trials comparing roxadustat with epoetin alfa: ROCKIES, SIERRAS, HIMALAYAS. A total of 3980 patients were randomized to open-label roxadustat (n=1943) or epoetin alfa (n=1947). Per local care protocols, intravenous iron was given for epoetin alfa and limited to need for roxadustat. Regardless of rescue therapy use, data were analyzed in patients treated continuously for ≥3 years. The researchers also assessed adverse events.

Overall, 288 patients in the roxadustat group and 360 in the epoetin alfa group were treated for ≥3 years. Of those, 95% and 94%, respectively, completed treatment. Baseline values in the two groups were generally balanced between the roxadustat and epoetin alfa groups: mean age 55 years versus 57 years, mean hemoglobin (Hb) 9.8 g/dL versus 9.7 g/dL, dialysis modality (hemodialysis, 94% vs 93%), and median dialysis vintage 21.9 months versus 17.4 months.

During the period of weeks 28 to 52, the change in Hg from baseline was greater in the roxadustat group than in the epoetin alfa group (+1.3 g/dL vs +1.0 g/dL; $P<.001$) and the proportion of patients with Hb 19 g/dL was higher (95% vs 85%). To week 156, higher Hb was maintained in the roxadustat group versus epoetin alfa, with 11% increase in mean roxadustat weekly dose from week 25 to 28 versus 20% increase in mean epoetin alfa weekly dose. The need for red blood cell transfusion appeared less with roxadustat versus epoetin alfa (11% vs 16% of patients, respectively).

Rates of serious adverse events were 18.0 per 100 patient-exposure years for roxadustat versus 16.9 per 100 patient-exposure years for epoetin alfa.

In conclusion, the researchers said, "In DD-CKD patients who remained on treatment for ≥3 years, Hb stability with roxadustat was achieved with minimal dose change and less need for red blood cell transfusion versus epoetin alfa. Safety was comparable with roxadustat versus epoetin alfa."

Funding for the analysis was provided by AstraZeneca, Astellas Pharma, and FibroGen, Inc.

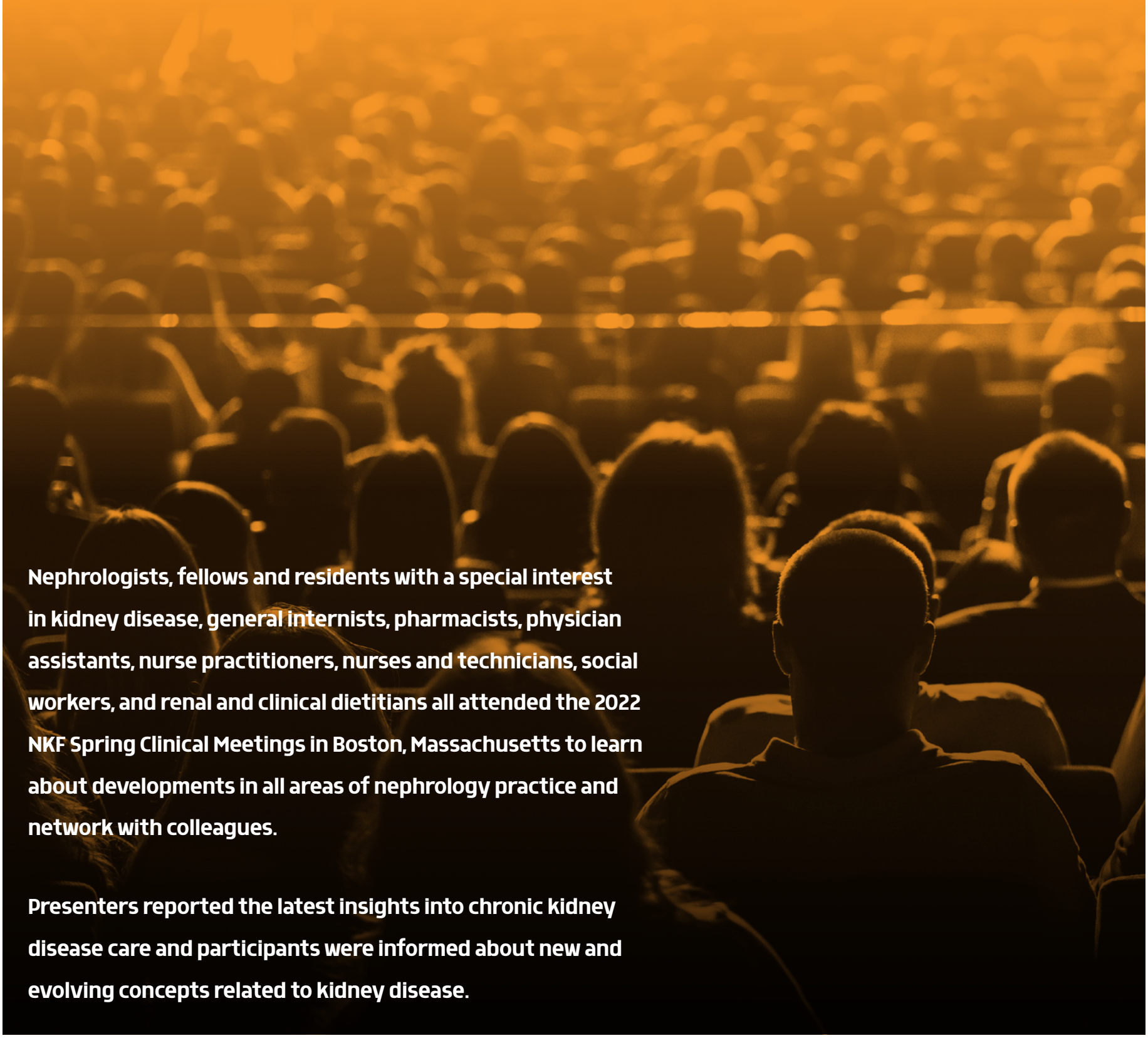
Source: Hao C-M, Dahl NK, Tham S, Orias M, Pecoits-Filho R. Efficacy and safety of roxadustat in patients with anemia of dialysis-dependent CKD (DD-CKD) treated continuously for ≥3 years. Abstract of a poster presented at the American Society of Nephrology virtual Kidney Week 2021 (Abstract PO0450), November 2021.

Conference Coverage

April 6-10, 2022

NATIONAL KIDNEY FOUNDATION

SPRING CLINICAL MEETINGS 2022



Nephrologists, fellows and residents with a special interest in kidney disease, general internists, pharmacists, physician assistants, nurse practitioners, nurses and technicians, social workers, and renal and clinical dietitians all attended the 2022 NKF Spring Clinical Meetings in Boston, Massachusetts to learn about developments in all areas of nephrology practice and network with colleagues.

Presenters reported the latest insights into chronic kidney disease care and participants were informed about new and evolving concepts related to kidney disease.

Patient Reported Burden of Pruritus Associated with CKD

Pruritus is an extremely uncomfortable condition with negative impacts on patient quality of life. Patients with chronic kidney disease (CKD) stages 4 and 5 are at increased risk for CKD-associated pruritus (CKD-aP). **Gail Torres, RN, MS, RD,** and Linda Singleton-Driscoll conducted a study to examine the impact of pruritus in patients with CKD stages 2, 3, 4, and 5 not on dialysis (5ND). Results of the study were reported during a poster session at the NKF SCM22 in a poster titled *Burden of Pruritus in Patients with Chronic Kidney Disease: A National Kidney Foundation Patient Survey.*

The study utilized an online survey of adults ≥18 years of age across the United States. Using links on the National Kidney Foundation Facebook, Twitter, and LinkedIn pages, the survey was conducted from June 16-22, 2021. The first 300 respondents with a valid email address received a $5 gift card. Patients who identified as being in CKD stages 4 and 5 ND were oversampled to ensure a sufficient number for analysis.

Of the 1870 initial respondents, 473 had incomplete surveys, 114 did not have CKD, 224 had an earlier stage of CKD, and 122 were receiving dialysis, resulting in a study cohort of 937 participants. Mean age was 31.4 years, 50% were female, 93% were employed or in school, 76% were non-Hispanic White, 24% were Black or African American, 5% were Hispanic, 4% were American Indian, and 3% were Asian.

Pruritus was common. Among patients with CKD stage 2, 58% (n=88/152) reported recurring itch at least somewhat intense on a Likert scale. In stages 3, 4, and 5, the proportion of patients reporting itch at least somewhat intense increased slightly to 61% to 62% (stage 3, n=69/113; stage 4, n=161/238; and stage 5, n=252/414). The severity of the itch increased in later stages: 57% in stage 4 (n=146/258) and 34% in stage 5 (n=142/414) rating their worst itch in the past 24 hours as ≥7 out of 10 compared with 10% in stage 2 (n=11/113) and 14% in stage 2 (n=22/152).

Patients with later stages of CKD also reported increased effects of pruritus: 44% (n=67/152) of patients with CKD stage 2 reported that itch affected them at least somewhat on a Likert scale. The proportion rose to 81% in stage 4 (n=208/258) and 62% in stage 5 (n=257/414). The proportion of patients reporting that itch interfered with daily activities also increased, from 22% in stages 2 and 3 (34/152; 25/113) to 50% in stage 4 (n=130/258) and 36% in stage 5 (n=149/414).

In summary, the researchers said, "This survey showed that pruritus is fairly widespread, even in earlier CKD. However, patients in CKD stages 4-5ND reported itch that is more severe in intensity, and with a greater burden on their daily activities compared with patients in earlier stages. These results suggest that the impact of pruritus on quality of life may worsen as CKD becomes more advanced."

Source: Torres G, Singleton-Driscoll L. Burden of pruritus in patients with chronic kidney disease: A National Kidney Foundation Patient Survey. Abstract of a poster (Poster #259) presented at the National Kidney Foundation 2022 Spring Clinical Meetings, Boston, Massachusetts, April 6-10, 2022.

Gout in Patients with Advanced Chronic Kidney Disease

Patients with chronic kidney disease (CKD) commonly experience gout, an inflammatory disease associated with higher comorbidity, mortality, and decreased quality of life. The risk for gout is increased in patients with impaired renal function; however, according to **Leonard Stern, MD.** and colleagues, there are few data available on the prevalence of effects of gout in patients with advanced CKD.

The researchers conducted a study to assess the health burden associated with gout in patients with CKD. Results of the study were reported during a poster session at the NKF SCM22 in a poster titled *Clinical Features of Gout in Advanced Chronic Kidney Disease.*

Data for the study were provided by nephrologists; patients with CKD stage 3-5 were included. Criteria for gout included gout listed as a comorbidity, use of urate-lowering therapy, or noted tophi/gout flare. Patients with uncontrolled gout had serum urate >6 mg/dL with tophi, two or more flares in the past year, or more than one swollen or tender joint. The study examined the prevalence of gout and compared patients with gout to those without gout.

A total of 111 physicians reported data on 746 patients. Mean age of patients was 56.2 years, 55.2% were male, mean body mass index was 31.4 kg/m^2, mean CKD duration was 4.0 years, and mean estimated glomerular filtration rate was 32.2 mL/min/1.73m^2 at baseline. A total of 173 (23%) patients had gout; of those 23 (13%) had uncontrolled gout. Twenty-nine percent had no diagnosis of gout and 38% were not using urate-lowering therapy. The prevalence of gout was highest among patients with CKD stage 3b and 4 (both 28%).

Patients with gout sought medical care more than patients without gout (30% vs 7% in the prior year), and, at presentation, more often had urination changes (15% vs 7%) and shortness of breath (21% vs 14%; *P*≤.02 for all).

Patients with gout had higher comorbidity prevalence. The most common comorbidities were hypertension (82%), diabetes mellitus (47%), CKD-associated anemia (42%), CKD-mineral bone disorder (40%), ischemic heart disease (23%), and congestive heart failure (21%). Patients with uncontrolled gout had higher disease burden and more pulmonary hypertension, joint issues, chronic pain, and use of febuxostat and colchicine compared with patients with controlled gout.

In conclusion, the researchers said, "In advanced CKD patients, gout is common and highly impactful with increased healthcare utilization and cardiovascular and bone/joint complication risk. Many gouty CKD patients were not on urate-lowering therapy, but uncontrolled gout patients had higher health burden. Improved diagnosis/management of comorbid gout is needed in advanced CKD patients."

Source: Stern L, Johnson RJ, Shakouri P, et al. Clinical features of gout in advanced chronic kidney disease (CKD). Abstract of a poster (Poster #205) presented at the National Kidney Foundation 2022 Spring Clinical Meetings, Boston, Massachusetts, April 6-10, 2022.

Remote Blood Pressure Monitoring in Patients with CKD and Hypertension

Patients in racial and ethnic minorities with chronic kidney disease (CKD) face increased risk of adverse outcomes associated with uncontrolled hypertension. Results of previous randomized trials have suggested an association between remote patient monitoring (RPM) of blood pressure and improvements in blood pressure. However, there are real-world barriers to implementation of successful RPM, including device assess and the lack of interdisciplinary teams.

Michel Terzibachi, MD, and colleagues created a pilot study designed to assess the feasibility and effectiveness of implementation of an RPM blood pressure program at a large urban health system in high risk patients with CKD and uncontrolled hypertension. Results were reported during a poster session at NKF SCM22 in a poster titled *A Remote Blood Pressure Monitoring Program in High Risk Patients with Chronic Kidney Disease and Hypertension.*

The study was conducted at the Montefiore Health System in the Bronx, New York. Nephrologists invited their patients to participate. Participating patients received instructions to measure blood pressure twice a day. Blood pressure readings were passively transmitted in real time via a cellular-enabled blood pressure device; readings were reviewed every 2 weeks or within 24 hours if a reading was ≥180/120 mm Hg. Patients also received education on lifestyle and adherence and had their medication adjusted if blood pressure was not at goal.

The researchers assessed both the feasibility (program acceptance, enrollment, participation), and the effectiveness of achieving blood pressure control. Descriptive statistics were performed and comparisons of the change in blood pressure from enrollment to 3 months were measured using paired t-tests.

A total of 38 patients were invited to participate. Of those, 36 accepted, 31 were enrolled, and 30 participated at 3 months. At enrollment, mean age was 59 years, 65% of participants were female, 55% were Black, 42% were Hispanic, 61% had diabetes, and mean estimated glomerular filtration rate was 43 mL/min/1.73 m^2.

Mean duration of hypertension was 12.5 years, and participants used a mean of 2.8 blood pressure medications. At enrollment, systolic blood pressure was 149 mmHg and diastolic blood pressure was 81 mm Hg. At 3 months, the mean reduction in systolic blood pressure was -11.2 mm Hg (95% confidence interval [CI], -2.2 to -20.3; *P*=.02); mean reduction in diastolic blood pressure was -6.2 (95% CI, -0.4 to -12; *P*=.03). Twenty of the patients (65%) achieved blood pressure <140/90 mm Hg, and 11 (35%) achieved blood pressure <130/80 mm Hg.

In summary, the authors said, "Implementation of an RPM blood pressure program for high-risk CKD patients with uncontrolled hypertension is feasible and demonstrates short-term effectiveness. Future studies in this population that assess long-term blood pressure reduction with an RPM program compared to usual care are needed."

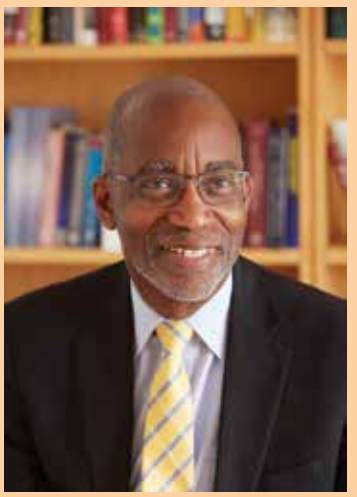
Source: Terzibachi M, Sebastian G, Rikin S, Stark A, Johns T, Fisher M. A remote blood pressure monitoring program in high risk patients with chronic kidney disease and hypertension. Abstract of a poster (Poster #366) presented at the National Kidney Foundation 2022 Spring Clinical Meetings, Boston, Massachusetts, April 6-10, 2022.

2022 Keynote Address

The keynote address at SCM22 was delivered by **David R. Williams, PhD.** The address was titled "Understanding and Effectively Addressing Inequalities in Health." According to Dr. Williams, a social scientist at Harvard University, there is a vital role to be played by healthcare professionals in addressing inequities in healthcare in America. He adds that while the issue is complicated, some solutions are not hard to implement.

"Healthcare professionals can play a vital role in reducing inequity in healthcare as well as in health," Dr. Williams said. "Professionals need to know the specific steps that everyone can take to make a difference for their patients and communities. Knowledge of the magnitude and determinants of health is limited even among many healthcare professionals and too many are unaware of the steps they can take to promote health equity."

Dr. Williams is Norman Professor of Public Health and chair of the Department of Social and Behavioral Sciences at the Harvard Chan School of Public Health. He is also a professor of African and African American studies at Harvard. He is the author of more than 500 scientific papers; his research focuses on the social influences on health. He is an elected member of the National Academy of Medicine, the American Academy of Arts and Sciences, and the National Academy of Sciences. He has been ranked as the Most Cited Black Scholar in the Social Sciences worldwide, and as one of the World's Most Influential Scientific Minds.



The address at NKF SCM22 provided participants with the ability to address ways socioeconomic status and racial/ethnic status affect health, identify ways in which the delivery of healthcare can be enhanced to improve patients' experience, and understand which interventions on social factors such as early childhood education, neighborhood and housing conditions, and employment opportunities can lead to improvements in health.

Risk Factors and Outcomes in Dialysis Patients with Gout

There are few data available on gout in patients with dialysis-dependent end-stage kidney disease. **Anthony J. Bleyer, MD, MS,** and colleagues conducted a study to examine the epidemiology, risk factors, and cardiovascular outcomes among dialysis-dependent patients with gout. Results of the study were reported during a poster session at NKF SCM22 in a poster titled *Risk Factors and Outcomes of Gout in Dialysis Patients from the United States Renal Data System (USRDS).*

Using data from the 2017 USRDS, the researchers identified adult patients ≥18 years of age who were Medicare beneficiaries and receiving dialysis. Characteristics and comorbidities were examined from January 1, 2018. Patients were followed from index diagnosis of gout until December 31, 2018. The study assessed gout diagnoses, all-cause mortality, and a composite outcome of death and hospitalization for myocardial infarction, strike, or congestive heart failure (CHF).

Of 231,841 dialysis patients, 13% (n=31,300) had one or more gout claims following initiation of chronic dialysis. Compared with patients without gout, those with gout were older (mean 66.9 years vs 61.4 years), more often male (62% vs 55%), were hospitalized more often (66% vs 57%), and underwent hemodialysis via central venous catheter more often (13% vs 11%). Length of hospital stays were also more likely to be longer for patients with gout than for patients without gout.

Gout patients had more comorbidities compared with patients without gout: diabetes (64% vs 61%), chronic obstructive pulmonary disease (26% vs 18%), hypertension (84% vs 73%), hyperlipidemia (54% vs 42%), CHF (42% vs 30%), ischemic heart disease (42% vs 29%), and peripheral vascular disease (27% vs 21%).

In adjusted regression analysis, there was a 2-fold increased risk of gout associated with older age (odds ratio [OR], 4.1 for ≥65 years vs <65 years, 95% confidence ratio [CI], 3.0-4.4), Asian race (OR, 2.4, 95% CI, 2.3-2.5) and higher body mass index (OR, 2.1; 95% CI, 2.0-2.2). Patients with gout had 10% higher erythropoietin stimulating requirements and 8% more red blood cell transfusions than patients without gout. Results of multivariable analyses demonstrated 6% higher risk in gout patients for the composite of death and hospitalization for cardiovascular disease (hazard ratio, 1.06; 95% CI, 1.03-1.09) in the year following diagnosis.

In conclusion, the authors said, "Gout prevalence was 13% in this US Medicare dialysis-dependent population. Gout patients had a higher comorbidity burden, anemia management challenges, and a higher risk for hospitalization/mortality. Further study is needed to assess whether improved gout recognition/management may improve outcomes among dialysis-dependent patients with gout."

Source: Bleyer AJ, Zhang Y, Ksirasgar O, Marder B, LaMoreaux B. Risk factors and outcomes of gout in dialysis patients from the United States Renal Data System (USRDS). Abstract of a poster (Poster #206) presented at the National Kidney Foundation 2022 Spring Clinical Meetings, Boston, Massachusetts, April 6-10, 2022.

Healthcare Costs among Patients on Phosphate Binders

In dialysis-dependent patients with end-stage kidney disease (ESKD), hyperphosphatemia is treated with phosphate binders. *Christine Ferro* and colleagues conducted a study to compare all-cause healthcare expenditures among Medicare fee-for-service beneficiaries with ESKD who were receiving phosphate binders during chronic outpatient dialysis.

The researchers presented results of the study during a poster session as NKF SCM22. The poster was titled *Real-World All-Cause Healthcare Costs among Dialysis-Dependent Patients with Chronic Kidney Disease on Phosphate Binders.*

The study utilized data from the Centers for Medicare & Medicaid Services (CMS) 100% Research Identifiable File (RIF). Prevalent patients with dialysis-dependent ESKD in the 2018-2019 RIF data were identified. Based on frequency of revenue codes, the patients were divided into hemodialysis and peritoneal dialysis. The researchers assessed monthly phosphate use for calcium acetate, ferric citrate, lanthanum carbonate, sevelamer (hydrochloride and carbonate), and sucroferric oxyhydroxide.

Phosphate binder use was defined as a filled prescription covering 15 or more days in a month. CMS ESRD risk scores (2019) were used to normalize all-cause healthcare allowed costs per patient per month (PPPM).

A total of 134,964 patients with dialysis-dependent ESKD with ≥1 month of phosphate use in 2019 were identified. The mean all-cause PPPM cost was $9723 ($3467 [36%] in outpatient dialysis; $2527 [26%] in inpatient facility; $2732 [28%] in other Part A/B services; $449 [5%] in phosphate binders; and $548 [6%] in other Part D drugs).

Mean PPPM costs were similar in patients receiving hemodialysis and those receiving peritoneal dialysis ($9722 vs $9743, respectively). However, there were differences in the components of cost. Among patients receiving hemodialysis, inpatient facility and outpatient dialysis costs were lower, but professional, skilled nursing, and transportation costs were higher than among patients receiving peritoneal dialysis.

There was variation in mean costs by primary phosphate binder. Patients on sucroferric oxyhydroxide had the highest PPPM costs while those on calcium acetate had the lowest costs ($10,532 vs $9104, respectively).

In conclusion, the researchers said, "After normalizing for the relative health status of patients, we found no difference in all-cause healthcare costs between hemodialysis and peritoneal dialysis; however, components of care varied by dialysis modality. Healthcare costs also varied by phosphate binder. Further studies are needed to determine if healthcare utilization and outcomes, particularly for services in the CMS ESRD bundle, also vary. These studies could identify opportunities for better control of phosphate levels among patients with CKD."

Source: Ferro C, Dieguez G, Metz S, et al. Real-world all-cause healthcare costs among dialysis-dependent patients with chronic kidney disease on phosphate binders. Abstract of a poster (Poster #189) presented at the National Kidney Foundation 2022 Spring Clinical Meetings, Boston, Massachusetts, April 6-10, 2022.

Hyperkalemia after Kidney Transplant

In studies evaluating electrolyte abnormalities in patients following solid organ transplant, a significant number of patients are described as developing hyperkalemia. Hyperkalemia after solid organ transplant has been attributed to the use of certain prophylactic antibiotics such as trimethoprim-sulfamethoxazole, as well as antirejection medications, particularly calcineurin inhibitors.

Isaac Pak, DO, and colleagues conducted a study designed to examine differences in the incidence of hyperkalemia in different solid organ transplants with an eye toward discerning the underlying cause of hyperkalemia (whether from medication or from dysfunction of the underlying organ). Results of the retrospective analysis were reported during a poster session at NKF SCM22 in a poster titled *Hyperkalemia in Solid Organ Transplantation*.

The analysis included all solid organ transplants performed at Westchester Medical Center, Valhalla, New York, from 2018 to 2021. Hyperkalemia was defined as potassium >5.0 mEq/L; severe hyperkalemia was defined as potassium ≥5.5 mEq/L. Potassium was measured at transplant, and at 1-month, 3-months, and 1-year post transplant. Fifty-five kidney transplants, 74 liver transplants, and 70 heart transplants were reviewed.

The risk of hyperkalemia was relatively low at any time in all transplant recipients. During the 1-year follow-up, 12% (24/199) of patients had documented potassium >5 mEq/L at any time. Kidney transplant recipients had the highest incidence of hyperkalemia >5.0 mEq/L at 1-month post-transplant (18.2%); the greatest risk of severe potassium was seen on the day of transplant in the kidney transplant recipients (7.27%).

The risk of hyperkalemia in other solid organ transplant recipients was significantly lower than in kidney transplant recipients, particularly within 1 month of transplant. The incidence of severe hyperkalemia was very low (<5%) in all heart and liver transplant recipients.

In conclusion, the authors said, "These data suggest that the risk of hyperkalemia in solid organ transplant recipients may be multifactorial and that kidney transplant recipients may be at highest risk of hyperkalemia, especially within 1 month of transplant. The relatively high incidence of hyperkalemia seen within 1 month of kidney transplant that eventually decreases to levels closer to other organ transplants at 3 months and 1 year suggests underlying renal dysfunction is the cause of hyperkalemia within this timeframe, rather than commonly used post-transplant medications. It also suggests that in the long term, medications may contribute to increased risk of hyperkalemia >5.0 mEq/L."

Source: Pak I, Fullmer J, Kore S, Chugh S. Hyperkalemia in solid organ transplant. Abstract of a poster (Poster #414) presented at the National Kidney Foundation 2022 Spring Clinical Meetings, Boston, Massachusetts, April 6-10, 2022.

Serum Ferritin Strong Predictor of Iron Status in Children

Several factors contribute to iron deficiency in patients with end-stage kidney disease (ESKD), including increased external loss, reduced circulating iron availability, and poor intestinal iron absorption. Standard of care includes monitoring of serum iron indices to guide administration of supplemental iron and recombinant human erythropoietin.

Shilpa Sharma, MD, and colleagues recently conducted a study designed to examine which indices of serum iron were predictive of bone marrow iron stones (gold standard) in children with dialysis-dependent ESKD (a state of co-existing inflammation). Results of the study were reported during a poster session at NKF SCM22. The poster was titled *Predictors of Iron Status in Children with ESKD*.

The cross-sectional study collected clinical, laboratory, and bone marrow data from 71 stable dialysis pediatric patients who underwent bone biopsy for chronic kidney disease-related mineral bone disorders. Patients were enrolled between 2007 through 2011.

The primary causes of kidney failure were birth defects and hereditary diseases (63.3%), followed by primary glomerulonephritis (36.7%). An independent pathologist who was blinded to the patients' iron parameters interpreted bone marrow smears stained with Perls' Prussian blue stain. Staining was scored on a scale of 0 to 4. Predictors of greater bone marrow iron stores were evaluated using linear regression.

Mean age of the cohort was 17.2 years and 30% were female. Median dialysis vintage was 1.2 years and 56.4% underwent peritoneal dialysis. At the time of biopsy, mean hemoglobin was 12.4 g/dL and 31% of the participants were on iron supplementation. There were independent associations between greater serum ferritin levels, older age, and higher transferrin saturation and greater bone marrow iron stores. The association appeared strongest for serum ferritin. When patients on hemodialysis and patients on peritoneal dialysis were evaluated separately, the association with ferritin remained similar.

"In children with ESKD, greater serum ferritin remained the strongest independent correlate of greater bone marrow iron stores followed by older age and transferrin saturation," the researchers said.

Source: Sharma S, Pereira R, Nemeth E, Ix J, Salusky I, Ganz T. Predictors of iron status in children with ESKD. Abstract of a poster (Poster #178) presented at the National Kidney Foundation 2022 Spring Clinical Meetings, Boston, Massachusetts, April 6-10, 2022.

Kidney Stone Risks May Vary by CKD Stage

Patients with recurrent kidney stones face an increased risk for chronic kidney disease (CKD). There is an association between hypercalciuria and increased risk for formation of kidney stones, but hypercalciuria does not increase the incidence of CKD. However, there is an association between uric acid stones and lower estimated glomerular filtration rate (eGFR).

Hari Nair and colleagues conducted a retrospective review of all patients with kidney stone at Yale Urology and Nephrology from November 1994 to May 2021. Results were reported during a poster session at NKF SCM22 in a poster titled *Kidney Stone Risk Factors and Stone Type Vary with CKD Stage*.

Automated query and manual chart review were used to extract medical histories, stone pathologies, blood chemistries, and 24-hour urine analyses. The analyses included serum and 24-hour urine chemistries obtained within 1 year of baseline stone pathologies. Prior to statistical analysis by one-way ANOVA and multiple linear regression, 24-hour urine chemistries were normalized to urine creatinine.

Of 10,163 kidney stone formers, 9.1% (n=929) completed a 24-hour urine and blood chemistry within 1 year of baseline stone pathology. Of those, 34.3% (n=319) were classified as CKD stage 1, 44.0% (n=409) as CKD stage 2, and 21.6% (n=201) as CKD stages 3 to 5.

As CKD progressed, the proportion of calcium stones declined and the proportion of uric acid stones increased. There was an association between lower urine phosphorous (P=.0001), calcium, urinary pH, citrate, and ammonium (P<.0001). There was significant variation in urinary oxalate by CKD stage (P=.025). However, there was no correlational trend.

Patients with advanced CKD and kidney stones were more likely to have an elevated supersaturation for uric acid, but reduced supersaturations for calcium salts.

In conclusion, the authors said, "Renal function may play a key role in modulating the risk factors for kidney stones, and ultimately, stone composition in those with CKD. Strategies to mitigate stone risk may need to vary with CKD stage."

Source: Nair H, Simmons K, Murphy E, et al. Kidney stone risk factors and stone type vary with CKD stage. Abstract of a poster (Poster #196) presented at the National Kidney Foundation 2022 Spring Clinical Meetings, Boston, Massachusetts, April 6-10, 2022.

Anti-Glycemic Medications and Risk of Adverse Renal Outcomes

Results of recent studies have demonstrated that the risk of decline in estimated glomerular filtration rate (eGFR), progression to end-stage kidney disease, and mortality in patients with chronic kidney disease (CKD) can be substantially reduced with the used of sodium-glucose cotransporter-2 (SGLT2) inhibitors compared with placebo. However, according to **Connie Rhee, MD**, and colleagues, there are few data available on the comparative effectiveness of SGLT2 inhibitors versus other newer anti-glycemic medications (dipeptidyl peptise-4 [DPP-4] inhibitors and glucagon-like peptide 1 [GLP1] agonists) on the risk of incident albuminuria and decline in GFR using real-world data in patients without underlying CKD.

Dr. Rhee et al. conducted an analysis of data from a national cohort of US veterans with diabetes and without underlying CKD to examine the effectiveness of the newer medications versus SGLT2 inhibitors. Results were reported during a poster session at NKF SCM22 in a poster titled *Comparative Effectiveness of SGLT2 Inhibitors, DPP-4 Inhibitors, and GLP-1 Agonists on Incident Albuminuria and Glomerular Filtration Rate Decline in US Veterans*.

The researchers utilized data from the Veterans Administration Healthcare System on 32,250 US veterans with diabetes and without CKD from 2004 to 2018 to identify incident users of SGLT2 inhibitors versus DPP4 inhibitors versus GLP1a agonist therapy. Combined users of the classes of interest were excluded from the analysis.

The study used multivariable Cox models to examine associations of SGLT2 inhibitor versus DPP4 inhibitor use versus GLP1 agonist use with the risk of incident albuminuria, defined as ≥2 urine-to-albumin-creatinine (UCAR) levels ≥30 separated by >90 days. The researchers then compared the risk of developing GFR decline, defined as ≥2 eGFR <45 mL/min/1.73 m^2 levels separated by >90 days, with the use of the anti-glycemic medications.

In Cox models adjusted for expanded case-mix + laboratory + other anti-glycemic covariates, compared with the use of DPP-4 inhibitors, there was an association between use of GLP1 agonists and a higher risk of incident albuminuria. There was no association between SGLT2 inhibitor use and a higher risk of incident albuminuria.

There was also an association between GLP1 agonists use and a higher risk of decline in eGFR. There was no association between SGLT2 inhibitor use and a higher risk of eGFR decline.

In conclusion, the researchers said, "In a national cohort of US veterans with diabetes and without underlying CKD, GLP1 agonists use was associated with a higher risk of incident albuminuria and eGFR decline, whereas use of SGLT2 inhibitors had comparable risk to DPP4 inhibitor use."

Source: Rhee C, Narasaki Y, You A, et al. Comparative effectiveness of SGLT2 inhibitors, DPP-4 inhibitors, and GLP-1 agonists on incident albuminuria and glomerular filtration rate decline in US veterans. Abstract of a poster (Poster #282) presented at the National Kidney Foundation 2022 Spring Clinical Meetings, Boston, Massachusetts, April 6-10, 2022.

Adherence among Dialysis Patients During the Pandemic

Results of previous studies have suggested that older patients adapt to maintenance dialysis better than younger patients. Researchers, led by **Judy Lee,** investigated the response by age of various stressors encountered by dialysis patients residing in the inner city during the COVID-19 pandemic. Results of the investigation were reported during a poster session at NKF SCM22. The poster was titled *Stress and Adherence During the COVID-19 Pandemic in an Inner-City Population of Dialysis Patients: Relationship to Age*.

The study utilized a survey conducted in a random sample of 32 dialysis patients. Questions included fluid intake, general attitudes regarding medical recommendations, and changes in well-being due to COVID-19. Measurement instruments also included the Perceived Stress Scale and the Kim Alliance Scale Revised.

Mean age of the respondents was 56.8 years, 46.9% (n=15) were <60 years of age (younger group) and 53.1% (n=17) were ≥60 years of age (older group). Mean dialysis duration was 88.0 months. Of the total sample, 62.5% (n=20) were male, 90.6% (n=29) self-identified as Black, 56% (n=18) had a high school diploma or less, and 44% (n=14) completed some college or more. There were no statistically significant differences between the two groups in sex, race, or education level.

When asked about following the fluid restriction recommendations, 7% (n=1) of the older patients and 46% (n=6) of the younger patients responded "some of the time" of "never" rather than "most of the time" (P=.034). When asked about difficulty following fluid restriction recommendations, 29% (n=4) of younger patients reported having difficulty following the recommendations, compared with none of the older patients. (P=.037).

When asked about their stress level prior to the pandemic, 33% (n=5) of the younger patients responded "poor" or "average" compared with 100% (n=15) of the older patients who reported their stress level pre-pandemic was "good" (P=.05). In rating their stress level during the pandemic, 64% (n=9) of the younger patients reported being somewhat or very stressed, compared with 79% (n=11) of the older patients who reported being not at all or a little stressed (P=.015).

Four of the younger patients (29%) reported they "sometimes" work well with their provided compared with 100% of the older patients who reported they "always" work well with their provider.

In summary, the authors said, "In our population during the pandemic (1) younger patients were less adherent to fluid restriction and found them more difficult to follow; (2) older patients were more likely to report feeling good prior to the pandemic and were less stressed following it; (3) older patients were more likely to report a good relationship with their provider; (4) younger patients may need more support through the pandemic as they appear to be coping less well, feel less connected, and are less able to follow important dietary restrictions."

Source: Lee J, Wei L, Flynn P, et al. Stress and adherence during the COVID-19 pandemic in an inner-city population of dialysis patients: Relationship to age. Abstract of a poster (Poster #231) presented at the National Kidney Foundation 2022 Spring Clinical Meetings, Boston, Massachusetts, April 6-10, 2022.

Associations Between Pruritus Severity and Adverse Outcomes

Patients with advanced chronic kidney disease (CKD) commonly experience pruritus. Pruritus is associated with depression, decreased quality of life, and poor sleep quality. There are few data available on clinical outcomes associated with pruritus in patients with CKD not on dialysis.

Angelo Karaboyas, PhD, and colleagues conducted an analysis of data from CKDopps (Chronic Kidney Disease Outcomes and Practice Patterns Study), a nephrology clinic-based cohort study of patients with estimated glomerular filtration rate <60 mL/min/1.73 m^2. Results of the analysis were reported during a poster session at NKF SCM22 in a poster titled Uremic Pruritus and Clinical Outcomes in Non-Dialysis CKD.

The analysis included data from 498 patients in Brazil and 1210 patients in the United States (total=1708) in 2013-2020. Patients self-reported the extent to which they were bothered by itch over the past 4 weeks. After adjustments for confounders, the association between severity of pruritus and time-to-event outcomes was examined using Cox regression.

More than half of the patients (53%) reported being at least somewhat bothered by itch. Of the patients reporting being at least moderately bothered by itch, 21% were taking an antihistamine, 11% were taking a gabapentin, and 0.6% were taking a pregabalin; 72% were not prescribed any of the medications commonly prescribed for itch.

Over a median follow-up of 1.2 years, there were associations between pruritus severity and higher incidence of progression to initiation of kidney replacement therapy (P for trend <.001), all-cause mortality (P for trend =0.12), and all-cause hospitalization (P for trend =.17).

In summary, the authors said, "The majority of CKD patients reported some level of pruritus, and these patients were largely untreated. Pruritus severity was associated with higher incidence of KRT, mortality and hospitalization. Further research is needed to evaluate the potential impact of pruritus treatment on these clinical outcomes."

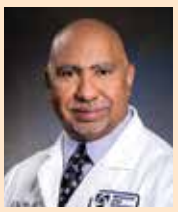
Source: Karaboyas A, Tu C, Speyer E, et al. Uremic pruritus and clinical outcomes in non-dialysis CKD. Abstract of a poster (Poster #221) presented at the National Kidney Foundation 2022 Spring Clinical Meetings, Boston, Massachusetts, April 6-10, 2022.

Awards and Honors

Healthcare professionals who have made significant contributions to the field of kidney disease were honored at the **National Kidney Foundation 2022 Spring Clinical Meetings**.

Jennifer E. Flythe, MD, MPH

The *Shaul G. Massry Distinguished Lecture* award was presented to **Jennifer E. Flythe, MD, MPH,** associate professor of medicine and vice chief of the Division of Nephrology and Hypertension at the University of North Carolina at Chapel Hill. Her research aims to improve the safety and experiences of individuals living with kidney disease by bettering patient-reported and biomedical outcomes.



J. Kevin Tucker, MD

The *Donald W. Seldin Award* was established to recognize excellence in clinical nephrology. The recipient for 2022 is **J. Kevin Tucker, MD.** Dr. Tucker is vice president for education at Mass General Brigham and assistant professor of medicine at Harvard Medical School. His clinical appointment is at Brigham and Women's Hospital, where he focuses on the management of chronic kidney disease patients, hemodialysis patients, and peritoneal dialysis patients.

Bernard Jaar, MD

The winner of the 2022 *Garabed Eknoyan Award,* given in recognition of an individual whose work promotes the mission of NKF in making lives better for people with kidney disease is **Bernard Jaar, MD,** of the Nephrology Center of Maryland and Johns Hopkins University, Baltimore. Dr. Jaar is a practicing nephrologist on the part-time faculty in the Division of Nephrology, Department of Medicine at the Johns Hopkins School of Medicine, with a joint appointment in the Department of Epidemiology at the Johns Hopkins Bloomberg School of Public Health.

Susan T. Crowley, MD, MBA, FASN, FNKF

The *David M. Hume Memorial Award* was created in memory of one of NKF's most distinguished members and is the highest honor given by the Foundation to a scientist-clinician in the field of kidney and urologic diseases. The winner of the 2022 David M. Hume Award, presented to a scientist-clinician in the field of kidney and urologic diseases, is **Susan T. Crowley, MD, MBA, FASN, FNKF,** a board-certified professor of medicine (nephrology) at Yale University School of Medicine and national program director for the Veterans Health Administration (VA) Kidney Disease and Dialysis Program.

Cari Maxwell

The 2022 *Celeste Castillo Lee Patient Engagement Award* was presented to **Cari Maxwell** of Lancaster, Pennsylvania, a member of the NKF Advocacy Committee and champion for patient education, early detection, and patient-centered research. She was diagnosed with polycystic kidney disease in 1989.

Daniel E. Weiner, MD, MS

The *J. Michael Lazarus Award* recognizes individuals whose research has yielded novel insights related to renal replacement therapy. The 2022 winner is **Daniel E. Weiner, MD, MS.** Dr. Weiner is a nephrologist at Tufts Medical Center and associate professor of medicine at Tufts University School of Medicine. His clinical interests include home and in-center dialysis, hypertension, and CKD. His research has focused on cardiovascular and cerebrovascular disease in CKD; clinical trials in CKD, dialysis, and hypertension; decision-making in advanced CKD; and policy.

Haewook Han, PhD, RD, LDN, FNKF

The recipient of the 2021 *Joel D. Kopple Award* for work in the field of renal nutrition is **Haewook Han, PhD, RD, LDN, FNKF.** She is a renal nutrition specialist at Atrius Health's (Harvard Vanguard Medical Associates) Department of Nephrology as well as at Tufts Medical Center in Boston. She has experience in clinical practice among stage 1-5 CKD, post-transplant, and dialysis patients and has participated in research including the Hemodialysis Study.

Amy Wilson, MD

Amy Wilson, MD, is the recipient of the 2021 *Medical Advisory Board Distinguished Service Award.* The award is given to highlight community service and activities that promote NKF's mission on a local level. Dr. Wilson joined the faculty at Indiana University School of Medicine and Riley Children's Hospital, in the division of Pediatric Nephrology & Hypertension in 2010, after completing pediatrics residency and pediatric nephrology fellowship training at Cincinnati Children's Hospital.

Sumit Mohan, MD, MPH

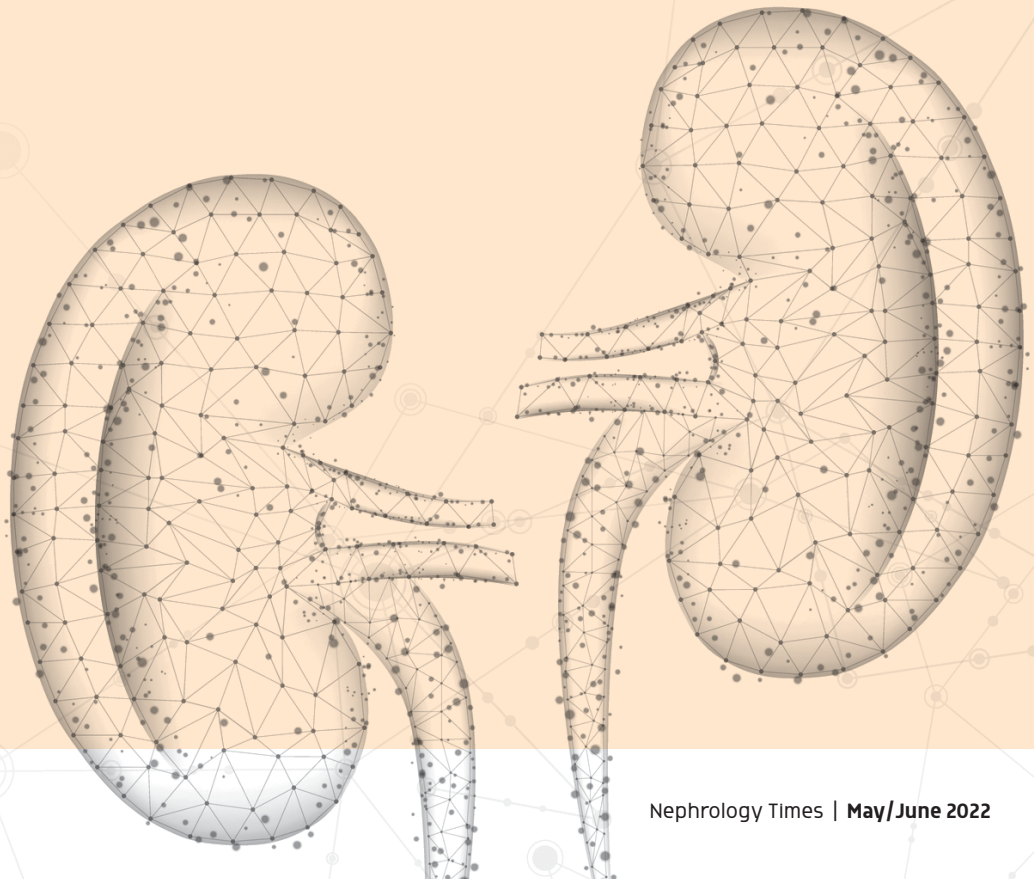
Sumit Mohan, MD, MPH, is the recipient of the 2021 *Excellence in Kidney Transplantation Award.* He is an associate professor of medicine and epidemiology at Columbia University, and the director of clinical research in the Division of Nephrology and the director of quality and outcomes research for the transplant initiative at New York Presbyterian Hospital. Dr. Mohan's clinical and research career has been focused on improving access to care and outcomes for patients with kidney disease–especially those with end-stage kidney disease–and kidney transplantation.

Rep. Rosa DeLauro (D-CT)

The *NKF Public Service Award* honors the work of a kidney health professional who has demonstrated exceptional dedication to public service and has significantly contributed to public policies or government programs aimed at improving outcomes for kidney patients. The 2022 recipient is **Representative Rosa DeLauro** (D-CT), Chair, House Appropriations Committee. She is also the chair of the Labor, Health, and Human Services, and Education Appropriations Subcommittee.

Cheyenne Fasce, BSN, RN

The *Carol Mattix Award* was created by the Council of Nephrology Nurses and Technicians to honor Carol Mattix who was a home dialysis training nurse whose tireless work improved the lives of kidney patients. The winner for 2022 is **Cheyenne Fasce, BSN, RN.** Ms. Fasce is a pediatric hemodialysis and peritoneal dialysis nurse and nurse trainer DCI at Upstate University Hospital, Syracuse, New York.



Print-only Content

Print-only Content

Print-only Content

Risk Factors for Mortality in COVID-19 Patients on Long-Term Dialysis

Risks for adverse outcomes associated with COVID-19 are increased in patients with pre-existing conditions, including obesity, diabetes, or chronic cardiovascular, lung, liver, and kidney diseases. There is also evidence of disparities based on sex, race, and region in the United States.

Patients with end-stage kidney disease (ESKD), particularly those with additional comorbidities, are at higher risk of worsened prognoses with COVID-19. Patients with ESKD undergoing in-center maintenance hemodialysis are extremely susceptible to SARS-CoV-2 infection. Previous studies have examined the impact of COVID-19 on dialysis patients in specific regions or within specific dialysis organizations.

However, according to **Stephen Salerno, MS,** and colleagues, there are few data available on outcomes in COVID-19 in a national population of patients receiving long-term dialysis. The researchers conducted a retrospective, claims-based cohort study to identify risk factors associated with COVID-19 and mortality in Medicare patients undergoing long-term maintenance dialysis. Results of the study were reported in *JAMA Network Open* [doi:10.1001/jamanetworkopen.2021.35379].

The study compared mortality trends of patients receiving long-term dialysis in 2020 with those of previous years (2013-2019) and fit Cox regression models to identify risk factors for contracting COVID-19 and postdiagnosis mortality. The primary outcomes of interest were COVID-19 and all-cause mortality. Associations of claims-based risk factors with COVID-19 and mortality were examined pre- and postdiagnosis.

Among the cohort of 498,169 Medicare patients undergoing dialysis, median age was 66 years, and 43.1% (n=215,935) were women and 56.9% (n=283,227) were men. Most (94%) lived in an urban area. Of the total cohort, 12.1% (n=60,090) received a diagnosis of COVID-19 during the study period.

COVID-19 RISK FACTORS

Rates of COVID-19 were higher among Black patients compared with non-Black patients (13.1% vs 11.5%) and among Hispanic patients compared with non-Hispanic patients (15.6% vs 11.3%). The most prominent differences in rates of COVID-19 were seen between patients with short stays in a nursing home and stays of ≥90 days compared with patients who did not receive care at a nursing home in the year prior to the COVID-19 diagnosis (14.0% and 35.6% vs 10.1%, respectively).

Following adjustment for all other risk factors and compared with no nursing home stay, there was an association between prior short-term stay in a nursing home and a 60% higher hazard for COVID-19 (hazard ratio [HR], 1.60; 95% confidence interval [CI], 1.56-1.65); extended stays were associated with a 448% higher hazard (HR, 4.48; 95% CI, 4.37-4.59). In addition to older age, higher body mass index (BMI), congestive heart failure, inability to ambulate, diabetes, cerebrovascular disease, and higher prevalent comorbidity burden, Black race (HR vs non-Black race, 1.25; 95% CI, 1.23-1.28) and Hispanic ethnicity (HR vs non-Hispanic ethnicity, 1.68; 95% CI, 1.64-1.72) were also associated with higher COVID-19 hazard. Conversely, urban residence, Medicare Advantage coverage, ESKD vintage, cancer, and tobacco use were associated with lower hazards of COVID-19.

NATIONAL MORTALITY TRENDS

Trends in mortality in the period 2013 to 2019 followed a seasonal pattern, with peaks in late January and early February. Beginning in 2020, there were deviations in those trends, commensurate with observed waves of the COVID-19 pandemic. Mortality for Black patients declined in May, returning close to normal historic differences by late summer. Sex differences were variable. Mortality has been high since March 2020; the initial increase was markedly higher in urban areas. The spike in April was driven by key hotspots, particularly New York New York, as well as Detroit, Michigan, and Chicago, Illinois. As COVID-19 became more widespread, the trends shifted.

POSTDIAGNOSIS MORTALITY RISK FACTORS

Of the 60,090 patients with COVID-19, 26.0% (n=15,612) died, compared with 16.9% of patients without COVID-19 (72,339/438,079), suggesting an association between COVID-19 and higher mortality in the study population. Kaplan-Meier curves for post-COVID-19 survival show attenuated differences in survival between Black and non-Black patients and worse survival outcomes among men and among patients with prior nursing home stays.

Also associated with higher mortality after a COVID-19 diagnosis were age, Hispanic ethnicity, higher BMI, congestive heart failure, and number of prevalent comorbidities. Nursing home residence for 1 to 89 days prior to COVID-19 diagnosis was associated with a 41% higher hazard for mortality (HR vs 0 days, 1.31; 95% CI, 1.25-1.37); extended nursing home stays were associated with a 12% higher hazard for mortality (HR vs 0 days, 1.12; 95% CI, 1.07-1.16).

Of the 60,090 patients with COVID-19, 26.0% (n=15,612) died, compared with 16.9% of patients without COVID-19 (72,339/438,079), suggesting an association between COVID-19 and higher mortality in the study population.

The hazard for postdiagnosis mortality was 20% higher in men than in women (HR, 1.20; 95% CI, 1.16-1.24). Mortality hazard was lower in Black patients than in non-Black patients (HR, 0.87; 95% CI, 0.84-0.90). There were also associations between home dialysis, longer ESKD vintage, Medicare Advantage coverage, and tobacco use and higher postdiagnosis mortality. Residing in an urban area was associated with lower postdiagnosis mortality.

In citing limitations to the study, the researchers included the difficulty in capturing COVID-19 cases, the short follow-up period, and the possibility that data on all events during the follow-up period were not available at the time of the analysis.

In conclusion, the authors said, "To our knowledge, this cohort study is the first national study using CMS claims data to evaluate COVID-19 outcomes in the Medicare dialysis population using all available 2020 data through December 2020. Our results identified several risk factors for COVID-19 and mortality, which include nursing home residence, race, sex, modality, and several comorbidity conditions, such as diabetes and obesity. There results improve our understanding of COVID-19 and complications in this high-risk population and could inform policy decisions to mitigate the added burden of COVID-19 and death." ■

TAKEAWAY POINTS

- Researchers conducted a retrospective, claims-based cohort study to identify risk factors associated with COVID-19 and mortality in Medicare patients undergoing long-term dialysis.
- Risk factors for COVID-19 that remained as risk factors for mortality included residence in a nursing home, time on dialysis, obesity, and diabetes.
- Also associated with higher mortality after a COVID-19 diagnosis were age, Hispanic ethnicity, higher body mass index, congestive heart failure, and number of prevalent comorbidities.

Treating Women with CKD and Metabolic Acidosis

Worldwide, the prevalence of chronic kidney disease (CKD) is higher in women than in men, with a ratio of approximately 4:3. Historically, women have been under-represented in nephrology clinical trials, limiting adequate generalization of some findings to women.

In patients with CKD, metabolic acidosis develops due to acid retention from impaired kidney acid excretion, which is associated with reduced ammoniagenesis and impaired ammonium excretion. Patients with metabolic acidosis face increased risk of progression of CKD as well as catabolism of muscle protein and loss of muscle mass.

In women, older age, gender, and postmenopausal status may combine with the catabolic effects of metabolic acidosis. Further, the muscular effects of metabolic acidosis may be more consequential in causing functional decline in women due to their lower baseline muscle mass.

Veverimer is an investigational, orally administered, non-absorbed polymer that is being developed as treatment for metabolic acidosis. The drug increases serum bicarbonate by selectively binding protons and chloride in the gastrointestinal tract and removing this bound hydrochloric acid via fecal excretion.

In a previous study of men and women with CKD and metabolic acidosis, veverimer significantly increased serum bicarbonate within 24 hours after the first dose. At the end of 2 weeks of treatment, serum bicarbonate had increased by 3-4 mmol/L. However, there are few data on the differential effects of veverimer on serum bicarbonate levels and muscle function in a larger multicenter randomized controlled trial by sex.

Vandana S. Mathur, MD, FASN, and colleagues conducted a phase 3, multicenter, randomized, blinded, placebo-controlled trial in 196 patients with CKD and metabolic acidosis who were treated for up to 1 year with veverimer or placebo. Findings from a pre-specified subgroup analysis evaluating the effects of veverimer on metabolic acidosis and physical function among women were reported online in *BMC Nephrology* [doi.org/10.1186/s12882-022-02690-1].

Of the 217 randomized patients in the 12-week parent study, 196 were enrolled in the 40-week extension study. Of those 77 were women (46 in the veverimer group and 31 in the placebo group). Study completion was achieved by 97.3% of the veverimer group (111/114) and 90.0% of the placebo group (74/82). Mean daily dose in the veverimer group was 7.9 g/day.

Patients who took >80% of the prescribed doses were considered dosing compliant. One hundred percent of patients in the veverimer group was dosing compliant, as were 99% of those in the placebo group.

Within both the subgroup of women and the overall study population, baseline characteristics, including demographics, serum bicarbonate, estimated glomerular filtration rate (eGFR), and urine to albumin to creatinine ratio were generally balanced across treatment groups. Among women patients, patient-reported physical function was numerically lower in the veverimer group than in the placebo group (48.4 vs 58.2). Among all women, mean age was 65.4 years, mean baseline eGFR was 28.4 mL/min/1.73 m^2, mean baseline serum bicarbonate was 17.3 mmol/L, and 9.1% were on background oral alkali.

At week 52, a significantly greater percentage of women in the veverimer group met the composite end point (a ≥4 mmol/L increase of normalization of serum bicarbonate) compared with the placebo group (66% vs 36%, *P*=.011). Among patients in the veverimer group, the increase from baseline in serum bicarbonate was significantly greater than among patients in the placebo group (least squares mean increase of 5.4 vs 2.2 mmol/L; *P*<001), findings that were consistent with those from the overall study population.

The significant effect of veverimer on serum bicarbonate was seen within 1 week of the first dose and was maintained through week 52. Effects of veverimer were similar in the subgroup of patients on proton pump inhibitors or H2 receptor blockers compared with the effects in the overall population.

In the subgroup of women, there were significant improvements in patient-reported limitations of physical function on the Kidney Disease Quality of Life physical function domain (KDQoL-PFD, measuring daily activities such as walking, bending/stooping, and climbing stairs, in the veverimer group compared with the placebo group (+13.2 vs –5.2 points, respectively; *P*<.0031). In the veverimer group, the mean KDQoL-PFD score increased (indicating better functioning) from 48.4 at baseline to 61.5 at week 52. In the placebo group, scores worsened (from 58.2 to 53.1).

At week 52, a significantly greater percentage of women in the veverimer group met the composite end point (a ≥4 mmol/L increase of normalization of serum bicarbonate) compared with the placebo group (66% vs 36%, *P*=.011).

Physical performance measured with the repeated chair stand test at week 52 also improved in the veverimer group to a significantly greater extent compared with the placebo group (–4.2s vs +0.08s; *P*<.0002). Mean chair stand time decreased (better functioning) in the veverimer group (21.7 seconds at baseline to 16.7 seconds at week 52). In the placebo group, mean chair stand time weas essentially unchanged (21.5 seconds to 22.2 seconds).

VEVERIMER SAFETY PROFILE

In the overall study population, treatment for up to 1 year with veverimer was well tolerated and the safety profile was similar to that observed in the placebo group. There were no deaths in the veverimer group and two in the placebo group. The rate of premature discontinuation of the study treatment was higher in the placebo group than in the veverimer group (10% vs 3%) and there were no premature discontinuations in the veverimer group due to an adverse event. Serious adverse events were reported in 2% of patients in the veverimer group and 5% of patients in the placebo group. None of the serious adverse events were considered related to the study drug by the investigator.

Among women, adverse events were reported in 91% of patients in the veverimer group and 84% of the placebo group. Treatment-related adverse events were reported int 42% of patients in the placebo group and in 26% of patients in the veverimer group.

The authors cited some limitations to the study, including preforming a subgroup analysis and the lack of significant racial heterogeneity.

In conclusion, the researchers said, "We found that veverimer, an investigational non-absorbed polymer drug, was effective in treating metabolic acidosis in women with CKD. Women treated with veverimer reported significantly improved ability to perform daily activities; their measured physical performance also improved significantly." ■

The study was funded by Tricida, Inc.

TAKEAWAY POINTS

- Veverimer is an investigational, non-absorbed polymer that is being developed as treatment for metabolic acidosis.
- Researchers reported findings from a pre-specified subgroup analysis analyzing the effects of veverimer on women with chronic kidney disease (CKD).
- Results demonstrated that veverimer was effective in treating metabolic acidosis in women with CKD and significantly improved physical function.

CONFERENCE COVERAGE KIDNEY WEEK 2021

RASi Suspension and Mortality in Patients with AKI

In individuals with chronic kidney disease, blockade of the renin-angiotensin system (RAS) may slow disease progression and prevent mortality. According to **Ana carolina Nakamura Tome, MD,** and colleagues, it is unclear whether RAS inhibitors (RASi) can increase the risk of developing acute kidney injury (AKI) and related complications among hospitalized patients. The researchers conducted an analysis to compare mortality of patients with AKI who discontinued RASi with that of patients who maintained use of RASi.

Results of the analysis were reported during a virtual poster session at ASN Kidney Week 2021. The poster was titled *Associations of RAS Inhibitor Suspension During AKI with Mortality in Hospitalized Patients.*

The analysis included data from a cohort of hospitalized patients in a RASi identified by an AKI alert based on Kidney Disease Improving Global Outcomes creatinine criteria. From January to December 2018, suspension of use of RASi medications was defined by the lack of its prescription until 3 days following AKI alert in the patient's electronic health records. The association between suspension of RASi use with all-cause mortality was tested using Cox models, adjusting for possible confounders including age, sex, race, baseline and worst achieved glomerular filtration rates, potassium, hemoglobin levels, and episodes of hypertension during the hospitalization.

The cohort included 1252 hospitalized patients who were on a RASi. Following the AKI alert, 493 remained on a RASi and 760 discontinued use of a RASi. Median time to follow-up was 11.9 days.

Patient characteristics were similar across treatment strategies. In the group that suspended RASi use, more patients needed dialysis (13% vs 4%) and were admitted to the intensive care unit (66% vs 55%), compared with the group that continued RASi use. Mean potassium levels were consistent across groups (4.45 mg/dL vs 4.39 mg/dL, respectively). There was a strong association between suspension of RASi use and mortality.

In conclusion, the authors said, "Among patients with AKI, the strategy of suspending RASi resulted in a twofold higher death rate than for those who remained on the medication, even after adjustment for possible confounders. These findings suggest that an individualized approach to RASi therapy may be warranted in the hospitalized patient with AKI."

Source: Tome ACN, Lopes M, Santos Menezes Lopes D, Ramalho RJ, Lima EQ. Associations of RAS inhibitor suspension during AKI with mortality in hospitalized patients. Abstract of a poster presented at the American Society of Nephrology virtual Kidney Week 2021 (Abstract P00193), November 2021.

Patiromer Monotherapy for Hyperkalemia in Acute Care Settings

Hospitalized patients often develop hyperkalemia, a common electrolyte disorder. However, according to **Katherine E. Di Palo, PharmD,** and colleagues there are few data available on the usefulness of administering patiromer for reduction of serum potassium levels in hospitalized patients with hyperkalemia.

Mean time from recording of baseline serum potassium levels in the EHR to administration of patiromer was 6.7 hours.

The researchers conducted a cohort study designed to evaluate the outcomes associated with patiromer as monotherapy in patients with acute hyperkalemia in an acute care setting. Results of the study were reported online in *JAMA Network Open* [doi:10.1001/jamanetworkopen.2021.45236].

The study utilized electronic health record (EHR) data from adult patients treated with patiromer for acute hyperkalemia in emergency departments, inpatient units, and intensive care units at an urban, academic medical center in the Bronx, New York, between January 30, 2018, and December 31, 2019. Data were analyzed between June 2020 and February 2021.

The study exposure was a single dose of patiromer (8.4 g, 16.8 g, or 25.2g). The primary outcome of interest was the mean absolute reduction in serum potassium level from baseline at three distinct time intervals following administration of patiromer: 0 to 6 hours, greater than 6 to 12 hours, and greater than 12 to 24 hours. Secondary outcomes were the incidence of hypokalemia and potassium reduction stratified by baseline potassium level and care setting.

During the study period, a total of 881 unique encounters of patiromer administration in an acute care setting were identified. Mean age of the cohort was 67.4 years and 52.6% of the encounters (n=463) were for male patients. Of the 881 encounters, 1.7% (n=15) of the patients identified as Asian; 37.9% (n=334) as Hispanic/Latinx; 38.4% (n=338) as non-Hispanic Black; 12.9% (n=114) as non-Hispanic White; and 9.1% (n=80) as other or unknown race/ethnicity.

In 42.0% of the encounters (n=370), patients were treated with renin-angiotensin-converting enzyme inhibitors prior to the hyperkalemia episode. Common comorbidities were heart failure with marked ejection fraction (161 encounters, 18.3%) and moderate-to-severe chronic kidney disease (665 encounters, 75.5%). Patiromer was administered in inpatient units (679 encounters, 77.0%); emergency departments (152 encounters, 17.3%); and intensive care units (50 encounters, 5.7%). Mean length of stay prior to patiromer administration was 5.4 days.

At baseline and prior to administration of patiromer, mean serum potassium concentration was 5.6 mEq/L, and most patients had mild or moderate hyperkalemia (potassium level, 5.1-5.5 mEq/L or 5.6-6.4 mEq/L, respectively). Patients had severe hyperkalemia (potassium level ≥6.5 mEq/L) in only 2.2% of encounters (n=19). The lowest dose (8.4 g) of patiromer was administered in 81.8% of encounters (n=721). Mean time from recording of baseline serum potassium levels in the EHR to administration of patiromer was 6.7 hours.

The mean reduction in serum potassium levels was 0.50 mEq/L at 0 to 6 hours, 0.46 mEq/L at greater than 6 to 12 hours, and 0.52 mEq/L at greater than 12 to 24 hours ($P<.001$ for all compared with baseline). The findings represent a mean relative reduction from baseline of 8.5%, 7.9%, and 9.0% at each respective time interval.

There was variation in both absolute and relative reduction in potassium across baseline potassium level categories; there was no variation by care setting. There appeared to be a trend toward a greater relative reduction in potassium levels associated with patiromer doses of ≥16.8 g compared with 8.4 g at greater than 12 to 24 hours.

In 82.3% of encounters (n=725), patients received no further doses of potassium binders in the 24 hours following the initial administration of patiromer; in 15.5% of encounters (n=137), patients received one additional dose and in 2.2% of encounters (n=19),patients received two or more additional doses. Of the patients receiving additional binder doses, mean time to administration was 14.8 hours. In 76 encounters, patients received at least one dose of insulin in the 24 hours following administration of patiromer within a mean of 13.5 hours from the initial dose. Other subsequent standard-of-care measures for hyperkalemia included furosemide treatment, hemodialysis, and intravenous calcium treatment.

In 0.2% of encounters (n=2), patients experienced an episode of hypokalemia, defined as serum potassium level of <3.5 mEq/L. In 10.0% of encounters (n=68), patients developed hypomagnesemia, defined as serum magnesium level of <1.7 mg/dL, following administration of patiromer. The two episodes of hypokalemia were mild and asymptomatic, with a serum potassium concentration between 3.2 and 3.4 mEq/L.

Limitations to the study findings cited by the authors included the lack of a control group, limiting the ability of the researchers to determine whether observed reduction in potassium levels were associated with patiromer alone; in addition, the absence of a protocol for treatment and monitoring of hyperkalemia necessitated the exclusion of observations in each time interval if a laboratory blood sample was not obtained.

In conclusion, the researchers said, "In this cohort study of patients with acute, non-life-threatening hyperkalemia, a single dose of patiromer was associated with a significant decrease in serum potassium level and a low incidence of hypokalemia. The findings suggest that episodes of non-life-threatening hyperkalemia may be treated with patiromer monotherapy in an acute care setting to help minimize the risk of hypokalemia associated with other potassium control measures." ■

Funding for this study was provided by Vifor Pharma, Inc.

TAKEAWAY POINTS

- Researchers reported results of a cohort study designed to examine outcomes associated with patiromer as monotherapy in patients with acute hyperkalemia in an acute care setting.
- The analysis included 881 encounters of patients treated for acute hyperkalemia; patiromer was associated with a significant reduction in serum potassium levels within the first 6 hours of administration.
- Both absolute and relative potassium reduction from baseline varied across severity of baseline hyperkalemia but not by care setting.

COVID-19 Outcomes in People with Chronic Kidney Disease

By May 2021, more than 151 million people were confirmed to have been infected with SARS-CoV-2, and more than 3.1 million deaths attributable to COVID-19 had been reported worldwide. Early in the pandemic, evidence suggested a higher incidence of severe COVID-19 in patients with chronic diseases, including chronic kidney disease (CKD), and an association with acute kidney injury (AKI). There was also evidence of poor prognosis in kidney transplant recipients who developed COVID-19, with a 25% mortality rate. Later evidence indicated CKD as a risk factor for severe COVID-19.

Edmund Y. M. Chung, MD, and colleagues performed a systematic review and meta-analysis of the incidence and outcomes of COVID-19 in adults and children with CKD, including those treated with kidney replacement therapy (KRT). Results were reported in the *American Journal of Kidney Diseases* [2021; 78(6):804-815].

The review included MEDLINE, EMBASE, and PubMed between November 1, 2019, and February 22, 2021. Retrospective and prospective cohort studies and case-control studies examining the incidence of COVID-19 or outcomes in adults and children with any stage CKD, including CKD treated with dialysis and kidney or kidney/pancreas transplant recipients with or without COVID-19. Gray literature included 29 conference abstracts, two government reports, and four preprints. CKD was defined using the Kidney Disease: Improving Global Outcomes CKD guideline and COVID-19 was defined using criteria from the World Health Organization based on a positive reverse transcriptase-polymerase chain reaction assay for SARS-CoV-2.

Data extraction included incidences of COVID-19, death, respiratory failure, dyspnea, recovery, admission to the intensive care unit, hospital admission, need for supplemental oxygen, hospital discharge, sepsis, short-term dialysis, AKI, and fatigue. The researchers adjudicated evidence certainty using an adapted GRADE (Grading of Recommendations Assessment, Development and Evaluation) framework for prognostic factor research.

The search revealed 6698 citations; of those, 348 studies were included, representing 382,407 participants with CKD and COVID-19 and 1,139,979 total participants with CKD. The analysis included 336 cohort studies (45 prospective, 245 retrospective, and 46 not identified as prospective or retrospective) and 12 case-control studies. The case-control studies included all eligible participants with CKD without KRT, participants with dialysis-dependent CKD, or kidney transplant recipients during the study period; however, CKD was not reported in controls, so only case participants with CKD were included.

A total of 110 studies reported the incidence of COVID-19 in individuals with CKD (366,931 participants with CKD and COVID-19; 772,389 total participants with CKD); 330 studies reported outcomes (381,422 participants with COVID-19), and 309 studies (373,141 participants with CKD and COVID-19 and 1,114,991 participants with CKD) reported on study duration for the calculation of incidence rates.

Participant age ranged from 11 to 79 years; five studies included children with CKD (165 participants). Eighteen studies of kidney transplant recipients reported baseline glomerular filtration rate. In 308 studies, study duration ranged from 7 to 274 days. Most of the studies were conducted in Europe, North and South America, and the Western Pacific region, and in high- to upper-middle-income countries.

In 88 studies of 14,972 participants with CKD and COVID-19 and 740,452 total participants with CKD, the incidence of COVID-19 in patients with CKD was 66 per 10,000 person-weeks (95% confidence interval [CI], 58-75). In participants with CKD without KRT, the incidence of COVID-19 was 16 per 10,000 person-weeks (95% CI, 4-33) in five studies of 701 participants with CKD and COVID-19 and 70,683 total participants with CKD.

In 59 studies of 12,208 participants with CKD and COVID-19 and 468,233 total participants with CKD, the incidence of COVID-19 in participants with CKD requiring KRT was 105 per 10,000 person-weeks (95% CI, 91-120) (low-certainty evidence). In 29 studies of 1893 participants with CKD and COVID-19 and 120,281 total participants with CKD, the incidence in kidney transplant recipients was 23 per 10,000 person-weeks (95% CI, 18-30) (low-certainty evidence).

Based on low-certainty evidence, the incidence of death in individuals with CKD and COVID-19 was 32 per 1000 person-week (95% CI, 30-35) in 229 studies with 70,922 total participants, which may be higher than in those with CKD without COVID-19 (incidence rate ratio, 10.26; 95% CI, 6.78-15.53). The incidence of death in people with COVID-19 and CKD without KRT was 40 per 1000 person-weeks (95% CI, 35-45); the incidence of death in those with CKD requiring KRT was 30 per 1000 person-weeks (95% CI, 26.35) in 107 studies with 34,639 participants.

In people with CKD and COVID-19, the overall incidence of respiratory failure was 31 per 1000 person-weeks (95% CI, 27-35), in 101 studies with 68,840 participants. The incidence of respiratory failure in those with COVID-19 and non-KRT CKD was 28 per 1000 person-weeks (95% CI, 29038) in 17 studies with 57,077 participants.

The researchers cited some limitations to the study, including the limited measurement of known confounding factors affecting the incidence and outcomes of COVID-19 in patients with CKD, including old age, male sex, being Black or South Asian, lower socioeconomic status, obesity, diabetes, malignancy, or respiratory, cardiovascular, liver, neurologic, or autoimmune diseases; the lack of reporting of prognostic outcomes in people with CKD but without COVID-19; lack of reporting on stages of CKD in most studies; reporting outcomes in only hospitalized patients in most studies; and variability in study definitions of COVID-19.

In summary, the authors said, "Our systematic review found that people with CKD may be at higher risk of COVID-19 than the general population and may be at higher risk of death than people with CKD without COVID-19. Decision-making by clinicians and policy makers should focus on preventive measures for people with CKD, particularly people receiving maintenance dialysis. Future studies that measure and adjust for confounders, and that are adequately powered to report the COVID-19 COS [Core Outcomes Set] and SONG [Standardized Outcomes in Nephrology] CKD core outcomes in people with CKD with and without COVID-19, are needed to better evaluate the prognostic effect of COVID-19 in people with CKD." ■

TAKEAWAY POINTS

- Researchers reported results of a systematic review and meta-analysis to examine the incidence and outcomes of COVID-19 in individuals with chronic kidney disease (CKD).
- Data for the analysis were pooled from 348 studies that included a total of more than one million individuals with CKD. COVID-19 occurred more frequently in people receiving maintenance dialysis than in those with non-dialysis dependent CKD.
- The risk of death may be 10-fold higher in people with CKD and COVID-19 than in those with CKD without COVID-19.

Extending Eligibility of Reinstatement of Waiting Time after Allograft Failure

The optimal treatment for kidney failure is kidney transplantation. The shortage of kidneys available for transplantation is intensifying, creating interest in the high proportion of deceased donor kidneys discarded after procurement. The discard rate for deceased donor kidneys recovered for transplant in the United States is approximately one in five, despite evidence that transplantation with even marginal deceased donor kidneys can improve survival, quality of life, and cost, compared with dialysis.

The high rate of discard exacerbates the organ shortage that results in long wait times. Deceased donor kidney discard occurs when the benefits of transplantation using kidneys thought to be at risk for shorter allograft longevity and earlier graft failure are outweighed by the risk of those adverse outcomes. However, according to **S. Ali Husain, MD, MPH, MA,** and colleagues, many discarded deceased donor kidneys are potentially transplantable, and improving utilization of those kidneys would expand access to transplantation.

TAKEAWAY POINTS

- Of 76,044 deceased donor kidneys procured from 2013-1027, 20% (n=60,895) were discarded.
- Researchers used decision analysis informed by clinical registry data to estimate the impact of a policy designed to increase organ utilization by extending eligibility for reinstatement to the waiting list for recipients with early graft failure following transplantation.
- With the exception of very low reduction in discards and very high failure rate of transplanted organs, reinstating a waiting time up to 1 year after transplantation yielded more additional transplants than growth in additions to the waiting list.

The researchers conducted a decision analysis to estimate the impact of a policy proposal to increase organ utilization by extending eligibility for waiting time reinstalment for recipients experiencing early allograft failure after transplantation. Results were reported in the *American Journal of Kidney Diseases* [2022;79(3):354-361].

The researchers utilized data from the Organ Procurement and Transplantation Network to identify deceased donor kidneys procured in the United States from 2013 to 2017. The analysis intervention was extension of waiting time reinstatement for recipients experiencing allograft failure from the current 90 days to 1 year after transplantation.

The outcome of interest was the net impact to the waitlist, defined as the estimated number of additional transplants minus estimated increase in waiting list reinstatements. The analysis aimed to estimate (1) the number of additional deceased donor kidneys that would be transplanted if there were a 5% to 25% relative reduction in discards and (2) the number of recipients who would regain waiting time under a 6-, 12-, 18-, and 24-month reinstatement policy.

A total of 76,044 deceased donor kidneys were included in the analysis; of those 80% (n=60,985) were transplanted and 20% (n=15,059) were discarded. The Kidney Donor Profile Index (KDPI) distribution for discarded deceased donor kidneys was most notable for the kidneys with higher KDPI; any reduction in the discard rate would disproportionally require improved use of high-KDPI organs (organs of lower relative quality). During the study period, a mean 4045 deceased donor kidneys were discarded annually, More than half of the discarded kidneys were from the highest two KDPI deciles (KDPI ≥81%), representing a mean 2123 annual discards. Approximately 16% of discarded deceased donor kidneys were from the lowest five KDPI deciles (KDPI ≤50%, 624 discards annually).

Based on a relative reduction in discards (R) of 5%, 10%, 15%, 20%, or 25% the researchers estimated that the number of additional transplants performed would be 202, 405, 607, 809, or 1011 deceased donor kidneys, respectively.

Based on the KDPI decile, the current observed failure rate for transplanted deceased donor kidneys at any time (T) varied, ranging from 1.3%-3.9% at 3 months, 1.5%-5.4% at 6 months, 1.9%-7.5% at 12 months, 2.6%-9.3% at 18 months, and 3.5%-10.7% at 24 months. Correspondingly, 410 transplants per year failed within 1 year; of those, 150 per year failed between 3 months and 1 year.

Based on those failure rates, the researchers assessed the expected net benefit to the waitlist of any permutation of R and T ($N_{R,T}$); $N_{R,T}$ exceeded 0 (greater number of additional transplants than excess returns to the waitlist) in all circumstances with the exception of at 18 and 24 months when R=5%. Assuming additional transplants (if a given relative reduction in current discard rate is achieved) failed at rates similar to currently transplanted kidneys, at T of 12 months, there would be an $N_{R,T}$ of 838 net additional transplants for R=25%, 641 for R=20%, 443 for R=15%, 245 for R=10%, and 47 for R=5%. At the best relative reduction in discards considered in the analysis (R=25%), $N_{R,T}$ ranged from 908 at T of 6 months to 574 at T of 24 months.

The authors cited some limitations to their proposal to allow recipients of deceased donor kidneys with early post-transplant allograft failure within an expanded time frame to regain their waiting time: (1) The estates of net benefit were calculated in rates of relative discard reduction and allograft failure rates that may be plausible but were arbitrary; (2) not taking into account other patient-level consequences of early graft failures, such as sensitization that may delay access to a second transplant or the risks associated with exposure to immunosuppression; (3) if the increased use of marginal organs that would have been previously discarded is associated with a significantly higher rate of early graft failure, the reinstatement of waiting time may not offset the risks of perioperative complications such as infection, prolonged hospitalization, and death; and (4) given that a loss of quality-adjusted life years (QALYs) associated with the use of lower quality organs may be offset by a gain in QALYs from reduction in waiting and increased probability of transplantation, the impact of increased utilization of marginal organs on QALYs realized from transplantation is difficult to predict.

"In conclusion," the researchers said, "We estimate that a policy change reinstating pretransplant waiting time for deceased donor kidney recipients who experience allograft failure within 1 year of transplant can result in a net benefit to the kidney waitlist even if it only results in a small decrease in the proportion of deceased donor kidneys that are discarded. Although there results are theoretical, we believe that such policies that aim to improve organ utilization by addressing cognitive processes underlying suboptimal organ offer acceptance warrant study." ■

Immunosuppression Adherence in Pediatric Kidney Transplant

Following solid-organ transplantation, the primary aim of care is preventing allosensitization. Despite potent immunosuppression, nonadherence often disrupts treatment, resulting in rejection. Among recipients of kidney transplant, the strongest predictors of allograft failure are nonadherence and subsequent antibody or T-cell-mediated rejection (AMR and TCMR, respectively).

Adolescent and young adult kidney transplant recipients are disproportionally affected by suboptimal adherence, due, in part, to normal development changes affecting adherence behaviors. Transplant recipients in that age group face rates of allograft failure that are three times those of older recipients, resulting in a need to return to dialysis, and contributing to a 25-year decrease in their life expectancy, worsened quality of life and much higher cost.

Results of previous clinical trials have demonstrated that adherence barriers are amenable to behavioral interventions, and provider-delivered, systems-based, multicomponent interventions have had substantial and durable effects. However, according to **David K. Hooper, MD,** and colleagues, there are few data available on whether improved adherence results in allograft rejection.

The researchers reported results of a quality improvement initiative implemented in 2015 at Cincinnati Children's Hospital aimed at decreasing late acute rejection in kidney transplant recipients by applying evidence-based adherence strategies as standard care. The strategies directly addressed barriers to adherence and correlated highly with adherence behaviors. Results of the initiative were reported in the *American Journal of Kidney Diseases* [2022;79(3):335-346].

The initiative included kidney transplants who were receiving care at Cincinnati Children's Hospital ≥1 year after transplant and who were taking one or more immunosuppressive medications from 2014 through 2017. Over a 14 month period, interventions collectively called MAPS (Medication Adherence Promotion System) were implemented: (1) adherence promotion training for clinical staff; (2) electronic health report-supported adherence risk screening; (3) systematic assessment of medication adherence barriers; (4) designation of specific staff to partner with patients to address adherence barriers; (5) patient-centered shared decision-making to develop action plans; (6) follow-up evaluation to address progress and adapt action plans if necessary; and (7) optional electronic medication adherence monitoring.

The primary outcome measure was biopsy-proven late acute rejection, acute TCMR grade 1a or higher or AMR according to the Banff 2013 criteria. Process measures were conducted to assess barriers, identify barriers, and perform interventions. Secondary outcomes/balancing measures were de novo donor-specific antibodies (DSA), biopsy rate, and rejections per biopsy.

Patient-days between acute rejections as well as monthly rejections per 100 patient-months before and after implementation of the program were evaluated using time series analysis with statistical process control. Multivariable analyses were performed to control for known rejection risk factors including changes in treatment and case mix.

Over the 4-year study-period, the researchers assessed 121,133 active patient-days in 130 patients. A total of 72 patients met inclusion criteria at the beginning of the observation period. During the study, 58 patients entered the cohort (49 new transplants and nine transfers). Forty-three left the cohort. Reasons for leaving the cohort were transferred care (n=33), allograft failure (n=4), loss to follow-up (n=3), death (n=2), or malignancy (n=1). All of the allograft failures occurred in the pre-MAPS period.

There were 51 rejections (34 prior to MAPS vs 17 after MAPS). Twenty-four patients had one rejection, four patients had two rejections, five patients had three rejections, and one patient had four rejections. Of all patients-days of observation among patients with multiple rejections, the proportion occurring in the pre-MAPS and post-MAPS periods were similar (59.9% vs 48.1%), which was comparable to the entire sample.

During the 26-month baseline and implementation period, there was a median of 1700 (upper control limit [UCL], 7939) patient-days between rejection episodes. Prior to implementation of MAPS, the monthly rejection rate was 1.61 rejections per 100 patient-months.

There were four rejection episodes in the 5 weeks following implementation of MAPS. After April 7, 2016, the researchers observed 11,658 patient-days between rejection episodes above the previous UCL of 7939. Following implementation of MAPS, the average monthly late acute rejection rate fell from 1.61 to 0.88 rejections per 100 patient-months. All but three of the 22 monthly data points after implementation of MAPS fell below the previous monthly average rejection rate, including the final 12 consecutive months indicating special cause on the U-chart.

In the multivariable model, the post-MAPS treatment period was associated with a 50% reduction in the incidence of rejection (incidence rate ratio [IRR], 0.51; 95% confidence interval [CI], 0.28-0.94; *P*=.03). The final model included DSA history, repeat kidney transplant, donor type, race, prior rejection, human leucocyte antigen mismatch, and time since transplant. None of the covariates significantly violated the proportionality assumption.

Following adjustment for covariates in the multivariable model, the post-MAPS treatment period was associated with a 50% reduction in the incidence of rejection (IRR, 0.50; 95% CI, 0.27-0.91; *P*=.02). There was an association between DSA history and a >2-fold increase in incidence of rejection (IRR, 2.27; 95% CI, 1.12-4.57; *P*=.02). There was also an association between each year after transplant and a 13% decreased incidence of rejection (IRR, 0.87; 95% CI, 0.77-0.97; *P*=.02).

There were no significant differences in the rate of kidney biopsies per 100 patient-months before and after implementation of MAPS (3.17 vs 2.91; *P*=.5). There was a significant decrease in the rate of biopsies positive for rejection (50% to 30%; *P*=.03). A total of 13 patients developed de novo DSA during the pre-MAPS period compared with seven patients in the post-MAPS period (*P*=.3). There were no significant differences in the severity and type of rejection before and after implementation of MAPS (*P*=.8).

Limitations to the findings cited by the authors included lack of direct measuring of adherence, the single-center study design, and the need to make inferences of causality.

In summary, the researchers said, "We adapted evidence-based adherence interventions and reliably implemented them at the point of care with clinical staff supported by the EHR. This multimodal, provider-delivered system to identify and mitigate patient and caregiver barriers to taking immunosuppression was associated with a 50% rejection in late allograft rejection. MAPS has become the standard of care in our clinic and should be tested in other settings." ■

TAKEAWAY POINTS

- Among pediatric kidney transplant recipients, suboptimal adherence to immunosuppression medications is associated with high risk of allograft rejection.
- Clinicians at Cincinnati Children's Hospital implemented a program to help patients identify barriers to medication adherence and work with clinicians to manage those barriers.
- Following full implementation of the system, the rate of acute allograft rejection decreased by nearly half.

Testing for Genetic Risk for Kidney Failure in Patients of African Ancestry

Approximately 26 million adults in the United States are affected by chronic kidney disease (CKD). The risk of CKD and progression to end-stage kidney disease (ESKD) is higher among those of African ancestry compared with those of European ancestry due in part to social determinants, clinical factors, and health system factors. Social constructs include race and ethnicity; ancestry has some biologic underpinnings.

High-risk genotypes at the apolipoprotein L1 (*APOL1*) locus confer a 5-fold to 10-fold increased risk for CKD and ESKD attributed to hypertension; the risk increment is attenuated among individuals with diabetes. High-risk variants of *APOL1* (OMIM 603734) on chromosome 22 are found in one in 17 people of African ancestry but are nearly absent in people of European ancestry.

Of late, interest in incorporating genetic testing into primary care has increased. The *APOL1* risk genotype is common and carries high risk for CKD in individuals of African ancestry who are disproportionally burdened by chronic diseases, creating a need for the incorporation of genetic testing into clinical care. Kidney function deterioration can be reduced with blood pressure control, but those of African ancestry have the highest age-adjusted prevalence of hypertension and the lowest rates of blood pressure control. Further, tests of kidney function are underused among patients at high risk for CKD.

There are few data available on whether disclosure of results of *APOL1* genetic testing to patients of African ancestry and their clinicians affects blood pressure, screening for kidney disease, or patient behavior. **Girish N. Nadkami, MD, MPH,** and colleagues conducted a pragmatic randomized clinical trial to examine the effects of testing and disclosing *APOL1* genetic results to patients of African ancestry with hypertension and their clinicians. Results were reported online in *JAMA Network Open* [doi:10.1001/jamanetworkopen.2022.1048].

The trial included adults of African ancestry with hypertension and without existing CKD in two healthcare systems in the United States from November 1, 2014, through November 28, 1016. Follow-up continued until January 16, 2018. Patients were randomly assigned to undergo immediate (intervention) or delayed (waiting list control group) *APOL1* testing in a 7:1 ratio. Statistical analyses were performed from May 1, 2018, to July 31, 2020.

Patients in the intervention group received *APOL1* genetic testing from trained staff. Their clinicians received results through clinical decision support in electronic health records (EHRs). Patients in the waiting list control group received results following their 12-month follow-up visit. The primary outcomes of interest were the change in 3-month systolic blood pressure and 12-month urine kidney disease screening comparing intervention patients with high-risk *APOL1* genotypes and those with low-risk *APOL1* genotypes. Secondary outcomes included comparison of those outcomes between patients in the intervention group with high-risk *APOL1* genotypes and those in the control group. Psychobehavioral factors were also analyzed.

During the enrollment period November 1, 2014, to November 20, 2016, 5481 patients identified in EHR queries were approached. Of those, 2052 were enrolled, 2783 were ineligible, 243 declined, and 412 were undecided at the end of the enrollment period. Of the 2052 enrolled, all but two were randomized. Mean age of participants was 53 years, 66% were women (1360/2050), 50% had very low income (1014/2050), 38% had low health literacy (769/2050), and 26% had very good or excellent self-rated health (530/2050).

At 3 months, 92% of participants remained in the study (1881/2050); 77% remained at 12 months (1587/2020). There were no differences between the two study groups in follow-up rates. The two groups were similar in sociodemographic characteristics with exception of higher educational attainment in the control group (more than some college: 64% [162/255) control patients vs 56% [1010/1975] intervention patients. Patients with high-risk *APOL1* genotypes had significantly higher mean systolic blood pressure at baseline (137 mm Hg) than those with low-risk genotypes (134 mm Hg; *P*=.003) and controls (133 mm Hg; *P*=.001).

All groups had some decreases in systolic blood pressure. It was greatest in patients with high-risk *APOL1* genotypes (mean, 6 mm Hg) compared with those with low-risk *APOL1* genotypes (mean, 3 mm Hg; *P*=.004) or controls (mean, 3 mm Hg; *P*=.01). The percentage change in systolic blood pressure was significantly different between patients with high-risk *APOL1* genotypes (3.6%), those with low-risk *APOL1* genotypes (1.0%; *P*=.003), and controls (1.3%; *P*=.04).

Following adjustment for age, sex, body mass index, comorbidity, education level, and marital status, the decrease in systolic blood pressure remained statistically significant between patients with high-risk *APOL1* genotypes and those with low-risk *APOL1* genotypes.

All three groups had protein excretion tests at baseline in similar proportions. At 12 months after the intervention, all three groups had a significant increase in the rate of urine protein testing over time. Patients with high-risk *APOL1* genotypes had the most significant increase (12% increase; from 39 of 234 [17%] to 68 of 243 [29%]) compared with those with low-risk *APOL1* genotypes (6% increase; from 278 of 1561 [18%] to 377 of 1561 [24%]) and controls (7% increase; from 33 of 255 [13%] to 50 of 255 [20%]). The difference was significant between patients with high-risk *APOL1* genotypes and controls (*P*=.01). Over time across groups, the difference did not remain statistically significant.

In response to testing, patients in the high-risk *APOL1* genotype group reported more changes in lifestyle (a subjective measure that included better dietary and exercise habits): 59% compared with 37% in the group with low-risk *APOL1* genotypes. Patients in the high-risk *APOL1* genotype group also reported greater increased use of blood pressure mediation than those in the low-risk *APOL1* genotype group (10% vs 5%).

The authors cited some limitations to the study findings, including exclusion of patients with CKD, the modest effect size, the lack of comprehensive data on lifestyle and dietary intake or medication refill, and conducting the study in only one urban area.

In conclusion, the researchers said, "Return of *APOL1* genetic testing results combined with EHR-based clinical decision support and disclosure of results to patients using laypersons improved systolic blood pressure control and increased guideline-appropriate kidney function testing. These results may support an approach of broad implementation of genetic medicine in primary care. This broad implementation will benefit racial and ethnic minority groups that have been traditionally under-represented in both clinical trials and genetic studies. Because it is imperative not to overlook the importance of social determinants of health in affecting chronic disease, it will also be important to understand and address the intersection of social and biological determinants in patient health." ■

TAKEAWAY POINTS

- Results of a pragmatic randomized clinical trial designed to examine the effects of testing and disclosing *APOL1* genetic results to patients of African ancestry with hypertension and their clinicians.
- Patients were randomized to receive immediate (intervention) or delayed (control) *APOL1* testing results. Patients in the immediate results group received results from trained staff; those in the delayed group received results after a 12-month follow-up visit.
- Patients with high-risk *APOL1* genotypes had greater improvement in blood pressure from baseline and more lifestyle changes than those with low-risk APOL1 genotypes or controls.

AKF Names 2022 Research Fellows

Recipients of 2022 American Kidney Fund (AKF) funding through the Clinical Scientist in Nephrology Program were announced in a recent press release from AKF: **Jillian Caldwell, DO,** nephrology fellow at Stanford University School of Medicine and **Janewit Wongboonsin, MD, MS,** a clinical and research fellow in the Brigham and Women's Hospital-Massachusetts General Hospital Renal Fellowship Program.

The Clinical Scientist in Nephrology Program has funded more than 40 nephrologists since 1989; funding includes support from Akebia Therapeutics, Inc. **LaVarne A. Burton,** AKF president and CEO, said, "We are very pleased to provide this year's AKF Clinical Scientist in Nephrology fellowships to two researchers who are dedicated to improving health outcomes for people affected by kidney disease through their innovative studies in the areas of health equity and genetics. Thanks to support from Akebia Therapeutics Inc., we are able to continue our decades-long commitment to funding groundbreaking research through this vital program."

John Butler, president and CEO of Akebia Therapeutics, Inc., said, "Akebia proudly supports the AKF Clinical Scientist in Nephrology Program, which has provided funding to help usher in a new generation of talented researchers investigating kidney disease. Approximately 37 million adults in the US are affected by kidney disease, which is an alarming number that reinforces the need to work with urgency to advance research on their behalf."

Dr. Caldwell's project will examine the interplay between immunologic matching in kidney transplants and equitable access to transplantation. Racial and ethnic minorities are less likely to receive fully matched kidneys; Dr. Caldwell's project will examine the reasons for the disparity and examine alternative strategies for kidney allocation that enhance access to well-matched kidney transplants. Her long-term goals include devising better systems, including policy changes, to enhance access and equity in kidney transplantation.

Dr. Wongboonsin will study the genetic signatures of nephrotic syndrome, using an existing electronic health record-linked biobank of 130,000 participants in the Mass General Brigham Biobank. He hopes to expand the understanding of the prevalence and clinical impact of nephrotic syndrome genetic variants and create a large, genetically mapped cohort of patients that will be valuable for both current and future clinical genetic epidemiology studies.

Study Results for Fabry Disease Treatment

In a press release in March, Chiesi Global Rare Diseases and Protalix BioTherapeutics announced final results from the BRIGHT study. The phase 3 multicenter, multinational, open-label, switch-over study assessed the efficacy, safety, and pharmacokinetics of pegunigalsidase alfa (PRX-102) for the treat-

ment of Fabry disease. The study cohort included 30 patients with Fabry disease previously treated with a commercially available enzyme replacement therapy (ERT). PRX-102 is an ERT created from a plant-based platform used to produce a chemically modified stabilized version of the recombinant a-Galactosidase-A (GLA) enzyme, which is deficient in patients with Fabry disease.

Results reported in the press release showed that treatment with PRX-102 was well tolerated and that Fabry disease, assessed by estimated glomerular filtration rate slope and concentration of plasma globotriaosylsphingosine, a biomarker of the disease, was stable. None of the patients developed treatment-induced anti-drug antibodies to PRX-102.

Dror Bashan, president and CEO at Protalix, said, "We are excited to share the final data from the BRIGHT study, an important milestone in the progress of our PRX-102 clinical program. The availability of this data for review by the US Food and Drug Administration, the European Medicines Agency ,and other regulators is another step forward towards the anticipated approval of PRX-102 as a potential good alternative for adult Fabry patients in both the regular 1 mg/kg every two weeks as well as the 2 mg/kg every four weeks regimen."

Print-only Content

Three-Way Merger to Provide Value-Based Kidney Care

In a recent press release, Fresenius Health Partners, InterWell Health, and Cricket Health announced an agreement to merge to create a new, independent company, which will result in the premier value-based kidney care provider in the United States. The agreement will bring together InterWell's more than 1600 nephrologists, Cricket Health's technology-enabled care model and patient engagement platform, and the value-based kidney care expertise of Fresenius Health Partners, the value-based division of Fresenius Medical Care North America.

Bill Valle, CEO of Care Delivery for Fresenius Medical Care, said, "The new InterWell Health will bring together physicians, care management teams, and providers to ensure we show up as one team and provide the best possible experience for the patients who entrust us with their care.

Print-only Content

Cricket Health's predictive analytics and patient engagement platform combined with the physician-led clinical approach of InterWell Health and Fresenius Health Partners' experience and expertise in value-based care will position the organization for accelerated growth."

Cricket Health CEO, **Robert Sepucha,** said, "At Cricket Health, our mission is to help our patients live their best lives. This combination advances our ability to do just that. Each patient's situation and needs are unique, and the new organization will offer groundbreaking solutions from machine learning to highly personalized engagement that keep patients healthy, at home, and out of the hospital."

George Hart, MD, co-chief medical officer of InterWell Health, said, "The big beneficiaries here are patients, through the strengthened relationships created with their physicians. Recognizing that nephrologists are the constant in an otherwise fragmented care delivery system, our goal is to further enhance the support to physician practices, giving them even greater opportunities to focus on what matters most—patient care. Patients will be empowered to identify issues and better manage their disease progression well before the onset of kidney failure."

The transaction is expected to close by the second half of 2022 and is subject to receipt of regulatory approvals and satisfaction of customary closing conditions.

Print-only Content

AKF Living Donor Protection Report Card

The American Kidney Fund (AKF) released its second annual State of the States: Living Donor Protection Report Card in late March. The report card rates progress in protections for living donors and highlights the continued need for baseline federal legislation that would protect living donors regardless of where they live. Living donor protection laws were passed in seven states in the past year: Connecticut, Kentucky, Maryland, New Jersey, Pennsylvania, Texas, and Washington.

The 2022 Report Card included: two states (Arkansas and Connecticut) continued to receive an A grade, 31 states received a B or C, and 18 states received a grade of D or F; four states (Kentucky, Pennsylvania, Texas, and Washington) improved to a C grade, bringing the total number of C states to 17; New Jersey moved up to a D grade and six other states remained a D; 11 states offer no protections at all for living donors and received an F (Alabama, Florida, Michigan, Montana, Nebraska, New Hampshire, South Dakota, Tennessee, Vermont, and Wyoming). The overall grade for the United States remains a D.

LaVarne A. Burton, president and CEO of AKF, said, “AKF applauds states that have chosen to

stand up for the remarkable Americans who make a lifesaving organ donation. We urge all states to continue to pass these important laws. A person's ZIP code should not dictate whether they can be a living organ donor. The Report Card make abundantly clear that there is a need for federal legislation that will provide nationwide, uniform protections for living organ donors, so that more people can consider giving the gift of life."

The Living Donor Protection Act of 2021 was introduced in both the US House of Representatives and Senate to provide baseline protections nationwide, ensuring that living donors have Family and Medical Leave and anti-discrimination protections. In 2021, the bill gained 32 cosponsors in the Senate and 102 cosponsors in the House. The passage of such an act would ensure that the lowest Report Card grade any state could receive would be a C.

Print-only Content

Fresenius Names Head of Strategy and Operations

Clinical researcher and nephrologist **Nwamaka (Amaka) Eneanya, MD,** has been named head of strategy and operations for the Global Medical Office of Fresenius Medical Care. According to a press release from Fresenius, Dr. Eneanya was an attending nephrologist and assistant professor of medicine and epidemiology at the University of Pennsylvania, where she served in the nephrology division as director of Health Equity, Anti-Racism, and Community Engagement. At Fresenius Medical Care, she will report directly to **Frank Maddux, MD,** Global chief medical officer, and will serve on the Global Medical Office executive leadership team.

Dr. Maddux said, "As both a board-certified clinician and expert researcher, Dr. Eneanya brings a wealth of knowledge and expertise that will advance our work in improving outcomes for people living with kidney disease. Her insights regarding health equity, patient-reported outcomes, and social engagement in healthcare and public health will be key elements to inform our ongoing medical strategy."

Dr. Eneanya's research has been supported by the National Institutes of Health and the American Society of Nephrology. Last year she received the Radhika Srinivasan Award for Humanism & Professionalism in Medicine from the University of Pennsylvania. In 2020, she was recognized as a "40 under 40 Leader in Minority Health" by the National Minority Quality Forum.

AKF Among Top 50 Nonprofit Employers

The Nonprofit Times has named the American Kidney Fund (AKF) as one of the top 50 nonprofit employers. The annual program highlights nonprofit organizations that have excelled in creating quality workplaces. According to a press release from AKF, the recognition was based on results of an employee survey that measured the employee experience as well as an evaluation of AKF's workplace policies, practices, philosophy, systems, and demographics.

LaVarne A. Burton, AKF president and CEO, said, "We are honored to once again receive such wonderful accolades for our workplace. We are especially proud to be acknowledged as one of the best nonprofits to work for during a time when AKF, like so many others, operated fully remotely.

A big part of what makes this a great place to work is the commitment and 'all in' spirit that each and every AKF team member brings to our mission of helping people fight kidney disease, and we have continued to make progress and serve the kidney community despite the challenges brought by the pandemic over the last two years."

AKF recently attained a milestone 20th consecutive 4-star rating from Charity Navigator, the leading independent evaluator of nonprofits, and a Platinum Seal of Transparency from Candid (formerly GuideStar).

AKF Releases Survey Results from UCKD

The American Kidney Fund (AFK) has released results of a survey that examined barriers and opportunities among healthcare providers to provide patients with a timely kidney disease diagnosis that identifies the cause of their kidney damage. The survey was part of the AKF's Unknown Causes of Kidney Disease Project (UCKD). The project, begun in late 2020, seeks to improve understanding of how undiagnosed or misdiagnosed causes of kidney disease directly impact patient care and outcomes.

Kidney disease is most often caused by diabetes and/or high pressure. Approximately 5% of cases of kidney failure are attributed to unknown causes. In the AKF survey, healthcare providers estimated 15% of their patients have kidney disease with no known cause.

LaVarne A. Burton, AKF president and CEO, said, "What we learned through this survey was enlightening and very much reinforced why the American Kidney Fund has taken action to improve diagnosis and treatment of kidney disease. Knowing the underlying cause of chronic disease is key to receiving effective, timely treatment and preventing disease progression. With these findings, we are better equipped to work together with stakeholders to address the challenges shared across the kidney community."

Fresenius Increases Benefit for Employees Who Are Living Organ Donors

Employees at Fresenius Medical Care North America (FMCNA) who act as living organ donors will receive 6 weeks of fully paid time off. According to a press release, the newly expanded benefit for eligible employees will provide full pay during the time needed to undergo a qualified organ donation or bone marrow transplant procedure and fully recover.

FMCNA has been named to the American Society of Transplantation's Circle of Excellence that honors companies that support employees who choose to be living organ donors. The Circle of Excellence recognizes companies that give employees at least 4 weeks of time off at 80% of their usual salary. FMCNA has exceeded that minimum standard in providing employees with 6 weeks off, fully paid.

Brian Silva, chief human resources officer and senior vice president, administration for FMCNA, said, "By increasing our paid donor leave benefit, we are increasing support for employees who selflessly choose to save lives through living donor donation. We recognize that transplant is a life-saving treatment for people living with kidney disease and our employees work tirelessly to provide superior care to patients. It was only natural for us to evolve this benefit which helps our employees while also improving the lives of those impacted by kidney disease."

John Gill, MD, president of the American Society of Transplantation, said, "We are thrilled to welcome Fresenius Medical Care as a Supporting Partner of the Living Donor Circle of Excellence. By joining, they will eliminate a significant barrier to living donation for their 68,000 employees. As the largest provider of dialysis in the United States, this partnership directly demonstrates their support for living kidney donors and their commitment to work with the transplant community to improve the care of patients living with kidney failure by removing barriers to transplantation."

Nearly 90,000 patients are currently waiting for a kidney transplant. Of the transplants performed in 2021, only 24% were from living donors. ■

Conference Coverage ACC.22

FIDELIO-DKD and FIGARO-DKD Criteria and the General US Population

Results of the FIDELIO-DKD (Finerenone in Reducing Kidney Failure and Disease Progression in Diabetic Kidney Disease) and FIGARO-DKD (Finerenone in Reducing Cardiovascular Mortality and Morbidity in Diabetic Kidney Disease) trials demonstrated the benefits of finerenone in reducing risks for adverse renal and cardiovascular outcomes in patients with type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD). According to **Nicholas Chiu, MD, MPH,** and colleagues there are few data available on comparisons of the trial populations or the population in the United States meeting criteria for trial enrollment.

The researchers conducted an analysis applying FIDELIO-DKD and FIGARO-DKD enrollment criteria to the US population to estimate the number of individuals who could benefit from finerenone. Results were reported at the American College of Cardiology's 2022 Scientific Session and Expo in a presentation titled *Generalizability of FIGARO-DKD and FIDELIO-DKD Trial Criteria to the United States Population Eligible for Finerenone*.

The researchers applied FIDELIO-DKD and FIGARO-DKD enrollment criteria to the National Health and Nutrition Examination Survey 2009-2018 data. The comparison analysis included adults ≥18 years of age with T2DM, serum potassium ≤4.8 mmol/L, and receiving angiotensin-converting enzyme inhibitor or angiotensin II receptor blocker therapy. Patients with heart failure were excluded.

In the FIGARO-DKD cohort, inclusion criteria included a urine albumin-to-creatinine ratio (UACR) of ≥30 mg/g and <300 mg/g with an estimated glomerular filtration rate (eGFR) of ≥25 and ≤90 mL/min/1.73 m^2 or included a UACR of ≥300 mg/g and ≤5000 mg/g with an eGFR ≥60 mL/min/1.73 m^2. Inclusion criteria in FIDELIO-DKD were a UACR of ≥30 and <300 mg/g with an eGFR of ≥25 but <60 mL/min/1.73 m^2 or an UACR ≥300 mg/g and ≤5000 mg/g with an eGFR of ≥25 to <75 mL/min/1.73 m^2.

The researchers further derived a combined cohort who met criteria for either trial. National projections of baseline characteristics were compared among groups.

Eligibility criteria for FIDELIO-DKD were applied to 1,022,705 individuals in the United States; FIGARO-DKD eligibility criteria were applied to 1,980,176. A total of 2,232,031 individuals in the United States met criteria for initiation of finerenone by at least one trial criterion.

When compared with participants in the FIDELIO-DKD trial, the corresponding eligible US population had a higher proportion of women (45.1% vs 31.3%) and non-Hispanic Black adults (14.5% vs 4.9%), The profiles in the US population varied from those in the trial populations: both the FIDELIO-DKD and FIGARO-DKD eligible US populations lad lower median UACRs at 144.3 mg/g and 93.6 mg/g, respectively, when compared with 833 mg/g and 302 mg/g for trial participants.

In conclusion, the authors said, "FIDELIO-DKD and FIGARO-DKD are broadly generalizable to the US population with CKD and T2DM and could benefit more than two million US adults."

Source: Chiu N, Aggarwal R, Bakris G, Pitt B, Bhatt DL. Generalizability of FIGARO-DKD and FIDELIO-DKD trial criteria to the United States population eligible for finerenone. Abstract of a presentation at the American College of Cardiology ACC.22, Washington, DC, April 2-4, 2022.

CHRONIC KIDNEY DISEASE

Acute Effects on GFR of Trial Interventions

Journal of the American Society of Nephrology. 2022;33(2):291-303

Following initiation of interventions aimed at targeting progression of chronic kidney disease (CKD) there may be acute changes in glomerular filtration rate (GFR) that complicate the interpretation of the long-term effects of treatment. **Brendon L. Neuen, MD,** and colleagues conducted a meta-analysis of data from randomized clinical trials for CKD progression to examine the magnitude and consistency of acute effects in trials and identify factors that might affect them.

The analysis included data from 53 trials enrolling a total of 56,413 participants with at least one estimated GFR measurement by 6 months following randomization. Acute treatment effects were defined as the mean difference in GFR slope from baseline to 3 months between randomized groups. Univariable and multivariable regression models were performed to assess the effect of intervention type, disease state, baseline GFR, and albuminuria on the magnitude of acute effects.

Across all studies, the mean acute effect was –0.21 mL/min/1.73 m^2 (95% confidence interval [CI], –0.63 to 0.22) over 3 months. There was substantial heterogeneity across interventions (95% coverage interval across studies, –2.50 to +2.08 mL/min/1.73 m^2). There were negative average acute effects in renin angiotensin system blockade, lowering of blood pressure, and sodium-glucose cotransporter 2 inhibitor trials, and positive acute effects in trials of immunosuppressive agents. In trials with a higher mean baseline GFR, there were larger negative acute effects.

In conclusion, the researchers said, "The magnitude and consistency of acute GFR effects vary across different interventions, and are larger at higher baseline GFR. Understanding the nature and magnitude of acute effects can help inform the optimal design of randomized clinical trials evaluating disease progression in CKD."

Developing a Model for Risk Prediction for ASCVD

Journal of the American Society of Nephrology. 2022;33(3):601-611

The risk for atherosclerotic cardiovascular disease (ASCVD) may be high among patients with chronic kidney disease (CKD). However, there are no ASCVD risk prediction models in CKD populations to inform clinical care and prevention.

Joshua D. Bundy, PhD, MPH, and colleagues developed and validated 10-year ASCVD risk prediction models in patients with CKD in participants from the CRIC (Chronic Renal Insufficiency Cohort) study without self-reported cardiovascular disease. ASCVD was defined as the first occurrence of adjudicated fatal and nonfatal stroke or myocardial infarction. The models utilized clinically available variables and novel biomarkers. Discrimination, calibration, and net reclassification were used to evaluate performance of the model

The analyses included 2604 CRIC partici-

pants; mean age was 55.8 years and 52.0% were male. Of the 2604 participants, 252 had incident ASCVD within 10 years of baseline. Compared with the American College of Cardiology/American Heart Association pooled cohort equations (area under the receiver operating characteristic curve [AUC]=0.730), a model with coefficients estimated within the CRIC sample had higher discrimination (*P*=.03), achieving an AUC of 0.736 (95% confidence interval [CI], 0.649-0.826). The CRIC model developed using clinically available variables had an AUC of 0.760 (95% CI, 0.678-0.851).

The CRIC biomarker-enriched model had an AUC of 0.771 (95% CI, 0.647-0.853), which was significantly higher than the clinical model (*P*=.01). Both the clinical and the bio-marker enriched models were well-calibrated and improved reclassification of nonevents compared with the pooled cohort equations (6.6%; 95% CI, 3.7% to 9.6% and 10.0%, 95% CI, 6.8% to 13.3%, respectively).

In summary, the authors said, "The 10-year ASCVD risk prediction models developed in patients with CKD including novel kidney and cardiac biomarkers, performed better than equations developed for the general population using only traditional risk factors."

DIABETES

Predicting Progression of Diabetic Kidney Disease

Nephrology Dialysis Transplantation. 2022;37(3):489-497

Prognosis of disease progression in patients with diabetic kidney disease (DKD) is challenging, particularly in the early stages of kidney disease. Patients with early stage diabetic kidney disease may develop anemia. **Masayuki Yamanouchi, MD, PhD,** and colleagues conducted a study to test the hypothesis that serum hemoglobin (Hb) concentration, as a reflection of incipient renal tubulointerstitial impairment, can be used as a marker to predict disease progression in patients with DKD.

The study utilized nationally representative data on patients with biopsy-proven DKD. The cohort included 246 patients with estimated glomerular filtration rate (eGFR) ≥60 mL/min/1.73 m^2 at the time of renal biopsy. Mean age was 56 years, 62.6% were male, mean Hb was 13.3 g/dL, mean eGFR was 76.2 mL/min/1.73 m^2, and mean urine albumin-to-creatinine ratio was 534 mg/g. Serum Hb concentration was divided into quartiles: ≤12, 12.1-13.3, 13.4-14,5 and 14.6 g/dL.

The risk of DKD progression was estimated using a multivariable Cox regression model. DKD progression was defined as new onset of end-stage kidney disease, 50% reduction of eGFR, or doubling of serum creatinine.

There was negative correlation between serum Hb levels and all renal pathological features, particularly with the severity of interstitial fibrosis. During a median follow-up of 4.1 years, 95 participants developed progression of DKD. After adjustment for known risk factors for DKD progression, the hazard ratios in the first, second, and third quartiles (the fourth quartile was the reference)

COVID-19

COVID-19-Related Mortality in Hemodialysis Patients

Clinical Kidney Journal. 2022;15(3):432-441

Among comorbidities associated with predisposition to severe COVID-19, dialysis confers the highest risk of mortality. However, according to **Sol Carriazo, MD,** and colleagues, reports of COVID-19 associated mortality most frequently refer to mortality occurring during the initial hospitalization in the first month following COVID-19 diagnosis.

Dr. Carriazo et al. reported results of a prospective observational study designed to analyze the long-term (1-year follow-up) serological and clinical outcomes of 56 patients on hemodialysis who were infected by severe SARS-CoV-2 during the first wave of the pandemic. COVID-19 was diagnosed by a positive polymerase chain reaction (PCR) test (n=37) or by the development of anti-SARS-CoV-2 antibodies (n=19).

After 1-year of follow-up, 35.7% of the hemodialysis patients infected by SARS-CoV-2 during the study period had died; of those, six (11%) died during the initial hospital admission and 14 (25%) in the following months, primarily within the first 3 months following diagnosis. Of the patients that died, 30% died from vascular causes and 40% from respiratory causes.

In adjusted analysis, there were associations between a positive SARS-CoV-2 PCR test for diagnosis (hazard ratio [HR], 5.18; *P*=.020), higher baseline C-reactive protein levels (HR, 1.10; *P*=.002), and lower hemoglobin levels (HR, 0.62; *P*=.005) and a higher 1-year mortality.

In the 144 patients who did not have COVID-19, mortality was 21 (14.6%) over 12 months; HR for death in COVID-19 patients 3.00; *P*=.00023. Over the first year, the percentage of patients having anti-SARS-CoV-2 immunoglobulin G (IgG) decreased from 73.4% (n=36/49) initially to 61.3% (n=27/44) at 6 months and 38.8% (n=14/36) at 12 months.

In conclusion, the authors said, "The high mortality of hemodialysis patients with COVID-19 is not limited to the initial hospitalization. Defining COVID-19 deaths as those occurring within 3 months of a COVID-19 diagnosis may better represent the burden of COVID-19. In hemodialysis patients, the anti-SARS-CoV-2 IgG response was suboptimal and short-lived."

Solid Organ Transplants in Patients after COVID-19

Current Transplantation Reports.
doi.1007/s40472-022-00362-5

Due to the continuing COVID-19 pandemic, it is important to determine the safety and timing of proceeding with solid organ transplantation in transplant candidates who have recovered form SARS-CoV-2 infection and are otherwise eligible for transplant. **Vivek Kute, MD,** and colleagues conducted a review of current protocols and outcomes of solid organ transplantation in patients who have recovered from SARS-CoV-2 infection.

The researchers identified 44 published reports through September 7, 2021. The reports represented 183 solid organ transplants: 115 kidney transplants, 27 lung transplants, 36 liver transplants, three heart transplants, one simultaneous pancreas-kidney transplant, and one small bowel transplant. The majority of the transplants involved a living donor.

A positive SARS-CoV-2 antibody test was not obligatory in most reports; however, a positive test was a useful tool in the decision to proceed with the transplant. In many reports, a key prerequisite for transplant was two consecutive real-time polymerase chain reaction (RT-PCR) negative tests. Some reports suggested that transplantation can proceed in select circumstances without waiting for a negative RT-PCR. In general, there were no changes in standard immunosuppression regimens.

In summary, the authors said, "In select cases, solid organ transplantation in COVID-19 recovered patients appears successful in short-term follow-up. Emergency solid organ transplantation can be performed with active SARS-CoV-2 infection in some cases. In general, continuing standard immunosuppression regimen may be reasonable, except in cases of inadvertent transplantation with active SARS-CoV-2. Available reports are predominantly in kidney transplant recipients, and more data for other organ transplants are needed."

were 2.74 (95% confidence interval [CI], 1.26-5.97), 2.33 (95% CI, 1.07-5.75), and 1.46 (95% CI, 0.71-3.64), respectively. The addition of serum Hb concentration to the known risk factors of DKD progression improved the prognostic value of DKD progression (the global Chi-statistics increased from 55.1 to 60.8; *P*<.001).

In summary, the researchers said, "Serum Hb concentration, which reflects incipient renal fibrosis, can be useful for predicting DKD progression in the early stages of kidney disease."

HEALTHCARE DISPARITIES

Racial Disparities in Access to Transplantation

Advances in Chronic Kidney Disease.
doi.org/10.1053/j.ackd.2021.10.009

Despite efforts of investigation and interventions, there are stark racial disparities in access to and receipt of kidney transplantation, particularly living donor and pre-emptive transplantation. **Dinushika Mohottige, MD, MPH,** and colleagues reviewed longstanding racial disparities in transplantation and examined structural barriers that contribute to racial transplant inequities.

The authors note that the causes of racial disparities in transplantation are complex, often inter-related, and result from a combination of structural barriers that disproportionately impact racial and ethnic minorities. The review discusses structural barriers that occur along the pathway to transplant including pretransplant healthcare, referral processes, and the evaluation of candidates for transplant. The review also examines the role of multilevel sociocontextual influences on the processes.

"We believe focused efforts which apply an equity lens to key transplant processes and systems are required to achieve greater structural competency and, ultimately, racial transplant equity," the authors said.

RENAL NUTRITION

Therapeutic Benefits of Biotics in Patients with CKD

Journal of Renal Nutrition.
doi.org/10.1053.j.jrn.2021.08.005

Patients with chronic kidney disease (CKD) commonly have gut flora imbalance. Biotic supplementation has been proposed to lessen inflammation and oxidative stress while reducing the risk of progressive kidney damage and cardiovascular disease. However, the effects of biotic supplementation in patients with CKD are uncertain. **Jing Liu, MD,** and colleagues conducted a meta-analysis to examine the therapeutic benefits of biotics in CKD.

The search included PubMed, EMBASE, and Cochrane databases. The researchers searched for randomized controlled trials evaluating any biotic (prebiotic, probiotic, symbiotic) supplements in patients with CKD stage 3-4 to end-stage kidney disease. Primary end points of interest included changes in renal function, markers of inflammation, and oxidative stress. Secondary end points included changes in levels of uremic toxins and variations in lipid metabolism.

The analysis included 23 studies representing 842 participants. In a pooled analysis, biotics did not change estimated glomerular filtration rate or serum albumin. Prebiotics reduced serum creatinine (standardized mean difference [SMD] = –0.23; *P*=.009) and blood urea nitrogen (SMD = –6.05; *P*<.00001). Biotics improved total antioxidative capacity (SMD = 0.37; *P*=.007) and malondialdehyde (SMD = 0.96; *P*=.006) and reduced the inflammatory marker interleukin-6 (SMD = –0.30; *P*=.01), but not C-reactive protein.

Some uremic toxins, including p-cresol sulfate and indoxyl sulfate, were reduced with biotic intervention in dialysis-dependent patients. There was no change in indole-3-acetic acid. Biotic intervention had no effect on lipids (total cholesterol, high-density lipoprotein, low-density lipoprotein, or triglycerides).

"The results highlight the favorable influence of biotics on circulating markers of creatinine, oxidant stress (malondialdehyde, total antioxidative capacity), inflammation (interleukin-6), and uremic toxins (p-cresol sulfate) in patients with CKD," the researchers said. "Biotics did not affect estimated glomerular filtration rate, albumin, indole-3-acetic acid, or lipids in either predialysis or dialysis patients." ■

Sarah Tolson

Keeping a Pulse on Financial Health

In the 13 years that I have worked in the renal industry, there are two main points I have found to be true in the dialysis program or nephrology practice of every client I have worked with:

- The goal is to provide every patient with the best possible care, helping them to achieve the best possible outcomes;
- The practice or dialysis program must generate enough revenue to cover expenses to continue to provide care.

My experience working with renal providers is that, generally, those that function in a clinical capacity are focused (and understandably so) on things that are directly related to patient care and have little time or energy to devote to the financial side of the practice. I have also noticed that often a surplus of revenue translates to growth in the practice, so that more patients can be treated, new services can be provided, or even amenities for patients can be improved, such as nicer waiting room furniture. Growth and improvements to a practice or dialysis program are benefits to patients that everyone can get behind, but finding time to monitor and improve the financial health of a practice can be difficult.

There are a few things I have found to be very beneficial for small-to-midsize practices and programs that readers of this column may find helpful. First and foremost, the biggest asset to financial well-being for a practice or program is to have at least one individual responsible for reviewing the practice's expenses and revenue. If possible, this individual should be in a position of trust and have the ear of those in the practice who have the authority to make financial decisions. Depending on the size of the practice and number of staff members, it may be difficult to find a person currently on staff who has both the skills and time to perform these tasks. In some cases, it may be worth looking for a workable third-party solution to assist with financial oversight.

After determining who is responsible for monitoring revenue and expenses, it is incredibly beneficial to establish several key performance indicators (KPIs) that make sense for the practice or program and will help demonstrate the financial health of the organization. Some examples of KPIs that the company I work for use to help our clients are collections per claim, collections per treatment, days in accounts receivable, and percentage of self-pay accounts. In addition to KPIs that measure revenue and accounts receivables, KPIs that measure cost should be included in the monthly review.

One important point to remember is that it is possible to look at too much data. In past years, I have performed financial reviews for our clients and made the mistake of reviewing nearly every data point available. In these instances, I ended up spending countless hours poring over data that, in the end, did not help me understand how the client's current financial health stacked up to prior years.

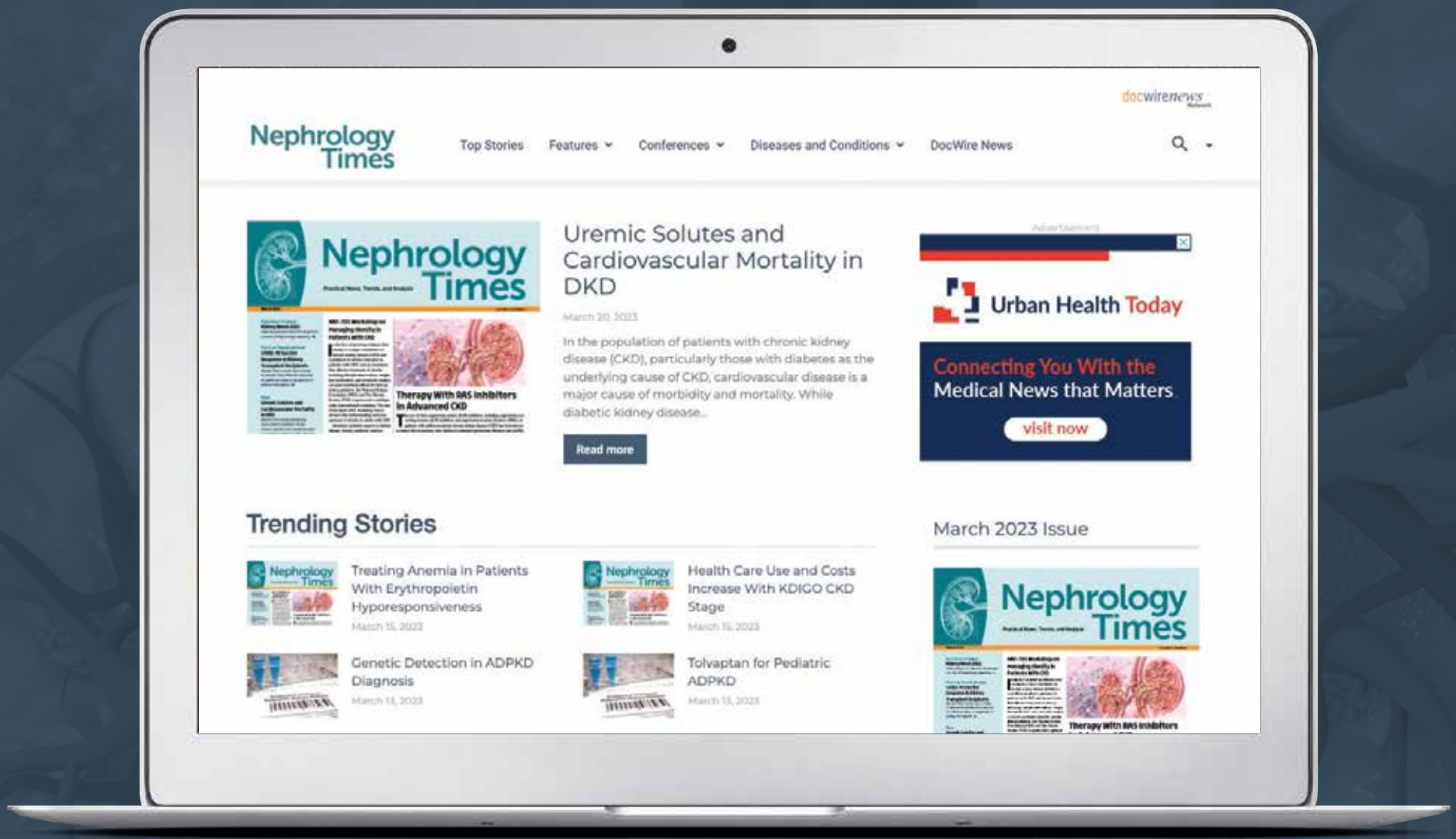
When finances are reviewed each month, any large variances from the expected or average KPIs should be investigated, and their cause should be reviewed and understood. Some variances, like insurance companies assigning large amounts to patient's deductibles, may be unavoidable, whereas variances caused by an issue with billing software or incomplete billing processes are often preventable with a thorough set of checks and balances.

In addition to key performance indicators (KPIs) that measure revenue and accounts receivable, KPIs that measure cost should be included in the monthly review.

Just as important as monitoring financial KPIs monthly is having a quarterly or at least biannual review of the KPIs with those in the organization involved in financial decisions. The purpose of the review is to compare the organization's current KPIs to the same KPIs from previous quarters or years. In the event there are notable increases or decreases to the KPIs, it is important to understand how billing practices, patient insurance coverage, and a host of other things that contribute to cost and revenue, change and plan for improvement where needed. ■

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.

DocWire News, your one-stop source for the latest medical industry news, now includes nephtimes.com.



Check out the online-exclusive content and round out your nephrology news experience.

Nephrology Times

Practical News, Trends, and Analysis

Print-only Content