Nephrology Times

Practical News, Trends, and Analysis

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Polypharmacy, Side Effects, and Nutrition in CKD

Significant changes in metabolism and nutrition, as well as extra-renal changes, occur in patients with progression of chronic kidney disease (CKD), and are associated with increased use of pharmacotherapy. Further, treatment of patients with end-stage renal disease (ESRD), dialysis or transplantation, requires additional specific medications, contributing to polypharmacy in that patient population.

As kidney function declines, there are changes in dietary intake and metabolism of nutrients, increasing the incidence and severity of poor nutritional status. Poor nutritional status in patients with CKD has been shown to be associated with increased morbidity and mortality. There are few available data on the association between nutritional status and the number of prescribed medications or side effects related to nutrition in patients with CKD.

Helene Dahl, MS, RD, and colleagues in Norway conducted a study designed to describe the prescribed medications in patients in different stages of CKD treatment and to examine the association of prescribed medications and nutritional status. The researchers also sought to test the hypothesis that there may be a specific association between the prescribed medications with nutrition-related side effects and poor nutritional status. Results were reported in the *Journal of Renal Nutrition* [2022;32(5):520-528].

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Development of Early-Stage CKD Treatments: NKF-FDA Workshop

Approximately 30 million individuals in the United States are living with chronic kidney disease (CKD); worldwide, the number is estimated to be 700 million. The most serious manifestation of CKD is kidney failure; however, those at earlier stages of CKD are at increased risk of other adverse outcomes that include cardiovascular disease and mortality. Caring for patients with CKD and related complications in the United States is estimated to cost $120 billion annually.

In the past 10 years there has been significant progress in identifying surrogate end points that can be used to evaluate the efficacies of therapies to slow CKD progression.

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Performance of Race-Free GFR Equations Among Kidney Transplant Recipients

Estimated glomerular filtration rate (eGFR) is the best marker of allograft function and is a predictor of allograft and patient survival among kidney transplant recipients. Measurement of true GFR is costly and time-consuming, while eGFR is a relatively inexpensive and efficient marker to track allograft function.

Serum concentrations of creatinine and/or cystatin C, surrogate markers of glomerular filtration, are commonly used to assess eGFR. Previous cohorts used to derive equations used to estimate GFR have included either no kidney transplant recipients or only a small minority of transplant recipients. According to **Gregory L. Hundemer, MD, MPH,** and colleagues, those eGFR equations have demonstrated low accuracy and poor precision among kidney transplant recipients. The 2008 and 2012 Chronic Kidney Disease (CKD) Epidemiology Collaboration (CKD-EPI) eGFR equations have shown improved bias and accuracy in that patient population.

New CKD-EPI eGFR equations that omit race from their calculations have been introduced recently. The new equations were developed to eliminate potential racial biases inherent in earlier eGFR equations, and have the greatest accuracy when both creatinine and cystatin C are included. The performance of the revised equations has not been validated among recipients of kidney transplantation.

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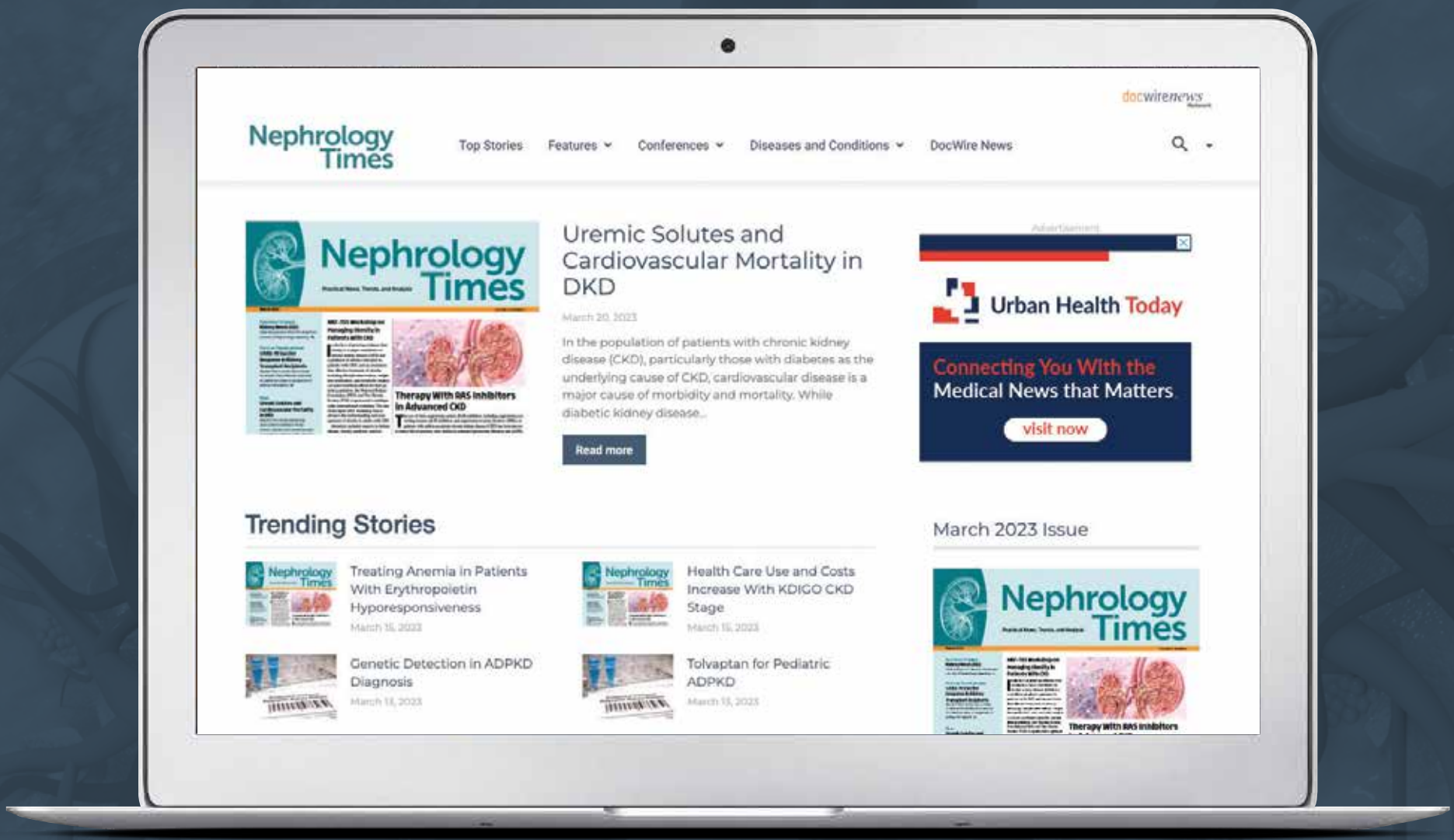

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Practical News, Trends, and Analysis

Do You Stop RAS Inhibitors in CKD Patients?

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Renin–angiotensin system (RAS) inhibitors are a class of agents that include angiotensin-converting enzyme (ACE) inhibitors, such as lisinopril, or angiotensin-receptor blockers, such as losartan, which are recommended for slowing of kidney disease.

We are often asked whether RAS inhibition should be discontinued to stave off initiation of dialysis because stopping the RAS inhibitor might increase the estimated glomerular filtration rate (eGFR). The idea is the mirror opposite of what happens when beginning a patient on a RAS inhibitor, where a small drop in eGFR is usually observed. Current guidelines do not speak to this issue, although post hoc analyses of the REIN and RENAAL trials[1,2] suggested that discontinuation of RAS inhibitors might be beneficial. Until now, however, there had not been a randomized controlled trial to examine this question.

The STOP ACEi trial[3], published very recently in the *New England Journal of Medicine* by Bhandari and colleagues from the UK, tested the hypothesis that discontinuation of RAS inhibitors in patients with advanced and progressive chronic kidney disease (CKD) would improve kidney function, quality of life, and/or exercise capacity. The trial was very well conducted.

Online publication in the journal coincided with a presentation at the American Society of Nephrology Kidney Week 2022. Surprisingly, the submission didn't make it into the high-impact clinical trials session (the late breaker session), but it was presented as a poster at the meeting.

In a nutshell, the STOP ACEi trial was a multicenter, randomized, controlled, open-label study that enrolled 411 patients with advanced and progressive CKD (stage 4 or stage 5). Patients were required to demonstrate kidney progression (an eGFR decrease of >2 mL/min/1.73 m^2 per year during the previous 2 years) and have received treatment with a RAS inhibitor for >6 months. A total of 206 patients were randomized to the "discontinue RAS inhibitors" arm and 205 to the "continue RAS inhibitors" arm.

Baseline characteristics were balanced. Overall, about one-third of patients had a history of diabetes mellitus. The median follow-up was 3 years. About 10% of patients in each arm discontinued the randomized treatment. The primary outcome was eGFR at 3 years and secondary end points included the development of end-stage renal disease (ESRD), a composite of a decrease of more than 50% in the eGFR, or the initiation of renal replacement therapy. Other secondary end points included hospitalization, blood pressure, exercise capacity, and quality of life.

The main finding from the trial was that stopping RAS inhibitors did not slow kidney decline. The eGFR was similar between the two arms (P=.42). Secondary outcomes and analysis by subgroups also did not show any meaningful differences between the two arms of the study. Serious adverse events were similar between the two arms.

There was a tantalizing observation suggesting that there might be a benefit from continuing RAS inhibition. ESRD or the initiation of renal replacement therapy occurred in 128 patients (62%) in the discontinuation group and in 115 patients (56%) in the continuation group (hazard ratio, 1.28; 95% CI, 0.99-1.65), just missing statistical significance. However, a word of caution: since the primary end point was null, and the result was a trend, this result needs to be confirmed in a larger trial.

The trial had several limitations that the authors acknowledged, including the open-label design that might have influenced reported outcomes or hospitalization and the under-representation of non-White patients and those with high levels of proteinuria (>2.6 g/g creatinine). As well, because this was a UK-based study and African American and Latino patients were not recruited, the results may not be generalizable to the US population.

The bottom line from a practice perspective is that you should not stop RAS inhibition unless the patient becomes intolerant or refractory hyperkalemia develops. Indeed, I keep patients on RAS inhibition even after they begin dialysis with the aim of preserving residual renal function. ■

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Performance of Race-Free GFR Equations

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Dr. Hundemer et al conducted a cross-sectional study to validate the performance of the 2021 CKD-EPI creatinine- and creatinine/cystatin C-based eGFR estimating equations ($eGFR_{cr}$ and $eGFR_{cr\text{-}cys}$, respectively). The researchers sought to examine the bias, precision, and accuracy of the equations along with the proportion of kidney transplant recipients classified according to CKD staging. Results were reported in the *American Journal of Kidney Diseases* [2022;80(4):462-472].

Among the overall study population, the median biases of the 2009 and 2021 CKD-EPI $eGFR_{cr}$ equations were -2.3 and -0.2 mL/min/1.73 m^2, respectively. Precision was similar between the 2009 and 2021 CKD-EPI $eGFR_{cr}$ equations (interquartile range [IQRs] of 14.5 and 14.9 mL/min/1.73 m^2, respectively). Accuracy was also similar between the 2009 and 2021 CKD-EPI $eGFR_{cr}$ equations, as demonstrated by P_{10}/P_{20}/P_{30} (32%/65%/84% vs 33%/63%/84%, respectively, root mean square error (12.9 [95% CI, 11.6-14.1] vs 13.0 [95% CI, 11.8-14.4] mL/min/1.73 m^2, and mean absolute error (9.7 [95% CI, 8.9-10.5] vs 9.7 [95% CI, 8.9-10.6] mL/min/1.73 m^2). The performance measures were also similar when stratified by the eGFR categories of ≥60, 30-59, and <30 mL/min/1.73 m^2.

In the overall study cohort, the median biases of the 2012 and 2021 CKD-EPI $eGFR_{cr\text{-}cys}$ equations were –3.6 and 0.3 mL/min/1.73 m^2, respectively. Regarding precision, IQRs of the 2012 and 2021 CKD-EPI $eGFR_{cr\text{-}cys}$ equations were 13.3 and 14.3 mL/min/1.73 m^2, respectively. Accuracy was also similar between the two equations. The measures were similar when stratified by the eGFR categories of ≥60, 30-59, and <30 mL/min/1.73 m^2.

Among the overall study population, the 2012 CKD-EPI eGFRcys equation had a median bias of –0.8 mL/min/1.73 m^2. The precision was reduced relative to the creatinine- and creatinine/cystatin C-based equations (IQR, 18.5 mL/min/1.73 m^2). Accuracy was also reduced relative to the creatinine- and creatinine/cystatin C-based equations.

Compared with the other eGFR equations, the Modification of Diet in Renal Disease (MDRD) Study equation demonstrated a relatively greater median bias (–5.0 mL/min/1.73 m^2). Precision of the MDRD Study equation was similar to the other GFR equations (IQR, 14.7 mL/min/1.73m^2).

There was no clear difference between the 2021 CKD-EPI $eGFR_{cr}$ and $eGFR_{cr\text{-}cys}$ equations (mean eGFR difference of –0.7; 95% CI, –18.7 to 17.4 mL/min/1.73 m^2).

In analyses of proportion of correct classification of CKD by eGFR equation, the 2009 CKD-EPI $eGFR_{cr}$ equation correctly classified 66% of participants compared with 68% with the 2021 version equation. The 2012 CKD-EPI $eGFR_{cr\text{-}cys}$ equation correctly classified 64% of participants compared with 69% correctly classified with the 2021 version. The MDRD Study equation classified a similar percentage of participants (67%); the 2021 CKD-EPI $eGFR_{cys}$ equation correctly classified a relatively lower percentage of participants (61%).

The researchers cited some limitations to the study, including the small sample size that may have limited the power to detect subtle differences in performance between the eGFR equations (eg, between $eGFR_{cr}$ and $eGFR_{cr\text{-}cys}$ as was shown among participants who were not kidney transplant recipients in the original study). The subset of participants with eGFR <30 mL/min/1.73 m^2 was small (n=45), limiting the ability to draw any definitive conclusions regarding eGFR equation performance in that subset. Another notable limitation was the small number of patients who self-identified as Black, limiting the ability to compare differences in eGFR equation by race.

In summary, the authors said, "Among kidney transplant recipients, the 2021 race-free CKD-EPI eGFR equations perform similarly to the previous CKD-EPI equations that included race correction terms. No significant difference in performance was observed between the 2021 CKD-EPI eGFR$_{cr}$ and eGFR$_{cr\text{-}cys}$ equations in the kidney transplant population." ■

TAKEAWAY POINTS

- Researchers reported results of a cross-sectional study designed to validate the 2021 race-free Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) estimated glomerular filtration rate (eGFR) equation based on creatine alone ($eGFR_{cr}$) or based on creatinine and cystatin C ($eGFR_{cr\text{-}cys}$) among kidney transplant recipients.
- The 2021 race-free CKD-EPI eGFR equations performed similarly to the previous CKD-EPI equations that included race correction terms.
- There was no significant difference in performance between the 2021 CKD-EPI $eGFR_{cr}$ and the CKD-EPI $eGFR_{cr\text{-}cys}$ equations among the cohort of kidney transplant recipients.

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Development of Early-Stage CKD Treatments

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There has also been increased interest in the development of treatments for early stages of CKD.

In December 2020, the National Kidney Foundation (NKF) sponsored a scientific workshop in collaboration with the US FDA. The meeting was titled the NKF-FDA Conference on Clinical Trial Considerations in Developing Treatments for Early Stages of Common, Chronic Kidney Diseases.

The workshop was designed to examine perceptions of the value of treating early CKD among patients, providers, and payers. More than 90 individuals representing a range of stakeholders, including faculty experts in clinical trials, nephrology, cardiology, and endocrinology, patient advocacy organizations, patients, payers, health economists, regulators, and policy makers took part in the virtual meeting. Results of the meeting were outlined by **Lesley A. Inker, MD, MS,** and colleagues on behalf of the workshop advisory group in a special report in the *American Journal of Kidney Diseases* [2022;80(4):513-526].

The report opened with a brief overview of CKD and its progression. Patients with CKD face increased risk for cardiovascular disease and death not related to kidney failure as well as other complications, including cognitive impairment and infections. There are robust associations between decreased glomerular filtration rate (GFR) and elevated albuminuria and cardiovascular disease, heart failure, hospitalizations, and mortality; more than 50% of deaths in CKD are the result of cardiovascular causes. Conversely, cardiovascular disease can precipitate decline in GFR.

ASSESSING RISK FACTORS FOR CKD PROGRESSION

Specific parameters are needed when estimating risk for inclusion in clinical trials as well as in clinical-decision making. Absolute risk, or the probability of an event occurring over a specific period, is most relevant to patients. For patients with CKD, the relevant time frame for the development of a serious adverse outcome may be a lifetime. For sponsors or investigators designing clinical trials, the relevant time frame is often the length of time needed to show the efficacy of an intervention.

Identification of the specific end point of interest is also a key parameter. The common end point of studies aimed at developing risk tools for CKD progression is kidney failure with the need for kidney replacement therapy (KFRT). This has two major limitations: (1) many patients, particularly older adults and those in settings with limited resources, may never receive KRT; and (2) progression of CKD in the relevant time horizon is not captured by kidney failure. More appropriate end points may be GFR slope, 30% and 40% declines in GFR, and reaching CKD GFR category 4 (G4; GFR <30 mL/min/1.73 m^2). In addition, cardiovascular disease could be an end point of interest in CKD trials, and incidence or progression of CKD could be an outcome of interest in cardiovascular trials.

RISK FACTORS AND TOOLS

Traditional risk factors for CKD progression are level of

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GFR and albuminuria, and the presence of hypertension, diabetes, hyperlipidemia, smoking, and variably, obesity. The most widely used tool to predict progression of CKD is the Kidney Failure Risk Equation that predicts risk of KFRT over 2-year and 5-year periods in individuals with GFR <60 mL/min/1.73 m^2. The risk tools can be used to inform patient counseling, referral to nephrology and multidisciplinary care, evaluation for transplant, and place of vascular access.

There are three tools for patients with higher GFR: (1) estimated risk of KFRT over 15 years and the lifetime; (2) 5-year risk of developing GFR <60 mL/min/1.73 m^2; and (3) 2- to 3-year risk of developing 40% decline in GFR. The first model was designed for potential kidney donors and is not useful in people with CKD; the second and third models are most appropriate in the identification of high-risk populations for trials designed to evaluate efficacies of therapies for development or prevention of CKD progression in early CKD.

COST VERSUS BENEFIT

Cost-effectiveness assessments require consideration value that is apparent in the immediate time frame as well as anticipated costs and savings. For treatment of early CKD, the potential costs and cost savings are key, because the benefits of treatment will likely be achieved after years, and due to the large number of individuals potentially eligible for treatment. In addition, due to uncertainties in clinical course, not all patients treated will derive benefit.

The two main sources of cost are direct and indirect. Direct costs are incurred by the health care system and include those related to prescriptions, outpatient appointments, visits to the emergency department, and inpatient episodes. In the US Medicare CKD population, following adjustment for age, sex, and relevant comorbidities, the annual direct spending cost per patient increased with worsening CKD stage ($8091 for stage 2; $46,128 for stage 4/5; and $87,399 for KFRT). Indirect costs are those incurred by patients and caregivers, as well as those related to absenteeism, presenteeism, unemployment, and lost productivity. Thus, higher direct costs in early CKD should be balanced by lower direct and indirect costs associated with late-stage disease.

SUMMARY

The workshop attendees agreed that there is value in preventing the development of and treating the progression of early-stage CKD in those at high risk for progression. End points in trials designed to examine the efficacy of such interventions are likely to be intermediate or surrogate end points. Cost analyses of early-stage CKD treatments should be holistic and include more than costs of the drug; savings on health care delivery and on treatment of kidney failure should be considered. Safety of treatment of early-stage CKD is crucial and will require additional assessment beyond that available during study periods.

"Successful drug development and implementation of effective therapies will require collaboration across sponsors, patients, patient advocacy organizations, medical community, regulators, and payers," the authors said. ■

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The cross-sectional observational study included adult, primarily White patients at different stages of CKD. Patient recruitment occurred from November 2014 until July 2018. Patients' electronic health records were used to obtain information on prescribed medications. Polypharmacy was defined as five or more medications simultaneously and excessive polypharmacy was defined as prescription of 10 or more medications simultaneously. Medications were grouped as per nutrition-related side effects (xerostomia and nausea).

Nutritional status was assessed using anthropometric measurements of height, weight, body mass index (BMI), mid-upper arm circumference (MUAC), skinfold thickness triceps (SFT triceps), and waist circumference (WC). Muscle strength was measured by handgrip strength. Nonfasting blood samples were obtained (prior to hemodialysis in the subset undergoing dialysis) and analyzed using standard methods.

Participants were grouped in three ways: (1) as per current CKD treatment (predialysis, dialysis, or transplant); (2) as per CKD stage defined by estimated glomerular filtration rate (eGFR); and (3) as per prescribed medications with nutrition-related side effects (xerostomia and nausea). Linear regression analysis adjusted for age, sex, and eGFR was used to examine the association between the number of prescribed medications and the measures of nutritional status.

> Polypharmacy was observed in 84% of study participants, and excessive polypharmacy was present in 37%.

The study cohort included 217 patients with CKD. Of those, 112 had predialysis CKD stages 3-5, 33 had ESRD receiving hemodialysis, and 72 had received a kidney transplant. Mean age was 60 years (range, 21-89 years) and 71% were male. Those in the kidney transplant group had the highest eGFR and the lowest mean age. The most common primary kidney disease was nephropathy caused by diabetes or hypertension (28%), followed by glomerular disease (25%), and polycystic or unspecified cystic kidney disease (14%).

On average, patients were prescribed nine medications. A total of 216 medications were prescribed for the entire study cohort. Polypharmacy was observed in 84% of study participants, and excessive polypharmacy was present in 37%.

Most patients had prescriptions from the group of cardiovascular system medications (94%) and from the group of prescriptions for the alimentary tract and metabolism (84%). When the medications were grouped according to nutrition-related side effects, 66% (n=143) of the patients were prescribed at least one medication with nausea as a side effect (36 different medications) and 24% (n=51) with xerostomia as a side effect (21 different medications).

There was a positive association between the number of prescribed medications with either nausea or xerostomia as a side effect and the total number of prescribed medications. There was a negative association between medications with either nausea or xerostomia as a side effect and eGFR.

Sixty-two percent of participants (n=133) were either overweight or obese (BMI >25 kg/m2) and 48% (n=104) had central obesity (WC >102 cm for men and >88 cm for women). A higher proportion of female participants had central obesity compared with male participants (62% vs 42%, respectively). Thirty-seven percent of participants (n=80) were normal weight (BMI= 18.5-24.9 kg/m^2) and three patients were underweight (BMI <18.5 kg/m^2).

The association between the number of prescribed medications and various measures of nutritional status was examined using linear regression analysis, adjusted for age, sex, and eGFR. There were inverse associations observed between the number of medications and MUAC, SFT triceps, handgrip strength, hemoglobin, and serum albumin.

Additional linear regression analyses with adjustments for sex, age, eGFR, and the total number of prescribed medication were conducted to investigate prescribed medications with nausea or xerostomia as a side effect. There was an association between medications with nausea as a side effect and lower MUAC, SFT triceps, albumin, and hemoglobin. Medications with xerostomia as a side effect were associated with lower handgrip strength.

In citing limitations to the study findings, the researchers included the cross-sectional design that precluded derivation of causal relationships, collecting data on prescribed medications from patients' health records that do not indicate actual intake, not accounting for over-the-counter medications, and lack of assessment of participants' physical activity.

In conclusion, the authors said, "In this study, medication prescriptions were associated with poor nutritional status in patients with CKD. Monitoring of nutritional status in patients with CKD with long medication lists is warranted to identify and treat patients with poor nutritional status. The methodology in our study offers a new approach to categorize medications, and larger longitudinal studies should be conducted to confirm our findings. Future studies should also focus on the mechanisms behind the observed associations between prescribed medications and nutritional status and offer a more comprehensive analysis of both side effects and specific medications for patients with CKD." ■

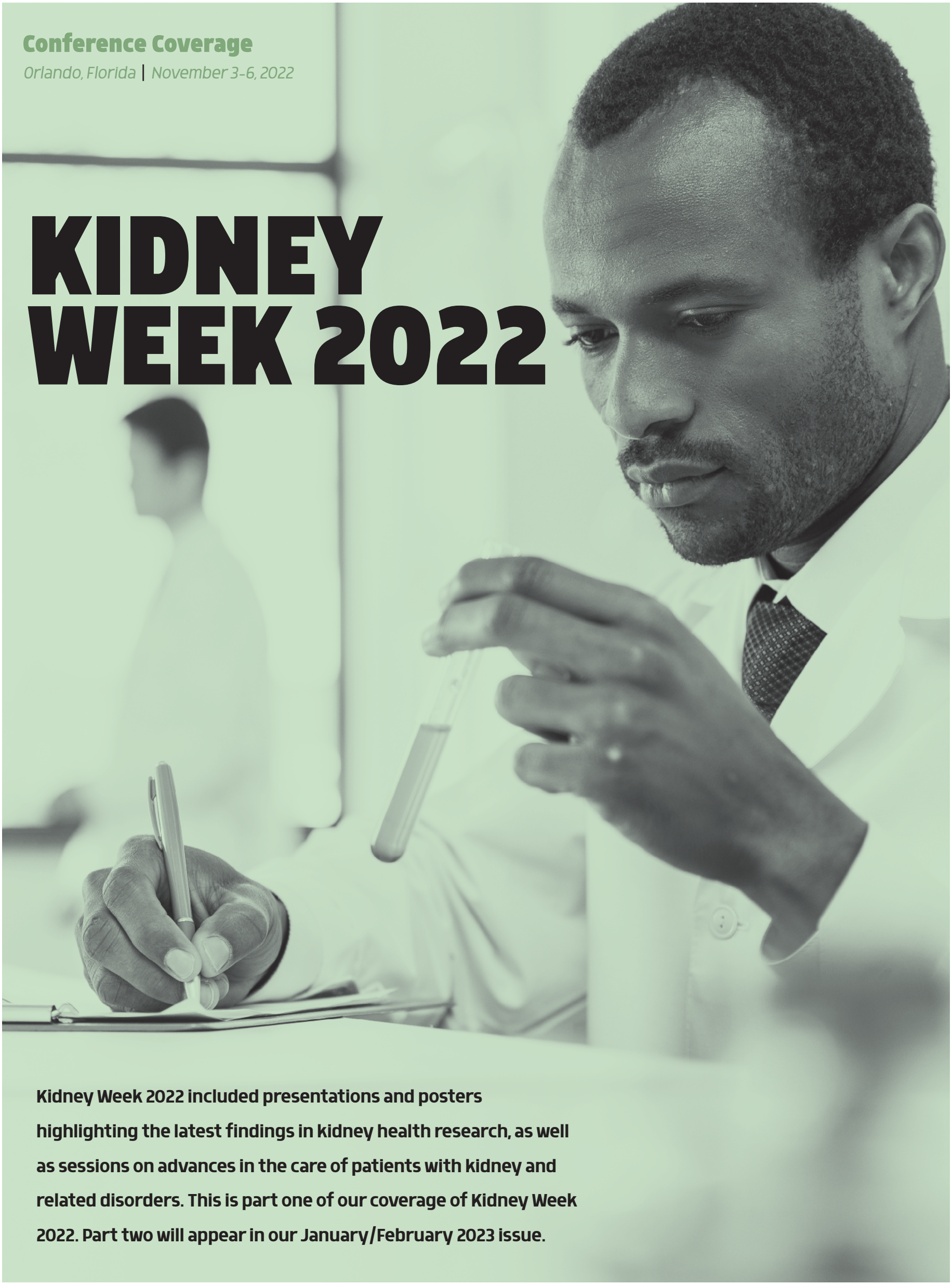
TAKEAWAY POINTS

- Researchers reported results of a cross-sectional study examining the association between prescribed medication and nutritional status in patients with chronic kidney disease.
- On average, patients in the study cohort were prescribed nine medications concurrently. There was an inverse association between the number of medications and mid-upper arm circumference, skinfold thickness triceps, handgrip strength, serum albumin, and hemoglobin.
- There was a positive association between the number of prescribed medications with either nausea or xerostomia as a side effect and the total number of prescribed medications.

Conference Coverage

Orlando, Florida | November 3-6, 2022

KIDNEY WEEK 2022



Kidney Week 2022 included presentations and posters highlighting the latest findings in kidney health research, as well as sessions on advances in the care of patients with kidney and related disorders. This is part one of our coverage of Kidney Week 2022. Part two will appear in our January/February 2023 issue.

Disease Progression and Variability of ADPKD

The most common monogenic nephropathy is autosomal dominant polycystic kidney disease (ADPKD). ADPKD is associated with variability in severity of kidney disease among affected relatives and families. Researchers in Ireland, led by **Elhussein A. E. Elhassan, MD,** conducted an analysis to examine variation in phenotype between families of adult Irish patients affected by ADPKD and assess the impact of kinship on disease progression.

Results were reported during a poster session at the American Society of Nephrology Kidney Week 2022 in a poster titled *Effects of Kinship on Disease Progression and Variability in Families With Autosomal Dominant Polycystic Kidney Disease*.

The researchers collected data on phenotype (age, sex, kinship with index patient, age at initial presentation, hypertension and urological events, and Predicting Renal Outcomes in Polycystic Kidney Disease score), as well as renal survival (time to end-stage renal disease [ESRD] and decline in estimated glomerular filtration rate [eGFR]). Patients with disease-causing *PKD1* and *PKD2* variants were included in the analysis. ADPKD was diagnosed using a combination of molecular methods, including targeted next-generation sequencing.

Variability between families was assessed based on the age at onset of ESRD. A frailty model using detailed phenotypic features of patients with available genetic diagnosis was used to account for the impact of kinship on disease progression.

The analysis included data on 103 unrelated families (369 patients). A majority (63.1%, n=65) had a diagnostic variant at PKD1 gene. Average age was 55.2 years, and 55.3% were female. Mean age at initial presentation was 30.2 years. At last follow-up, 71% of the patients (n=262) developed ESRD. The remaining patients had chronic kidney disease, with average creatinine 133.2 mg/dL and average eGFR 51.2 mL/min/1.73 m^2. Mean annual eGFR decline was 3.1 mL/min/1.73 m^2 per year.

Median variance in age at time of ESRD between families was 7 years. Among families with at least two ESRD patients, 33% (n=34) of families had wide delta difference in age at ESRD (eg, >10 years difference).

In the univariate frailty model, there was a significant association between kinship and time to renal failure (P<.001), taking into account phenotypic and genetic factors that are associated with disease severity. In multivariate analyses, there was no statistical impact of kinship in age at ESRD, with the exception of those with earlier initial presentation (hazard ratio, 0.96; 95% CI, 0.94-0.98; P<.001).

"Wide variability in age of ESRD among families with ADPKD is present in at least 33% of families, and the impact of family effects was evident on factors related with disease progression," the researchers said.

Source: Elhassan EAE, Collins KE, Gilbert EH, Cavalleri G, Benson KA, Conlon PJ. Effects of kinship on disease progression and variability in families with autosomal dominant polycystic kidney disease. TH-P0364. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 3, 2022; Orlando, Florida.

Anxiety Associated With Hypertension in Adolescents

With the increase in the prevalence of primary pediatric hypertension comes an emphasis on active research to identify modifiable risk factors for the condition. Anxiety, a common problem in childhood, may be associated with activation of the sympathetic system, plasma renin, and hypothalamic-pituitary-adrenal axis, resulting in increased peripheral vascular resistance and hypertension.

Anxiety has been shown to be associated with elevated blood pressure in adults; however, according to **Yaritzy Michelle Astudillo, MD,** and colleagues at New York Medical College, Valhalla, there are few data available on the relationship between anxiety and increased blood pressure in children.

The researchers recently conducted a cross-sectional study to examine the association between anxiety and hypertension in adolescents. Results were reported during a poster session at the American Society of Nephrology Kidney Week 2022 in a poster titled *Association Between Anxiety and Hypertension in Adolescent Patients: A Single-Center Cross-Sectional Study*.

Patients 12 to 18 years of age referred to the center's pediatric nephrology clinic were eligible to participate in the study. Hypertension was defined as either systolic or diastolic blood pressure above the 95th percentile for age, height, and sex. The validated Screen for Child Anxiety Related Disorders (SCARED) questionnaire was used to evaluate for anxiety. The questionnaire was completed independently by the child (SCARED-C) and by the parent (SCARED-P). A score of ≥9 was defined as a positive screen for anxiety.

Chi-square tests were used to compare proportions, and the Mann-Whitney U test was used to compare the difference in blood pressure between groups.

A total of 200 adolescents were included in the study. Of those, 130 were not on any blood pressure medication. In that subgroup, mean age was 15.18 years, 50% were male, 45% (n=58) had positive SCARED-C scores, and 29% (n=37) had positive SCARED-P scores.

Of the group with positive SCARED-P scores, 43% (n=16) had diastolic hypertension compared with 19% (n=18) of those with negative SCARED-P scores (P=.005). Diastolic blood pressure was significantly higher in adolescents with SCARED-P positive scores and in those with SCARED-C positive scores compared with SCARED-P negative and SCARED-C negative participants.

In summary, the researchers said, "In this cohort of adolescents, those who were anxious by parental reporting were more likely to have diastolic hypertension. For adolescents not treated with antihypertensive medications, diastolic blood pressure but not systolic blood pressure was significantly higher in the anxious cohort both by self and parental reporting. The impact of anxiety on the pathogenesis of hypertension in children warrants further study."

Source: Astudillo YM, Krishnan S, Pereira TE, Solomon S, Samsonov DV. Association between anxiety and hypertension in adolescent patients: a single-center cross-sectional study. FR-P0436. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 4, 2022; Orlando, Florida.

Progression to CKD After COVID-19-Related AKI

Patients with acute kidney injury (AKI) are at risk of progression to chronic kidney disease (CKD) and end-stage renal disease (ESRD). AKI is a common complication associated with COVID-19. **Thiago Terzian Ganadjian, MD,** and colleagues at Universidade Federal Sao Paulo, Sao Paulo, Brazil, conducted a study to examine the frequency and association of clinical variables in patients who developed CKD and ESRD following AKI related to COVID-19.

The researchers reported results of the 1-year follow-up study during a poster session at the American Society of Nephrology Kidney Week 2022. The poster was titled *The Emergence of CKD After COVID-19 Related AKI*.

The study included 182 survivor patients who were admitted to the center's ward and intensive care unit with COVID-19 between April 2020 and March 2021. Inclusion criteria were age ≥18 years and COVID-19 confirmed on reverse transcription-polymerase chain reaction test. Exclusion criteria included ESRD prior to hospitalization.

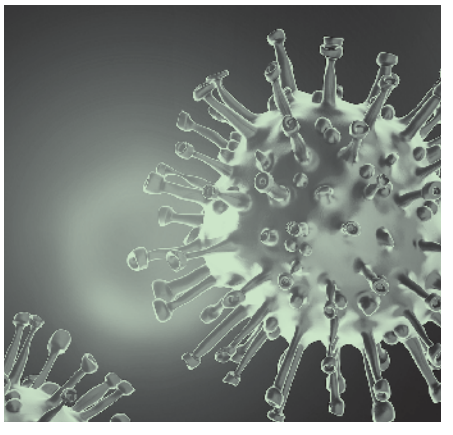
Kidney Disease: Improving Global Outcomes criteria were used to define AKI and CKD. The researchers assessed the frequency of AKI and then compared selected clinical variables in two subgroups: CKD after COVID-19-related AKI and non-CKD after COVID-19. Univariate and multivariate analyses were conducted.

A total of 137 patients (75.3%) developed AKI. Of those, 30.8% (n=56) required renal replacement therapy (RRT) in hospital. In the CKD after COVID-19-related AKI group, there were higher frequencies of diabetes and hypertension with lower estimated glomerular filtration rate (84.2 mL/min/1.73 m^2 vs 94.4 mL/min/1.73 m^2; P=.08) and mean arterial pressure at baseline (74.9 mm Hg vs 79.1 mm Hg; P=.03).

In binary logistic regression, there was an independent association between hypertension and CKD (odds ratio, 4.472; 95% CI, 1.356-13.886; P=.001). All patients who progressed to ESRD (3.9%, n=7) had nondialytic CKD exacerbated by COVID-19 requiring RRT.

"Hypertension was the independent clinical factor associated with progression to CKD after COVID-19-related AKI. All patients who progressed to ESRD had CKD exacerbated by COVID-19 requiring RRT," the authors said.

Source: Terzian Ganadjian T, Nakamura PL, Silva BM. The emergence of CKD after COVID-19 related AKI. TH-P0904. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 3, 2022; Orlando, Florida.



Kidney Biopsy Safety and Adequacy in Patients With Obesity

Obesity is associated with risk for complications related to kidney biopsy. **Long Qian, MD,** and colleagues conducted an analysis to compare the safety and adequacy of kidney-biopsy procedures between obese and nonobese patients.

Results were reported during a poster session at the American Society of Nephrology Kidney Week 2022. The poster was titled *Safety and Adequacy of Kidney Biopsy Procedure in Patients With Obesity.*

The analysis included data from patients in the Yale University kidney biopsy cohort enrolled between 2015 and 2017. Following adjustment for prebiopsy risk factors and needle gauge, linear regression analysis was used to examine the association between class 2 obesity (defined as body mass index ≥35 kg/m^2) with postbiopsy drop in hematocrit and with the number of glomeruli sampled. A supplementary analysis using data from Johns Hopkins University was also performed.

The Yale cohort included 337 patients, and of those, 23% (n=76) had obesity. Patients with obesity were more likely to undergo biopsy using an 18-gauge needle (vs 16-gauge needle) compared with nonobese patients (66% [n=48] vs 45% [n=113]; *P*=.002). In univariable analysis, patients with obesity had a lesser drop in hematocrit from pre- to postbiopsy (2.1% vs 3.0%; unadjusted difference, -0.95%; 95% CI, -0.14% to -1.75%). Following adjustment for prebiopsy factors, the difference was -0.92% (95% CI, -1.73% to -0.11%). There was no association between obesity and drop in hematocrit following further adjustment for needle gauge. Fewer glomeruli were sampled from patients with obesity.

The Johns Hopkins cohort included 78 patients, and of those, 12 were obese. All biopsies at Johns Hopkins were performed using an 18-gauge needle. There was no association between obesity and drop in hematocrit. Results of meta-analyses of the two cohorts found no association between obesity and drop in hematocrit.

In conclusion, the researchers said, "Obese patients did not have a greater risk of postbiopsy hematocrit drop than those without obesity but tended to have fewer glomeruli available for diagnosis. Future studies could examine techniques to improve diagnostic yield of kidney biopsy for obese patients."

Source: Qian L, Weinstein JN, Melchinger HC, et al. Safety and adequacy of kidney biopsy procedure in patients with obesity. TH-P0564. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 3, 2022; Orlando, Florida.

Kidney Delayed Graft Function After Combined Liver-Kidney Transplant

Among patients with liver failure with renal dysfunction, combined liver-kidney transplantation improves patient survival. However, according to **Paolo Vincenzi, MD,** and colleagues, kidney delayed graft function is a common and challenging complication that has a negative impact on clinical outcomes.

The researchers conducted a retrospective study to examine the incidence, potential risk factors, and prognostic impact of development of kidney delayed graft function following combined liver-kidney transplant in a cohort of patients with recent combined transplant. Results were reported during a poster session at the American Society of Nephrology Kidney Week 2022 in a poster titled *Predictors of Kidney Delayed Graft Function and Its Prognostic Impact Following Combined Liver-Kidney Transplantation.*

The study cohort included 115 consecutive combined liver-kidney transplant recipients who were transplanted at the Miami Transplant Institute between January 2015 and February 2021. All transplanted kidneys received hypothermic pulsatile machine perfusion prior to transplant.

The primary outcome of interest was development of kidney delayed graft function. Secondary outcomes were the combined incidence and severity of postoperative complications; postoperative infections; biopsy-proven acute rejection; renal function at 1, 3, 6, and 12 months posttransplant; and death-censored graft and patient survival.

Kidney delayed graft function was observed in 37.4% of the cohort (n=43/115). Results of multivariable analysis revealed five independent predictors of kidney delayed graft function: (1) preoperative dialysis, *P*=.0003; (2) lower recipient body mass index, *P*=.006; (3) older donor age, *P*=.003; (4) utilization of donor after cardiac death donors, *P*=.007; and (5) longer delay of kidney transplantation after liver transplantation (*P*=.0003).

Median follow-up was 36.7 months posttransplant. During follow-up, there was an association between kidney delayed graft function and a significantly increased risk of developing more severe postoperative complications (*P*<.000001), poorer renal function (*P*<.000001), and worse death-censored graft (*P*=.00004) and patient survival (*P*=.0002).

In conclusion, the researchers said, "kidney delayed graft function may be responsible for remarkable negative effects on immediate and potentially longer-term clinical outcomes after combined liver-kidney transplant. Understanding the important risk factors for kidney delayed graft function development in combined liver-kidney transplant may better guide recipient and donor selection(s) and improve clinical decisions in this increasing group of transplant recipients."

Source: Vincenzi P, Gaynor JJ, Ciancio G. Predictors of kidney delayed graft function and its prognostic impact following combined liver-kidney transplantation. FR-P0806. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 4, 2022; Orlando, Florida.

Changes in Renal Function in MIRROR RCT Participants

Results of the MIRROR randomized controlled trial comparing cotherapy of pegloticase plus methotrexate (MTX) with pegloticase plus placebo found increased urate-lowering response rate with MTX versus placebo (71.0% vs 38.5% during month 5). Infusion reaction rate was also lower in patients in the pegloticase + MTX group compared with those in the placebo group (4% vs 31%).

Gout is a common comorbidity in patients with chronic kidney disease (CKD). Methotrexate is used cautiously in patients with CKD, making the impact of pegloticase + MTX cotherapy of interest. During a poster session at the American Society of Nephrology Kidney Week 2022, **Abdul A. Abdellatif, MD,** and colleagues presented changes in estimated glomerular filtration rate (eGFR) among participants in the MIRROR trial. The poster was titled *eGFR Changes in Uncontrolled Gout Patients Randomized to Receive Methotrexate or Placebo as Co-Therapy to Pegloticase: MIRROR RCT Findings.*

Uncontrolled gout was defined as serum uric acid ≥7 mg/dL, urate-lowering therapy failure/intolerance, and ≥1 gout symptom. Following a 2-week MTX tolerance test and a 4-week blinded MTX/placebo run-in, patients with uncontrolled gout were randomized 2:1 to receive pegloticase (infusion of 8 mg every 2 weeks) and blinded oral MTX (15 mg/week) or placebo (patients with eGFR <40 mL/min/1.73 m^2 were excluded).

Baseline eGFR was measured prior to MTX exposure (week 6). Mean change from baseline in eGFR was assessed via treatment and baseline eGFR status (<60 mL/min/1.73 m^2 and ≥60 mL/min/1.73 m^2). Analyses were performed on all randomized patients (intent-to-treat).

The pegloticase + MTX group included 100 patients. Mean age was 56 years, 91% were male, and mean eGFR was 68.9 mL/min/1.73 m^2. The pegloticase + placebo group included 52 patients. Mean age was 53 years, 85% were male, and mean eGFR was 71.1 mL/min/1.73 m^2.

In both treatment groups, eGFR was stable during the MTX/placebo run-in and after initiation of pegloticase (day 1). At week 24, mean change in eGFR from baseline was +5.3 mL/min/1.73 m^2 in the MTX group (n=70; 69 responders) and +4.3 mL/min/1.73 m^2 in the placebo group (n=19; 19 responders). There was no difference in change from baseline in eGFR at week 24 between the eGFR <60 mL/min/1.73 m^2 and the ≥60 mL/min/1.73 m^2 groups in the MTX cohort (+4.1 mL/min/1.73 m^2 and +6.3 mL/min/1.73 m^2, respectively) or in the placebo group (+2.5 mL/min/1.73 m^2 and +7.8 mL/min/1.73 m^2, respectively) (both *P*≥.48).

In summary, the researchers said, "eGFR did not appear to decrease after oral MTX initiation when administered as cotherapy with pegloticase. This was true for patients with and without pretherapy eGFR <60 mL/min/1.73 m^2. These findings suggest MTX cotherapy did not negatively impact renal function in MIRROR RCT trial participants."

Source: Abdellatif A, Botson JK, Obermeyer KL, LaMoreaux B, Marder BA. eGFR changes in uncontrolled gout patients randomized to receive methotrexate or placebo as co-therapy to pegloticase: MIRROR RCT findings. SA-P0898. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 5, 2022; Orlando, Florida. Funding for this study was provided by Horizon Therapeutics.

Magnesium Intake and Incident CKD

Results of recent studies have suggested an association between low levels of serum magnesium and kidney injury. However, there are few data available on whether dietary magnesium intake is related to kidney function.

Hee Byung Koh, MD, and colleagues at the Yonsei University College of Medicine, Seodaemun-gu, Seoul, Republic of Korea, conducted an observational study to examine the association between dietary intake of magnesium and incident chronic kidney disease (CKD). Results were reported during a poster session at the American Society of Nephrology Kidney Week 2022 in a poster titled *Association Between Dietary Magnesium Intake and Incident CKD.*

The researchers screened 210,984 European adults (40 to 70 years of age) in the UK Biobank cohort who completed dietary questionnaires from April 2009 to June 2012. Patients with underlying CKD (defined as baseline estimated glomerular filtration rate [eGFR] <60 mL/min/1.73 m^2 or urine to albumin-to-creatinine ratio >30 mg/g) or dietary energy intake <500 kcal or >6000 kcal were excluded.

Eligible participants were categorized into quartiles based on energy-adjusted dietary magnesium intake. The primary outcome of interest was incident CKD diagnosed using *International Classification of Diseases, Tenth Edition* and Office of Population Censuses and Surveys *Classification of Interventions and Procedures* codes. A sensitivity analysis was conducted, with the outcome of CKD defined as eGFR <60 mL/min/1.73 m^2.

The final analysis included 144,408 participants. Mean age was 55.8 years and 51.8% were female. The average magnesium intake per person was 352.0 mg/day. During follow-up of 1,431,716.4 person-years, 4438 patients developed incident CKD. The prevalence of CKD was progressively lower in patients with higher magnesium intake (3.5%, 3.1%, 2.9%, and 2.7% in quartiles 1-4, respectively).

In Cox regression analysis, relative to quartile 4, hazard ratios (HRs) for incident CKD decreased in a stepwise manner toward higher magnesium intake quartiles: quartile 1 HR, 0.90; 95% CI, 0.83-0.97; quartile 2 HR, 0.83; 95% CI, 0.77-0.90; quartile 3 HR, 0.80; 95% CI, 0.74-0.87 (*P* for trend<.001). Following adjustments for confounding factors, the association was maintained.

Results were similar with the eGFR-defined CKD outcome: quartile 1 adjusted HR (aHR), 0.93; 95% CI, 0.84-1.04; quartile 2 aHR, 0.86; 95% CI, 0.76-096; quartile 3 aHR, 0.83; 95% CI, 0.74-0.94, relative to quartile 4 (*P* for trend=.002).

In conclusion, the researchers said, "Higher intake of dietary magnesium may relate with lower risk of kidney function decline in adults with normal kidney function."

Source: Koh HB, Heo GY, Kim HJ, Ko YE, Kang S-W, Park JT. Association between dietary magnesium intake and incident CKD. TH-P0873. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 3, 2022; Orlando, Florida.

Efficacy of COVID-19 Vaccination in Dialysis Patients

Patients with end-stage renal disease (ESRD) are at increased risk for adverse outcomes from COVID-19 infection. The gold standard for prevention of mortality associated with COVID-19 is vaccination. **Jose E. Navarrete, MD,** and colleagues at Emory University, Atlanta, Georgia, performed an analysis to examine the efficacy of the COVID-19 vaccine in patients with ESRD receiving dialysis.

Results of the analysis were reported during a poster session at the American Society of Nephrology Kidney Week 2022. The poster was titled *COVID-19 Infection in Dialysis Patients: Efficacy of Vaccination.*

The study population included all patients undergoing dialysis at Emory dialysis centers from December 1, 2020, until February 2022. The date of vaccine series completion was recorded, and confirmed cases of COVID-19 were registered.

The researchers also recorded time from vaccination to COVID-19 and from COVID-19 to death. The risk of COVID-19-related mortality was compared between vaccinated and unvaccinated patients. Patients who received vaccination following an episode of COVID-19 were excluded from the analysis (n=89).

During the study period, 935 patients received maintenance dialysis at Emory dialysis centers. Of those, 68% completed two doses of COVID-19 vaccine, and 46% of vaccinated patients received a booster after a mean 294 days following completion of the primary vaccination series. Nonvaccinated patients were younger (55 years of age vs 60 years of age) and had shorter dialysis vintage (1.0 years vs 2.8 years) compared with vaccinated patients.

The two groups were similar in the proportion of home and in-center dialysis modality. The prevalence of diabetes, congestive heart failure, peripheral vascular disease, chronic obstructive pulmonary disease, atrial fibrillation, and previous transplants was also similar between vaccinated and nonvaccinated patients.

During follow-up, 11% of patients in the vaccinated group (n=71) died after 196 days compared with 24% of patients in the nonvaccinated group (n=70) who died after 86 days (*P*<.001). Following adjustment for age, dialysis vintage, and congestive heart failure, vaccinated patients with ESRD had a 78% reduction in mortality risk.

A total of 73 patients (11%) in the vaccinated group developed COVID-19 after 250 days compared with 48 unvaccinated patients (16%) who developed COVID-19 after 64 days (*P*<.001). Among the unvaccinated patients, the mortality odds ratio (OR) after infection with COVID-19 was 3.9 at 30 days after infection, 4.7 at 60 days, and 4.1 at 90 days.

"Vaccination against COVID-19 infection resulted in a 78% reduction in mortality risk in patients receiving dialysis. Nonvaccinated patients diagnosed with COVID-19 had higher mortality rates than vaccinated patients (OR, 4.1 at 90 days postinfection)," the researchers said.

Source: Navarrete JE, Cobb J, Apata IW, Masud T, Lea JP. COVID-19 infection in dialysis patients: efficacy of vaccination. TH-P0930. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 3, 2022; Orlando, Florida.

Phosphate Wasting Predicts Adverse Renal Outcomes in ADPKD

The most common inherited chronic kidney disease (CKD) is autosomal dominant polycystic kidney disease (ADPKD). Patients with ADPKD commonly progress to kidney failure.

Levels of the phosphaturic hormone fibroblast growth factor 23 (FGF23) are disproportionately high among patients with ADPKD for their CKD stage. However, according to **Laixi Xue, MD,** and colleagues, only a subgroup of patients develop kidney phosphate wasting. Kidney phosphate wasting is considered a marker for tubular dysfunction.

The researchers conducted an analysis to test the hypothesis that phosphate wasting is associated with worse kidney outcomes in patients with ADPKD. Results were reported during a poster session at the American Society of Nephrology Kidney Week 2022 in a poster titled *Kidney Phosphate Wasting Predicts Worse Outcomes in Patients With Polycystic Kidney Disease.*

The analysis included data on 670 patients with ADPKD from the DIPAK observational cohort with serial measurements of kidney function (estimated glomerular filtration rate [eGFR]) and magnetic resonance imaging-based total kidney volume (TKV). Serum c-terminal FGF23 levels were measured at baseline. The Bijvoet formula was used to calculate the ratio of tubular maximum reabsorption rate of phosphate to GFR (TmP/GFR). Kidney phosphate wasting was defined as TmP/GFR ≤0.8 mmol/L.

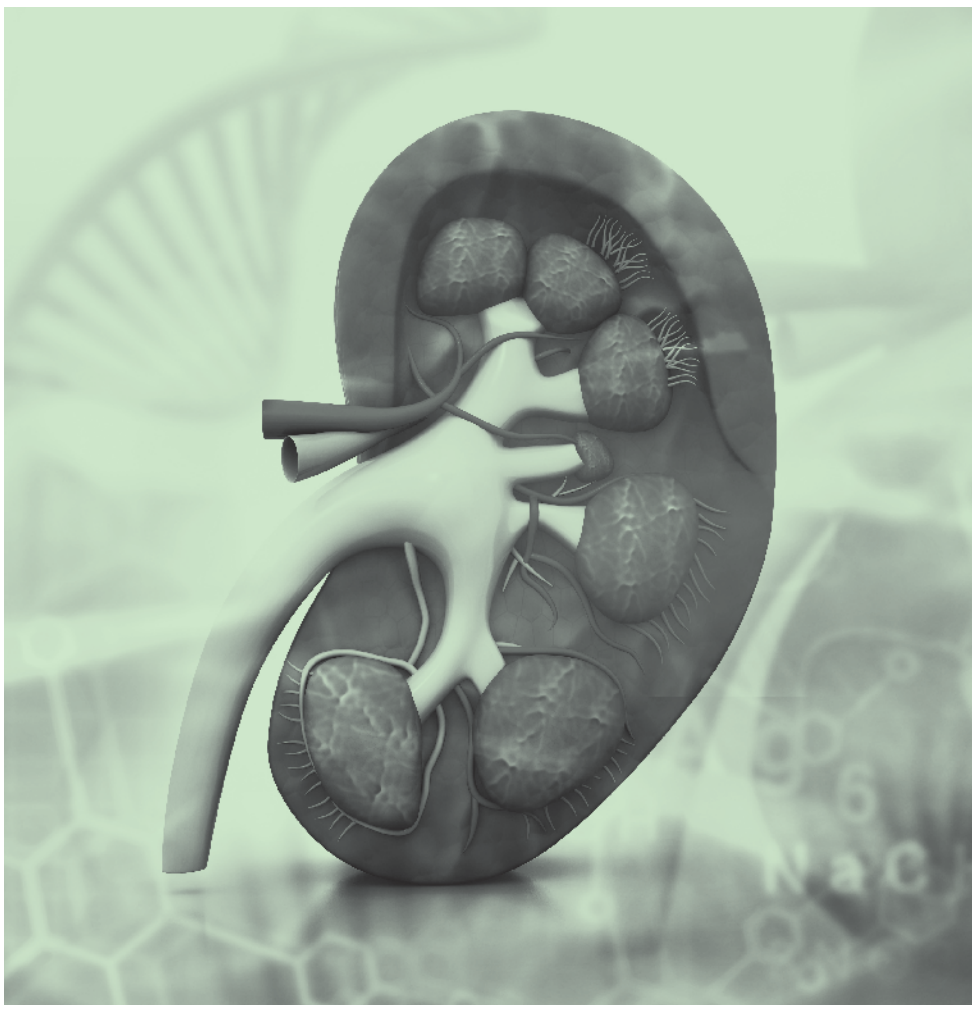
Linear mixed models and Cox regression analysis models were used to examine the association of TmP/GFR ratios with eGFR decline over time and the hazard ratios for the composite kidney outcome of >40% decline in eGFR, incidence of kidney failure, or initiation of kidney replacement therapy.

The cohort with measured phosphate excretion included 604 patients. Mean age was 48 years, 39% were male, and mean eGFR was 63 mL/min/1.73 m^2. Mean TmP/GFR was 0.76 mmol/L, and mean FGF23 was 121 RU/mL. Kidney phosphate wasting was observed in 59% of the cohort (n=357). There were independent associations between TmP/GFR and male sex, eGFR, and FGF23 (P<.05 for all).

During follow-up of 3 years, 145 kidney outcomes were observed. Following adjustment for risk factors for decline in kidney function (sex, genotype, and TKV), every 0.1 mmol/L decrease in TmP/GFR was associated with a steeper eGFR decline of 0.15 mL/min/1.73 m^2 per year (P=.01) and 1.17 times higher risk of the composite kidney outcome (95% CI, 1.04-1.31; P=.007). There were no associations between FGF23 or hypophosphatemia and the composite kidney outcome.

"In patients with ADPKD, phosphate wasting is highly prevalent and is independently associated with an increased risk for disease progress," the researchers said. "This effect was not mediated by FGF23 or serum phosphate levels. Our results suggest that TmP/GFR adds to the current prognostic models for ADPKD."

Source: Xue L, Meijer E, De Borst MH, et al. Kidney phosphate wasting predicts worse outcomes in patients with polycystic kidney disease. TH-P0382. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 3, 2022; Orlando, Florida.



Changes in eGFR in Patients Treated for Gout With Pegloticase + Methotrexate

Decline in renal function is associated with hyperuricemia and gout. Independent of chronic kidney disease (CKD) stage, pegloticase has been shown to lower uric acid in patients with CKD and uncontrolled gout. Data from recent trials and case data support use of an immunomodulator with pegloticase to limit formation of antidrug antibody, increase urate-lowering response rate, and decrease the risk of infusion reaction.

CKD may limit immunomodulator use. Patients with estimated glomerular filtration rate (eGFR) <40 mL/min/1.73 m^2 were excluded from clinical trials of pegloticase plus immunomodulator (methotrexate [MTX]). However, according to **Brad A. Marder, MD**, and colleagues, gout is common in patients with CKD and use of pegloticase plus immunomodulator has been reported.

The researchers performed an analysis of case data to examine changes in eGFR during cotherapy with pegloticase + MTX in patients with and without CKD. Results were reported during a poster session at the American Society of Nephrology Kidney Week 2022 in a poster titled *eGFR Changes in Uncontrolled Gout Patients Undergoing Pegloticase Plus Methotrexate Co-Therapy.*

The retrospective analysis included pooled deidentified case data of pegloticase + MTX cotherapy. Patients were labeled as CKD (defined as baseline eGFR <60 mL/min/1.73 m^2) or non-CKD (baseline eGFR ≥60 mL/min/1.73 m^2). Serum uric acid, eGFR, blood cell counts, and liver function tests were monitored. Patient characteristics, treatment parameters, response rate (≥12 infusions, pre-infusion 12 serum uric acid <6 mg/dL), eGFR, and adverse events were assessed. Response analyses excluded patients with <12 infusions who remained on therapy at time of data collection.

The analysis included data on 42 patients with uncontrolled gout. Of those, 15 were in the CKD group (13 stage 3 and 2 stage 4) and 27 were categorized as non-CKD. The comorbidity profiles of the two groups were similar; more patients in the CKD group were female and ≥65 years of age.

In both groups, MTX was initiated approximately 4 weeks prior to pegloticase; the patients with CKD had a lower dose (15 vs 19 mg/week). The pegloticase response rates were similar in both groups (CKD, 92% vs non-CKD, 86%). In patients without CKD, 44% had an increase in eGFR (mean increase, +4.2 mL/min/1.73 m^2). In patients with CKD, 60% had an increase in eGFR (mean increase, +11.5 mL/min/1.73 m^2).

A total of 13 patients in the CKD group had stability/improvement in CKD stage (87%, both stage 4 improved to stage 3a and two stage 3a improved to stage 3b). There were no new safety signals identified. Seven patients in the CKD group (47%) and 13 in the non-CKD group (48%) had one or more adverse events (most commonly gout flare, 47 % and 41%, respectively). Pancytopenia (n=1) and mild immune response (n=1) were reported in the non-CKD group.

"These limited data show similar pegloticase + MTX urate-lowering efficacy in CKD and non-CKD patients. Most CKD patients had renal stability/improvement during therapy, but further study is needed," the authors said.

Source: Marder BA, Albert JA, Broadwell A, Padnick-Silver L, LaMoreaux B. eGFR changes in uncontrolled gout patients undergoing pegloticase plus methotrexate co-therapy. SA-P0897. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 5, 2022; Orlando, Florida. Funding for this study was provided by Horizon Therapeutics.

Sarcopenia Prevalence and Adverse Cardiovascular Events

Among patients with end-stage kidney disease (ESKD) receiving maintenance dialysis, sarcopenia is a frequent, yet under-recognized, complication. **Wannasit Wathanavasin, MSc,** and colleagues in Thailand conducted a systematic review and meta-analysis designed to assess the global prevalence of sarcopenia and examine whether the condition has an impact on clinical outcomes, particularly cardiovascular events and mortality in dialysis patients.

Results of the study were reported during a poster session at the American Society of Nephrology Kidney Week 2022. The poster was titled *The Prevalence of Sarcopenia and Its Impact on CV Events and Mortality Among ESKD Patients on Dialysis: A Systematic Review and Meta-Analysis.*

Eligible studies were identified via searches in PubMed, Scopus, and Cochrane Central Register of Controlled Trials through March 31, 2022. Cross-sectional and cohort studies that reported the prevalence of sarcopenia were included. Other outcomes of interest were low muscle mass and low muscle strength, as well as adverse events, including cardiovascular events and death.

The pooled prevalence rate was calculated using the random-effects model. Associations between sarcopenia and clinical outcomes were expressed as odds ratio (OR) and 95% CI. The presence of heterogeneity was measured using Cochran's Q statistic and I2 test. Funnel plot and Egger's test also tested publication bias.

The meta-analysis included 41 studies representing 7576 patients. The pooled prevalence of sarcopenia in patients on dialysis was 25.6% (95% CI, 22.1%-29.4%). Among various diagnostic criteria, the highest prevalence was found in the Asian Working Group for Sarcopenia 2019 criteria (36.9%; 95% CI, 30.4%-44.2%).

There was a significant association between sarcopenia and higher mortality risk (adjusted OR [aOR], 1.83; 95% CI, 1.40-2.39) and cardiovascular events (aOR, 3.80; 95% CI, 1.79-8.09). There were independent associations between both low muscle mass and low muscle strength and increased risk of mortality in dialysis patients (OR, 1.71; 95% CI, 1.20-2.44 and OR, 2.15; 95% CI, 1.15-3.07, respectively).

In conclusion, the researchers said, "This meta-analysis revealed that sarcopenia was highly prevalent among dialysis patients and shown to be an important predictor of cardiovascular events and mortality. Future intervention research to alleviate this burden of disease in dialysis patients is needed."

Source: Wathanavasin W, Banjongjit A, Avihingsanon Y, Praditpornsilpa K, Eiam-Ong S, Susantitaphong P. The prevalence of sarcopenia and its impact on CV events and mortality among ESKD patients on dialysis: a systematic review and meta-analysis. TH-P0790. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 3, 2022; Orlando, Florida.

Urinary Copper Excretion in Kidney Transplant Recipients

Patients who develop proteinuria experience increases in urinary copper excretion. **Manuela Yepes Calderon, PhD,** and colleagues conducted a prospective cohort study to examine whether proteinuria in kidney transplant recipients is associated with urinary copper excretion. The researchers also sought to determine if there is an association between urinary copper excretion and the biomarker of tubular damage urinary liver-type fatty acid-binding protein (u-LFABP) and the development of graft failure. Results were reported during a poster session at the American Society of Nephrology Kidney Week 2022 in a poster titled *Urinary Copper Excretion Is Associated With Graft Failure in Kidney Transplant Recipients.*

The study included kidney transplant recipients with a functioning allograft ≥1 year posttransplant. Urinary copper was measured in 24-hour urine samples by coupled plasma mass spectrometry. The researchers conducted multivariable linear regression and Cox regression analyses.

The study cohort included 693 kidney transplant recipients. Of those, 57% were male, and mean age was 53 years. Baseline copper excretion was 23.57 µg. There was a direct association between copper and proteinuria independent of graft function (Std ß 0.45; $P<.01$) and with u-LFABP independent of proteinuria (Std ß 0.34; $P<.001$).

Median follow-up was 5.3 years. During follow-up, 12% of the cohort (n=83) developed graft failure. There was an association between being on the third tertile of urinary copper excretion and an increased risk of graft failure (hazard ratio, 2.94; 95% CI, 1.34-6.45; $P<.001$). The association was independent of adjustment by multiple potential confounders. The association was significantly mediated by u-LFABP, accounting for 46% of the total effect.

"We concluded that in kidney transplant recipients, proteinuria is associated with increased copper excretion, and this is further associated with the risk of graft failure apparently by enhancing tubular damage," the researchers said. "Further studies seem warranted to elucidate whether copper-targeted interventions may decrease the burden of graft failure on kidney transplant recipients."

Source: Yepes Calderon M, Kremer D, Knobbe TJ, et al. Urinary copper excretion is associated with graft failure in kidney transplant recipients. FR-P0810. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 4, 2022; Orlando, Florida.

Intervention to Reduce Contrast-Associated AKI After Coronary Procedures

Among patients undergoing coronary angiography or percutaneous coronary intervention (PCI), between 4% and 10% experience acute kidney injury (AKI). The costs of care in the United States attributed to AKI in that patient population has been estimated as high as $1.67 billion annually. AKI is associated with adverse renal and cardiovascular adverse outcomes, including acute dialysis, end-stage renal disease, heart failure, atherosclerotic events, and death.

According to **Matthew T. James, MD, PhD,** and colleagues, uptake of the recommended strategies for care to avoid contrast-associated AKI during those procedures varies. The researchers conducted a stepped-wedge, cluster randomized clinical trial to determine whether a multifaceted intervention would be effective to prevent AKI after coronary angiography or PCI. Results were reported in *JAMA* [2022;328(9):839-849].

All invasive cardiologists at three cardiac catheterization laboratories in Alberta, Canada, were randomized to one of eight start dates for the intervention between January 2018, and September 2019. The intervention included three components: (1) educational outreach that included information about AKI, prevention approaches, and the components of the intervention; (2) computerized clinical decision support on contrast volume and hemodynamic-guided intravenous fluid targets; and (3) audit and feedback every 3 months following initial introduction to the intervention. During the preintervention period (control), the cardiologists provided usual care and did not receive the intervention.

The primary outcome of interest was AKI defined by serum creatinine-based criteria form the Kidney Disease: Improving Global Outcomes AKI guidelines. Secondary outcomes included contrast volume, intravenous

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fluid administration, and major adverse cardiovascular and kidney events. Time-adjusted models were used in all analyses.

Of the 34 invasive cardiologists who contributed data to the trial, three retired from practice before receiving the intervention and contributed data only to the control group (preintervention period). Of the 31 physicians who received the intervention as planned, 12.9% (n=4) were women, mean age was 51.2 years, and mean length of practice was 19.6 years. During the study period, a total of 29,418 coronary angiography or PCI procedures were performed in 26,110 patients.

Following exclusion of 19,004 patients undergoing dialysis, urgent primary PCI for ST-segment elevation myocardial infarction, and those with less than a 5% risk of AKI, a total of 7820 procedures in 7106 patients were eligible for inclusion in the analysis. Of the 7820 procedures, 4327 were performed by the 31 cardiologists in the intervention group among 4032 patients (mean age, 70.3 years; 32.0% [n=1384] women). The remaining 3493 procedures were performed by the 34 cardiologists in the control group among 3251 patients (mean age, 70.2 years; 33.0% [n=1151] women). Of total procedures, 10.2% (n=794) were

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missing data for the primary outcome and 8.9% (n=698) were missing data on contrast volume.

During the intervention period, the range of the number of procedures performed by each physician among patients with a more than 5% risk of AKI across the 31 physicians was from 4 to 334 (median, 130 procedures per physician); during the control period, the range across the 34 physicians was from 22 to 325 (median, 87 procedures per physician). There were small differences in procedure indication between the intervention group and the control group. The two groups were similar in patient demographic characteristics, comorbidities, preprocedure estimated glomerular filtration rate (eGFR), predicted risk of AKI, and fluoroscopy time (a surrogate of procedure complexity).

PRIMARY OUTCOME

During the 2-year study period, there were 310 AKI events after 4327 procedures (7.2%) performed by physicians in the intervention group compared with 299 AKI events after 3493 procedures (8.6%) performed by physicians in the control group (between group difference, –2.3% [95% CI, –0.6% to –4.1%]). In the primary analysis accounting for clustering and adjustment

for time, the intervention resulted in a significant odds reduction in AKI (time-adjusted odds ratio [OR], 0.72; 95% CI, 0.56 to 0.93; *P*=.01). There was a consistent effect over the duration of the trial (*P*=.27 for treatment × time interaction).

In multivariable analyses with additional adjustments for age, sex, comorbidities, eGFR, and procedure indication, results were similar (adjusted OR, 0.67; 95% CI, 0.52-0.86), and in the complete case analysis. In subgroups defined by age, sex, with or without heart failure or CKD, at moderate or high risk of AKI, and in patients who underwent coronary angiography alone or procedures including PCI, the effect was seen consistently. The effect was also seen consistently when alternate serum creatinine-based definitions for AKI were assessed. In a post hoc analysis following exclusion of data from the three physicians who retired before receiving the intervention, the results remained consistent.

SECONDARY OUTCOMES

Of the 12 prespecified secondary outcomes, eight showed no significant difference. The proportion of procedures using excessive contrast volumes was reduced from 51.7% during the control period to 38.1% during the intervention period (between-group difference, –12.0%; 95% CI, –14.4% to –9.4%; time-adjusted OR, 0.77; 95% CI, 0.65 to 0.90; *P*=.002). The proportion of procedures in eligible patients in whom insufficient intravenous fluid was given was reduced from 75.1% during the control period to 60.8% during the intervention period (between-group difference, –15.8%; 95% CI, –19.7% to –12.0%; OR, 0.68; 95% CI, 0.53 to 0.87; *P*=.002). There were no significant between-group differences in major adverse cardiovascular events or major adverse kidney events.

The researchers cited several limitations to the study, including the cluster randomized clinical trial design that may have lower risk of bias than nonrandomized designs, the vulnerability of the stepped-wedge design to contamination if the physicians who had not yet received the intervention were aware of the trial and changed their behaviors prior to receiving the intervention, 10.2% of the cohort having missing data for AKI, the relatively small number of physician clusters, and the possibility that the findings may not be generalizable to countries other than Canada.

In conclusion, the researchers said, "Among cardiologists randomized to an intervention including clinical decision support with audit and feedback, patients undergoing coronary procedures during the intervention period were less likely to develop AKI compared with those treated during the control period, with a time-adjusted absolute risk reduction of 2.3%. Whether this intervention would show efficacy outside this study setting requires further investigation." ■

TAKEAWAY POINTS

- Contrast-associated acute kidney injury (AKI) is a common complication of coronary angiography and percutaneous intervention (PCI).
- Researchers in Canada conducted a stepped-wedge, cluster randomized clinical trial to determine whether a multifaceted intervention is effective for the prevention of AKI after those procedures.
- Patients who underwent coronary procedures during the intervention period were less likely to develop AKI compared with those treated during the control period.

Low-Carbohydrate Diet Score and All-Cause Mortality in Patients With CKD

Obesity and being overweight is the fifth leading cause of mortality worldwide, resulting in the growing popularity and mainstream use of low-carbohydrate diets (LCDs) as a way to lose weight. While previous studies have demonstrated the effectiveness of LODs to produce short-term weight loss and improvements in several risk factors for cardiovascular disease, such as insulin resistance and cholesterol levels, the long-term safety of adhering to a LCD remains controversial.

Most of the previous studies of the safety and long-term effectiveness of LCDs were conducted in the general population and focused on the effects of the dietary components rather than the health conditions of individuals who adhere to a LCD. Diets lower in carbohydrates and higher in protein and fat than more balanced diets may pose the risk of nephrotoxicity, in addition to concerns that saturated fats are risk factors for atherosclerosis, creating the possibility that LCDs pose particular problems for individuals with chronic kidney disease (CKD).

Nanhui Zhang, MD, and colleagues conducted a study designed to examine the association of LCD with all-cause mortality among individuals with and without CKD. Results of the study were reported in the *Journal of Renal Nutrition* [2022;32(3):301-311].

The study utilized data from the Third National Health and Nutrition Examination Survey (NHANES III), a nationally representative sample of the noninstutionalized US population conducted between 1988 and 1994 by the National Center for Health Statistics of the Centers for Disease Control and Prevention. The study cohort included nonpregnant adults >20 years of age who had (1) complete data on total nutritional intake obtained from dietary interview (n=15,358); (2) complete data on serum creatinine, urine creatinine, and albumin (n=14,388); (3) CKD, defined as an estimated glomerular filtration rate (eGFR) <90 mL/min/1.73 m^2 or urinary albumin-to-creatinine ratio ≥30 mg/g (n=2072); and (4) total caloric intake per day between 800 and 4200 kcal per day for men and between 500 and 3500 kcal per day for women (n=1954).

Patients with a history of diabetes, cardiovascular disease, or cancer were excluded (n=703). For the group without CKD participants with an eGFR >60 mL/min/1.73 m^2 and albumin-to-creatinine ratio ≤200 mg/gm, with all other inclusion criteria remaining, were included. The primary outcome of interest was all-cause mortality. The final cohort included 1158 participants with CKD and 9523 participants without CKD.

The LCD score was calculated based on a 24-hour dietary recall interview. The score ranged from 0 (lowest fat and protein intake and highest carbohydrate intake) to 30 (highest protein and fat intake and the lowest carbohydrate intake). Mortality was from baseline until December 31, 2015. Multivariable-adjusted hazard ratios and 95% confidence intervals were estimated using Cox proportional hazards regression models. For analyses of all-cause mortality, participants were divided into four categories (quarters) for each of the LCD score, with the lowest quarter always used as a reference.

In the group with CKD, mean daily carbohydrate intake ranged from 61.9% of total energy intake in the first quarter LCD score to 37.9% of total energy intake in the fourth quarter. Compared with participants in the lowest quarter of LCD score, those who had a higher LCD score were more likely to smoke, had a higher body mass index (BMI), a lower intake of dietary fiber, and a higher intake of sodium.

Among the group without CKD, mean daily carbohydrate intake ranged from 61.4% of total energy intake in the first quarter LCD score to 37.6% of total energy intake in the fourth quarter. Those with a higher LCD score had a higher BMI, and a higher intake of sodium and potassium.

Median follow-up was 24 years. During follow-up, there were 751 (65%) documented all-cause deaths in the CKD group and 2624 (28%) all-cause deaths in the non-CKD group. Following adjustment for all potential confounders, there were significant positive associations between the LCD score and all-cause mortality in participants with CKD. Participants in the fourth quarter LCD score group had a higher risk for all-cause mortality compared with those in the first quarter of the LCD score (hazard ratio [HR], 1.51; 95% CI, 1.01-2.25; *P* for trend=.045). There was no association between the LCD score and all-cause mortality in the group without CKD, following adjustment for all potential confounders.

In analyses of the association between each macronutrient and all-cause mortality in the group with CKD, compared with the highest total carbohydrate intake, those with the lowest total carbohydrate intake had a significantly higher risk of all-cause mortality (HR, 1.56; 95% CI, 1.11-2.19; *P* for trend=.006). There was a negative association between intake of vegetable protein and the risk of all-cause mortality (HR, 0.61; 95% CI, 0.44-0.84; *P* for trend=.003). Intake of saturated fatty acids was associated with an increased risk of all-cause mortality for the comparison of the highest quarter with the lowest quarter (HR, 1.53; 95% CI, 1.17-1.99; *P* for trend=.034).

Limitations to the study cited by the authors included the self-reported design of the study exposure and most of the covariates, the lack of longitudinal data on participants' dietary intake during the follow-up period, the use of data from NHANES III (1988-1944) rather than more contemporary data, and the lack of data on the progression of CKD.

In conclusion, the researchers said, "The LCD scores were found significantly positively associated with all-cause mortality in adults with CKD, but not in adults without CKD." ■

> Following adjustment for all potential confounders, there were significant positive associations between the LCD score and all-cause mortality in participants with CKD. Participants in the fourth quarter had a higher risk for all-cause mortality compared with those in the first quarter of the LCD score.

TAKEAWAY POINTS

- Researchers reported results of a study examining the association of a low carbohydrate diet with mortality in a cohort of individuals with and without chronic kidney disease (CKD).
- In participants with CKD, there was an association between higher LCD scores (indicating highest protein and fat intake and lowest carbohydrate intake) and all-cause mortality.
- There was no association between higher LCD scores and all-cause mortality among participants without CKD.

Healthy Lifestyle and Mortality in Dialysis Patients

Approximately 2.5 million people with stage 5 chronic kidney diseases (CKD) worldwide are treated with long-term dialysis. The prognosis of patients on dialysis is poor, with an annual mortality rate of 10% to 20%, due largely to cardiovascular diseases. Use of statins as pharmacological interventions have yielded few results in reducing mortality in dialysis patients.

There are a number of lifestyle recommendations from the American Heart Association (AHA) for cardiovascular prevention that have been combined into a health lifestyle score. The recommendations include avoiding smoking, engaging in regular physical exercise, maintaining an appropriate body mass index, adhering to a diet rich in fruits, vegetables, and fish and low in salt and sugar, and maintaining blood pressure, cholesterol, and glucose within recommended targets. There are associations with higher lifestyle scores and 30% to 50% lower cardiovascular disease risk in the general population. Those benefits may be related to reversing or reducing obesity, hypercholesterolemia, diabetes, and hypertension, key risk factors for cardiovascular disease.

There are few data available on the benefits of a healthy lifestyle in patients with CKD receiving maintenance hemodialysis. **Guobin Su, MD, PhD,** and colleagues conducted a prospective cohort study to examine the association of a modified AHA healthy lifestyle score and its individual components with all-cause and cardiovascular mortality in patients treated with hemodialysis. Results of the study were reported in the *American Journal of Kidney Diseases* [2022;79(5):688-698].

The study was conducted in a large, multinational private dialysis network. The study exposure was a modified healthy lifestyle score based on the AHA recommendations for cardiovascular prevention, the sum of four components addressing the use of smoking tobacco, physical activity, diet, and control of systolic blood pressure. The outcomes of interest were cardiovascular and all-cause mortality.

Adjusted proportional hazards regression analyses with country as a random effect was used to estimate the associations between lifestyle score and mortality. Lifestyle score was stratified as low (0-2 points) as the referent, medium (3-5 points), and high (6-8 points). Associations were expressed as adjusted hazard ratio (aHR), with 95% CI.

The study utilized data from the DIET-HD (Dietary Intake, Death and Hospitalization in Adults with End-Stage Kidney Disease Treated with Hemodialysis) study. A total of 9757 patients participated in the DIET-HD study and completed the Food Frequency Questionnaire (FFQ). Of those, 5483 (56%) had complete lifestyle data (all individual components of the lifestyle score) and were included in the primary analysis. Compared with patients without complete lifestyle data, those with complete lifestyle data were older, had more comorbidities, and had a higher mortality rate.

TAKEAWAY POINTS

- Results of a prospective cohort study evaluating the association of a modified AHA healthy lifestyle score and its individual components with all-cause and cardiovascular mortality.
- The cumulative incidence of cardiovascular death in those with low, medium, and high lifestyle scores was 63, 47, and 40 per 100 person-years, respectively.
- For all-cause death, the corresponding values were 156, 124, and105 per 1000 person-years, respectively.

Across increasing healthy lifestyle score categories, there were more women, a lower proportion of comorbidities, and a shorter dialysis vintage.

Overall, the mean age of the cohort was 66 years, 42% were female, 87% had hypertension, 31% had diabetes, and 43% had a history of CKD. Sixty-seven percent had never smoked, 20% engaged in physical activity more than once a week, 25% had systolic blood pressure before dialysis <120 mm Hg, and 20% adhered to a high recommended food score.

A total of 982 participants (18%) had a high lifestyle score (score 6-8), 3945 (72%) had a medium lifestyle score (score 3-5), and 556 (10%) had a low lifestyle score (score 0-2). Across increasing healthy lifestyle score categories, there were more women, a lower proportion of comorbidities, and a shorter dialysis vintage.

Median follow-up was 3.8 years. During the follow-up period, there were 2163 deaths (39%). Of those, 39% (n=826) were attributed to cardiovascular causes. The cumulative incidence of cardiovascular death was 63 per 1000 person-years in the group with low lifestyle score, 47 per 1000 person-years in the group with medium lifestyle score, and 40 per 1000 person-years in the group with high lifestyle score (log-rank $P<.001$). For all-cause death, the corresponding values were 156, 124, and 105 per 1000-person years (log-rank $P=.002$).

When the lifestyle score was treated as a continuous variable, the aHRs of cardiovascular death and all-cause death were 0.92 (95% CI, 0.89-0.95) and 0.94 (95% CI, 0.89-0.98), respectively, for every unit greater healthy lifestyle score.

Compared with patients with a low lifestyle score, the aHRs of cardiovascular death among those with medium and high lifestyles scores were 0.73 (95% CI, 0.49-0.85) and 0.65 (95% CI, 0.49-0.85), respectively (P for trend=.003). For all-cause mortality, the aHRs were 0.75 (95% CI, 0.65-0.85) for those with medium lifestyle scores and 0.64 (95% CI, 0.54-0.76) for those with high lifestyle scores (P for trend <.001).

Smoking and physical activity were consistently associated with higher risk of both cardiovascular and all-cause mortality. Compared with being a current smoker, the aHRs for all-cause and cardiovascular mortality for the participants who never smoked were 0.75 (95% CI, 0.65-0.86) and 0.71 (95% CI, 0.57-0.88). Compared with participants who did not engage in physical activity, the aHRs for all-cause and cardiovascular mortality for participants who engaged in physical activity more than once a week were 0.75 (95%CI, 0.66-0.85) and 0.79 (95% CI, 0.65-0.96), respectively. There were no significant associations between either recommended food score or blood pressure targets and mortality.

The researchers cited some limitations to the study findings, including the observational design, the self-reported nature of the FFQ, and the data-driven approach.

In conclusion, the authors said, "A healthier lifestyle is associated with lower all-cause and cardiovascular mortality among patients receiving maintenance hemodialysis." ■

Serum Phosphate and Predialysis Blood Pressure in Hypertensive Patients

Among patients with end-stage renal disease (ESRD) on hemodialysis, mineral bone disease (MBD) is a nontraditional cardiovascular risk factor that contributes to high mortality rate in that patient population. Hyperphosphatemia and related increases in parathyroid hormone (PTH) are each independently associated with mortality in patients with MBD.

It is known that chronically elevated serum phosphate contributes to structural changes in blood vessels including vascular calcification. According to **Jinwoo Jung, MD,** and colleagues, there is emerging evidence that elevated serum phosphate is also associated with other functional abnormalities of the blood vessels that may be more easily reversable.

The researchers conducted a cross-sectional study among patients with hypertension on maintenance hemodialysis to test the hypothesis that there would be an independent association between elevated serum phosphate and blood pressure, as well as with measurements of vasoconstriction and markers of endothelial cell dysfunction (ECD). Results were reported online in *BMC Nephrology* [doi.org/10.1186/s12882-022-02918-0].

Baseline data from a previously conducted prospective cohort of hypertensive ESRD patients on maintenance hemodialysis that included a predefined subset with recurrent intradialytic hypertension were used for the current analysis. Inclusion criteria were age >18 years, hemodialysis vintage >1 month, and peri-dialytic hypertension, defined as prehemodialysis systolic blood pressure >140 mm Hg or posthemodialysis systolic blood pressure >130 mm Hg.

Measurements of total peripheral resistance index (TPRI, noninvasive cardiac output monitor) and plasma levels of endothelial-1 (ET-1) and asymmetric dimethylarginine (ADMA) were obtained before and after a midweek hemodialysis treatment, as were blood pressure measurements. Generalized linear regression analyses were used to determine independent associations between serum phosphate and blood pressure, TPRI, ET-1, and ADMA, while controlling for demographic variables, PTH, and interdialytic weight gain.

The cohort for the current analysis included 54 patients with complete data available (serum phosphate and the outcomes of prehemodialysis blood pressure, TPRI, ET-1, and ADMA, as well as other analyzed covariates). Sixty-one percent were male and 63% had diabetes. Nearly all were receiving at least one oral phosphate binder (56% on calcium-containing binders, 41% on non-calcium-containing binders). Eighty percent were receiving some form of active vitamin D and 33% were receiving cinacalcet. Phosphate levels were collected from a range of 0 to 32 days from the time the blood pressure, TPRI, ET-1, and ADMA measurements were obtained. Mean serum phosphate, calcium, and PTH levels were 1.90 mmol/L, 2.29 mmol/L, and 631 ng/L, respectively.

There were significant correlations between serum phosphate and systolic blood pressure for both the supine and the seated measurements taken prior to hemodialysis (r=0.3; P=.03; and r=0.4; P=.002, respectively). There were no significant correlations between serum phosphate and systolic blood pressure for the supine and seated measurements taken following hemodialysis.

For the supine and seated diastolic blood pressure measurements prior to hemodialysis, there were significant correlations with serum phosphate (r=0.5; P<.0001; and r=0.5; P=.0003, respectively). There were also significant correlations between serum phosphate and posthemodialysis seated and supine blood pressure measurements taken following hemodialysis (r=0.4; P=.003; and r=0.4; P=.002, respectively).

In a model that controlled for demographic variables, there were positive associations between serum phosphate and diastolic blood pressure as well as systolic blood pressure, although the significance was attenuated in systolic blood pressure. In models that included PTH and percentage of interdialytic weight gain, the positive association between serum phosphate and diastolic blood pressure persisted; the significant association between serum phosphate and systolic blood pressure remained a trend.

The Pearson correlation coefficients for serum phosphate with prehemodialysis TPRI, ET-1, and ADMA were 0.3 (P=.01), 0.4 (P=.007), and 0.3 (P=.04), respectively. There were independent associations between serum phosphate and higher TPRI and ET-1 in models that included demographic variables, PTH, and weight gain. There was no association between serum phosphate and ADMA. In the univariate Pearson correlation analysis, PTH was positively associated with AMDA (r=0.3; P=.01); the statistical significance was slightly attenuated in the Spearman correlation and with the regression analysis.

The researchers cited some limitations to the study, including the relatively small sample size and the observational design that limited the ability to draw conclusions regarding causality. Further, the study utilized ET-1 and AMDA as biomarkers for ECD because there were no alternative measurements. Finally, measurements of serum phosphate and other hemodialysis laboratory values were gathered in the context of routine clinical care and did not occur on the same data as the blood pressure and TPRI measurements.

In conclusion, the authors said, "We found that there is a positive association between serum phosphate and peridialytic blood pressure. The association with diastolic blood pressure was particularly strong and was independent of PTH, interdialytic weight gain, and other variables. We found that phosphate was also related to prehemodialysis vasoconstriction and ECD markers, although the association with ADMA was not fully independent of other factors. These findings require further investigation to determine the hemodynamic benefits of aggressive phosphate lowering in ESRD and even possible in pre-ESRD chronic kidney disease. They also introduce the possibility of more targeted approaches to blood pressure management among patients with refractory hyperphosphatemia. Such research will require comprehensive assessment of the numerous mediators of MBD." ■

TAKEAWAY POINTS

- Researchers reported results of a study designed to test the hypothesis that elevated serum phosphate would be independently associated with blood pressure and with measurements of endothelial cell dysfunction (ECD) and measures of vasoconstriction in hypertensive hemodialysis patients.
- The study found independent associations between serum phosphate concentration and higher predialysis blood pressure, vasoconstriction, and markers of ECD.
- The findings demonstrated an additional negative impact of hyperphosphatemia on cardiovascular health beyond vascular calcification.

Discontinuation of RAAS Inhibitors and Risk of Mortality in CKD

Patients with proteinuric chronic kidney disease (CKD) are commonly treated with renin-angiotensin-aldosterone system (RAAS) inhibitors, with well-established beneficial outcomes. Results of large, randomized trials have demonstrated that use RAAS inhibitors among patients with CKD is associated with kidney-protective and antiproteinuric effects, as well as a lowering of risk of cardiovascular disease. Guidelines recommend the use of RAAS inhibition as first-line treatment for patients with CKD.

RAAS inhibitors have also been shown to have an association with an increased risk of hyperkalemia, an independent risk factor for arrhythmias, mortality, and hospitalization. Patients likely to gain the potential renal and cardiovascular benefits from RAAS inhibitors are also at the highest risk for hyperkalemia.

At present, there is no standard of care for management of chronic hyperkalemia in patients with CKD. Results of observational studies have identified discontinuation or dose reduction of RAAS inhibition as the most common management strategy in patients with chronic hyperkalemia.

Silvia J. Leon, MD, MSc, and colleagues conducted a retrospective cohort study to examine the risk of all-cause and cardiovascular mortality, fatal and nonfatal cardiovascular events, and initiation of dialysis with discontinuation of RAAS inhibitors in patients with CKD and hyperkalemia. Results were reported in the *American Journal of Kidney Diseases* [2022;80(2):164-173].

The study included adults in Manitoba and Ontario, Canada. Eligible patients had an episode of de novo RAAS-related hyperkalemia, defined as serum potassium ≥5.5 mmol/L, and CKD. The study exposure was a prescription for an RAAS inhibitor. The primary outcome of interest was all-cause mortality. Secondary outcomes included cardiovascular mortality, fatal and nonfatal cardiovascular events, and initiation of dialysis.

The association between the continuation (vs discontinuation) and outcomes was examined using Cox proportional hazards models using intent to treat. Sensitivity analyses included time-dependent, dose-dependent, and propensity-matched analyses.

The Manitoba cohort included 8534 patients who met eligibility criteria. Ninety days after the hyperkalemia episode, a total of 7200 surviving patients were included in the analysis. In the Ontario cohort, 78,938 patients ≥66 years of age met inclusion criteria. Ninety days following the hyperkalemia episode, 71,290 were included in the analysis. In the Manitoba cohort, 24% of the patients experienced the hyperkalemia episode in the inpatient setting.

Mean age of participants in the Manitoba cohort was 72.39 years, and approximately 48% were female. Mean serum potassium was 5.84 mmol/L, and mean estimated glomerular filtration rate (eGFR) at baseline was 40.87 mL/min/1.73 m^2. In the Ontario cohort, mean age was 79.48 years, and 52% were female. Mean serum potassium was 5.75 mmol/L and mean eGFR was 41.16 mL/min/1.73 m^2.

In Manitoba, participants who discontinued RAAS inhibitors were older (74 vs 72 years; $P<.001$), had lower eGFR (39 vs 41 mL/min/1.73 m^2; $P<.001$), and had higher serum potassium at baseline (5.90 vs 5.80 mmol/L; $P<.001$). Differences were similar in the Ontario cohort: those who discontinued RAAS inhibitors were older (80 vs 79 years), had lower eGFR (38 vs 41 mL/min/1.73 m^2), and had higher serum potassium at baseline (5.85 vs 5.73 mmol/L).

In unadjusted analyses, compared with continuation of RAAS inhibitor, discontinuation was associated with a higher risk of all-cause mortality in both the Manitoba (hazard ratio [HR], 1.48; 95% CI, 1.38-1.58) and Ontario (HR, 1.78; 95% CI, 1.75-1.85) cohorts. The association remained in adjusted Cox proportional hazards regression models (Manitoba: adjusted HR [aHR], 1.32; 95% CI, 1.22-1.41; Ontario: aHR, 1.47; 95% CI, 1.41-1.52).

In both study cohorts, there was also an association between discontinuation of RAAS inhibitors and a 30% higher risk of cardiovascular mortality compared with continuation of RAAS inhibition (Manitoba: aHR, 1.28; 95% CI, 1.13-1.44; Ontario: aHR, 1.32; 95% CI, 1.25-1.39). Participants who discontinued use of RAAS inhibitors also had a higher risk of fatal and nonfatal cardiovascular events compared with those who continued RAAS inhibitor therapy (Manitoba: aHR, 1.17; 95% CI, 1.11-1.24; Ontario: aHR, 1.18; 95% CI, 1.15-1.22)

In both cohorts, the risk of dialysis initiation was greater among participants who discontinued RAAS inhibitor therapy compared with those who continued use of RAAS inhibitors (Manitoba: aHR, 1.65; 95% CI, 1.41-1.85; Ontario: aHR, 1.11; 95% CI, 1.08-1.16).

In analyses that utilized a time-dependent approach, results were similar. There were associations between RAAS inhibitor discontinuation and higher risk of all-cause and cardiovascular mortality, fatal and nonfatal cardiovascular events, and initiation of dialysis. In analyses in a subset of participants with serum potassium level of ≥5.8 mmol/L, there were associations between hyperkalemia and all-cause mortality (aHR, 1.33; 95% CI, 1.20-1.48) and cardiovascular mortality (aHR, 1.30; 95% CI, 1.09-1.56).

In Cox regression models, with further adjustment for acute kidney injury and sepsis at baseline, the results were similar (all-cause mortality: aHR, 1.23; 95% CI, 1.20-1.39; cardiovascular mortality: aHR, 1.26; 95% CI, 1.12-1.42).

At the time of the hyperkalemia episode, ~35% of the Manitoba cohort and ~40% of the Ontario cohort were on the maximal RAAS dose. Of the participants on the maximal dose, 12.33% in the Manitoba cohort and 14.46 % in the Ontario cohort were down-titrated to a submaximal dose. Further, 32% of the Manitoba cohort and 11% of the Ontario cohort at a maximal dose at baseline discontinued use of an RAAS inhibitor.

Compared with a maximal dose of RAAS inhibitors, there were associations between submaximal dose use and increased all-cause mortality (Manitoba: HR, 1.24; 95% CI, 1.12-1.37; Ontario: HR, 1.11; 95% CI, 1.08-1.14).

The researchers cited some limitations to the study findings, including the observational design with retrospective cohorts, leading to the possibility of unmeasured confounders. In addition, because medications associated with hyperkalemia are commonly provided over the counter, it was not possible to fully capture their concomitant use. Finally, there were no data available on blood pressure measurements.

In conclusion, the authors said, "Our results demonstrate that continuation of RAAS inhibitors after an episode of hyperkalemia is associated with improved all-cause and cardiovascular event free survival in patients with CKD. Moreover, the maximal recommended dose was associated with a larger survival benefit than submaximal doses. Newer medications for the treatment of hyperkalemia may enable patients to continue their RAAS inhibitors after an episode of hyperkalemia." ■

TAKEAWAY POINTS

- The most common management strategy for management of hyperkalemia in patients with chronic kidney disease (CKD) is discontinuation or dose reduction of renin-angiotensin-aldosterone system (RAAS) inhibitors.
- Researchers reported results of a study designed to examine the association between discontinuation of RAAS inhibitors following an episode of hyperkalemia with clinical outcomes in patients with CKD.
- There were associations between discontinuation and dose reduction of RAAS inhibitors and increased risk of all-cause mortality, cardiovascular mortality, and cardiovascular events compared with continuation.

Sickle Cell Trait Associated With Adverse Outcomes Following COVID-19

Some demographic and preexisting medical conditions are associated with adverse outcomes in COVID-19, including chronic kidney disease (CKD), chronic obstructive pulmonary disease, and sickle cell disease (SCD). SCD has two copies of hemoglobin beta sickle alleles (rs334-T). Sickle cell trait (SCT) has one rs334-T and one wild-type allele; SCT affects more than 3 million people in the United States and 300 million people worldwide. Largely considered a benign condition, there are associations between SCT and increased risk for adverse outcomes, including chronic kidney disease.

During the COVID-19 pandemic, the Centers for Disease Control and Prevention advised that patients with SCD were highly susceptible to the infection. However, the advice did not extend to individuals with SCT. According to **Anurag Verma, PhD,** and colleagues, there are few data available on the association between SCT and outcomes in COVID-19.

The researchers conducted an analysis of data from the Million Veteran Program (MVP) to examine the association of SCT with preexisting conditions, severity of COVID-19 outcomes, and conditions post-COVID-19. Results were reported in *JAMA Internal Medicine* [doi.10.1001/jamainternmed.2022.22141].

A total of 132,577 participants in the MVP had COVID-19 data; mean age at the index date was 64.8 years. Of study participants of African ancestry, 7.8% had the sickle allele (rs334-T), as did 1% of participants of Hispanic ancestry. The researchers conducted ancestry-specific analysis. The primary findings were focused on participants of African ancestry.

The researchers performed a phenome-wide association study (PheWAS) analysis to test for associations between rs334-T and preexisting conditions preceding the COVID-19 pandemic among 658,358 MVP participants. The test identified 31 phecodes with significant association in participants of African ancestry. The most significant association was sickle cell anemia/trait-related condition (phecode: 282.5; odds ratio [OR], 93.17; 95% CI, 78.60-110.44; P=1 ×.10^{-300}).

There were also associations with conditions related to COVID-19 severity and mortality, including CKD (OR, 1.45; 95% CI, 1.36-1.55; P=1.8 × 10^{-28}), type 2 diabetes with kidney complications (OR, 1.33; 95% CI, 1.23-1.43; P=3.7 × 10^{-13}), pulmonary embolism (OR, 1.43; 95% CI, 1.27-1.60; P=1.73 × 10^{-9}), pulmonary heart disease (OR, 1.30; 95% CI, 1.19-1.42; P=5.3 × 10^{-9}), and hypertensive kidney disease (OR, 1.19; 95% CI, 1.12-1.26; P=2.77 × 10^{-9}).

In analyses of the association of the 31 preexisting conditions identified from comorbidity association studies with COVID-19 outcomes among MVP participants of African ancestry, 13 of the conditions were associated with COVID-19-related death. The most significant associations were with kidney disorders such as chronic kidney failure (OR, 1.95; 95% CI, 1.44-2.62; P=9.3 × 10^{-7}), CKD (OR, 1.94; 95% CI, 1.44-2.62; P=1.2 × 10^{-5}), and kidney dialysis (OR, 2.07; 95% CI, 1.24-3.45; P=.005).

The researchers examined the association between SCT and four COVID-19 outcomes: (1) susceptibility; (2) hospitalization; (3) severe conditions where patients required ventilator support or admission to the intensive care unit; and (4) COVID-related death. In individuals with African ancestry, there was a statistically significant association between SCT and increased risk of death from COVID-19 (OR, 1.77; 95% CI, 1.13-2.77; P=.01). Meta-analysis of the estimates across two ancestral groups provided more statistical power and a stronger association between SCT and COVID-19-related deaths (OR, 1.77; 95% CI, 1.13-2.77; P=.005).

In contrast, there were no associations between rs33930165-T, an HbC allele with a prevalence of 1.7% among individuals with African ancestry, and any COVID-19 outcomes. Results of association analyses demonstrated that the HbC allele was not associated with the clinical/kidney conditions associated with SCT.

The researchers also investigated the incidence of acute kidney failure and declining kidney function within 60 days of diagnosis of COVID-19 and their interaction with SCT. A total of 31,287 individuals of African ancestry who were tested for COVID-19; 66.8% had stable and normal kidney function, 31% had declining kidney function, and 27.4% had kidney impairments, including acute kidney failure, prior end-stage kidney failure, CKD, chronic kidney failure, or nephrosis within 2 years before the COVIID-19 diagnosis.

Compared with those without SCT, there was a statistically significant increase in postindex acute kidney failure in individuals with SCT (OR, 1.40; 95% CI, 1.09-1.90; P=.02). The interaction model suggested a significant interaction effect of COVID-19 with SCT on acute kidney failure (P=.02). In separate models, following adjustment for preexisting kidney impairment based on *International Classification of Diseases* codes in stepwise regression analysis or declining kidney function based on primarily laboratory values, the ORs for acute kidney failure remained largely unchanged with a nominally significant P value in all the models.

SCT was significantly associated with death in patients with COVID-19, and those with SCT had a higher risk of acute kidney failure due to COVID-19. Mediation analysis was used to determine how much of the effect of SCT on COVID-19-related death was mediated through acute kidney failure due to COVID-19. On average, 22% (95% bootstrap CI, –3% to 83%) of the total effect of SCT on death related to COVID-19 was mediated through acute kidney failure within 60 days of COVID-19.

The researchers cited some limitations to the study findings, including the MVP participants being predominately male and the possibility of residual confounding.

In conclusion, the authors said, "In this genetic association study, SCT was associated with increased COVID-19 mortality and a number of preexisting chronic medical conditions in African ancestry individuals. Our findings support the inclusion of SCT as an adverse prognostic factor for COVID-19 and development of SCT-tailored interventions. Our work has broad implications for the detection and clinical management of SCT." ■

TAKEAWAY POINTS

- Researchers conducted a genetic association study to examine the association of sickle cell trait (SCT) with outcomes in patients with COVID-19.
- The study cohort included 2729 individuals with SCT and 129,848 who were SCT negative; those with SCT had various preexisting conditions that were associated with adverse outcomes post- COVID-19.
- The results support including SCT as an adverse prognostic factor for COVID-19.

Waitlist Eligibility and Racial Disparities in Access to Kidney Transplantation

The optimal treatment for those with kidney disease at risk of kidney failure is kidney transplantation. Transplantation policy in the United States requires a glomerular filtration rate (GFR) ≤20 mL/min/1.73 m^2 for activation on the kidney transplant list for all patients. However, according to **Chi D. Chu, MD, MAS,** and colleagues, this policy is at odds with a higher rate of chronic kidney disease (CKD) progression among persons of color.

Due to the use of commonly used serum creatinine-based equations for estimated GFR (eGFR) that incorporate a race term that assigns higher eGFR to Black patients, there are concerns that the use of those equations may be associated with delayed waitlisting, thus contributing to racial disparities in access to kidney transplantation.

Both the Modification of Diet in Renal Disease Study and the CKD Epidemiology Collaboration (CKD-EPI) creatinine equation incorporate race terms that result in 21% or 16% higher eGFR, respectively, for Black patients compared with non-Black patients. Apart from ethical considerations of using race, which is not a biological construct, in a model that drives clinical decisions, there are also concerns that higher eGFR may delay access to various aspects of kidney care, including transplantation.

Dr. Chu et al conducted a retrospective cohort study to compare time from meeting transplant eligibility threshold of eGFR ≤20 mL/min/1.73 m^2 to kidney failure with replacement therapy (KFRT) among Black, Hispanic, and White patients and to examine the impact of incorporating race into eGFR expressions on establishment of eligibility for waitlisting and time from eligibility to KFRT. Results were reported in the *American Journal of Kidney Diseases* [2022;79(6):841-848].

The researchers utilized the OptumLabs Data Warehouse to assemble a cohort of patients 18 to 75 years of age with an outpatient eGFR decrease to ≤20 mL/min/1.73 m^2 from January 1, 2008, to December 31, 2018 (ie, patients having an outpatient eGFR value of ≤20 mL/min/1.73 m^2 during the study with at least one earlier value between 20 and 60 mL/min.1.73 m^2 within the preceding 2 years).

The total cohort included 52,130 patients; of those, 40,042 were non-Hispanic White, 8519 were non-Hispanic Black, and 3569 were Hispanic. When the cohort derivation was repeated assigning Black patients the eGFR CKD-EPI non-Black ($eGFR_{non\text{-}Black}$) value, it resulted in a cohort of 11,269 Black patients with an outpatient $eGFR_{non\text{-}Black}$ decline to <20 mL/min/1.73 m^2 during the study period.

At the time of incident eGFR <20 mL/min/1.73 m^2, non-Hispanic White patients were older (mean age 64 years) compared with non-Hispanic Black or Hispanic patients who were on average 3 to 6 years younger. Non-Hispanic White patients on average had lower blood pressure compared with non-Hispanic Black and Hispanic patients (mean blood pressure 127/70 vs 135/76 and 135/73 mm Hg, respectively). Median urinary albumin-creatinine ratio was higher among non-Hispanic Black patients (672 mg/g) and Hispanic patients (247 mg/g) than among non-Hispanic White patients (133 mg/g).

During median follow-up of 24 months, there were a total of 18,002 KFRT events; of those, 9401 were among non-Hispanic White patients, 3411 were among non-Hispanic Black patients using $eGFR_{Black}$, 3718 among non-Hispanic Black patients using $eGFR_{non\text{-}Black}$, and 1472 among Hispanic patients. The number of deaths was 13,532 among non-Hispanic White patients, 1849 among non-Hispanic Black patients using $eGFR_{Black}$, 2577 among non-Hispanic Black patients using $eGFR_{non\text{-}Black}$, and 490 among Hispanic patients.

Regardless of how eGFR was calculated among Black patients, they were substantially more likely to progress to KFRT than non-Hispanic White patients; Hispanic patients were also more likely to progress to KFRT than non-Hispanic White patients.

By 3 years of follow-up, the risk of KFRT among non-Hispanic Black patients using $eGFR_{Black}$ and the Hispanic cohorts was 36.0% (95% CI, 34.9%-37.0%) and 40.9% (95% CI, 39.0%-42.7%), respectively, compared with non-Hispanic White patients, who had a KFRT risk of 20.5% (95% CI, 20.0%-20.9%). When the $eGFR_{non\text{-}Black}$ value was used, the disparity was modestly attenuated (KFRT risk over 3 years, 28.7%; 95% CI, 27.8%-29.6%).

In unadjusted analyses, non-Hispanic Black patients using $eGFR_{non\text{-}Black}$ and Hispanic patients had a 1.51-fold (95% CI, 1.46-1.56) and 2.25-fold (95% CI, 2.13-2.38), respectively, increased hazard of KFRT. Following multivariable adjustment, the increased risk of KFRT was attenuated but remained statistically significant among non-Hispanic Black (hazard ratio [HR], 1.28; 95% CI, 1.15-1.43) and Hispanic (HR, 1.66; 95% CI, 1.18-2.13) patients.

In secondary analysis examining decline in eGFR, median eGFR slope for White patients was –4.2 mL/min/1.73 m^2 per year, which was slower relative to CKD progression in non-Hispanic Black (–6.4 mL/min/1.73 m^2 per year) and Hispanic patients (–7.6 mL/min/1.73 m^2 per year. The differences between the racial/ethnic groups were statistically significant (P<.001).

For Black patients, the potential time delay between an $eGFR_{non\text{-}Black}$ versus an eGFRBlack of 20 mL/min/1.73 m^2 based on the eGFR slopes was a median of 0.5 years.

Study limitations cited by the authors included the inability to exclude individuals who would not be candidates for kidney transplantation if they were comprehensively evaluated, and the possibility that data in the electronic health records were incomplete for patients whose care was not within a single health system.

In conclusion, the researchers said, "A uniform eGFR threshold provides less opportunity for being placed on the transplant waitlist among Black and Hispanic patients. For many Black patients, estimation of GFR as if their race category were non-Black would allow substantially earlier waitlisting but would not eliminate their shorter time to KFRT and reduced opportunity for preemptive transplantation compared with White patients." ■

TAKEAWAY POINTS

- United States policy for activation on the waitlist for a kidney transplant requires a GFR of ≤20 mL/min/1.73 m^2; however, current GFR estimating equations assign a higher value to Black patients compared with non-Black patients.
- Researchers conducted a study to examine progression of chronic kidney disease in patients who developed an estimated GFR based on incorporation of race.
- The study found that classifying all patients as non-Black for purposes of estimation of GFR would allow Black patients to be eligible for earlier waitlisting, but would not eliminate shorter time to KFRT.

Inclusion in Medicare Part D Star Ratings Adherence Measures

Among recipients of kidney transplantation, adherence to prescribed medication is key in graft survival as well as in treating comorbidities common in transplant recipients, including diabetes, hypertension, and dyslipidemia. Given the association between medication adherence and positive outcomes in transplant recipients, there are policies in place designed to encourage adherence.

Measures of adherence to oral medications for the treatment of diabetes, hypertension, and dyslipidemia are included in the Centers for Medicare & Medicaid Services (CMS) Five-Star Quality Ratings System (Star Ratings). The measures were developed by the Pharmacy Quality Alliance (PQA) in partnership with CMS.

Star Ratings programs for Medicare Parts C and D (Medicare Advantage plans and Medicare prescription drug coverage, respectively) were created by CMS. Star Ratings range from one to five, with higher ratings indicating higher quality or better performance on Star Ratings measures.

There are two types of Part D plans: independent prescription drug plans (PDPs) and Medicare Advantage prescription drug plans (MAPDs). MAPDs receive bonus payments based on their Star Ratings; the plans are required to use the bonus payments to lower premiums and/or offer extra benefits to enrollees.

Not all patients enrolled in a MAPD are included in the assessment of each Star Rating measure for that MAPD. There are criteria developed by the PQA that define who qualifies for inclusion in the assessment of each rating on adherence. However, according to **Marie A. Chisholm-Burns, PharmD,** and colleagues, the criteria may have the unintended consequence of adding to racial and ethnic disparities in care by causing MPADs to concentrate on patients who meet the inclusion criteria and disincentivizing those who do not.

The researchers conducted a cross-sectional analysis designed to assess whether criteria for inclusion in the assessment of Star Ratings medication adherence measures among kidney transplant recipients with diabetes, hypertension, and/or dyslipidemia are associated with racial and ethnic disparities in which patients are included in the Star Ratings assessment. Results of the study were reported in the *Journal of Managed Care Pharmacy* [2022;28(6):688-699].

The researchers utilized the 2017 Medicare Part D database linked to the Master Beneficiary Summary File, Parts A/B claims , and Area Health Resources Files. The Part D database includes data on dispensed prescriptions and drug costs for prescriptions paid for by the Part D program. The Medicare Beneficiary Summary Files includes demographic and enrollment data for Medicare recipients, and the Parts A and B claims provide diagnosis records for beneficiaries from inpatient and outpatient providers.

The outcomes of interest were the likelihood of being included in the assessment of Star Ratings Part D medication adherence measures for oral diabetes medications, hypertension medications (defined by the PQA as angiotensin 2 receptor blockers, angiotensin-converting enzyme inhibitors, and direct renin inhibitors), and statin medications to treat dyslipidemia.

The sample included 94,822 kidney transplant recipients with continuous coverage of Medicare Parts A/B/D who filled at least one prescription for diabetes, hypertension, or dyslipidemia in 2017. The majority of the eligible patients were White (51.4%), and 24.4% were Black. The White patient group was significantly older than all racial/ethnic groups ($P<.0001$). A larger proportion of Hispanic and other patients were male compared with White patients ($P<.0001$); a smaller proportion of Black patients were male compared with White patients ($P<.05$)

White patients were more likely to live in counties with higher proportions of married couples ($P<.001$) and individuals ≤25 years of age with at least a high school education ($P<.05$) compared with all racial and ethnic minority groups; more likely to live in countries with lower rates of uninsured individuals compared with Black, Hispanic, and other patients ($P<.001$); and more likely to live in counties with lower per capita income compared with Asian patients ($P<.0001$).

White patients had a significantly lower risk of adjustment summary score (higher risk adjustments indicate worse health status and greater expected health care costs) compared with Black patients ($P<.0001$).

Across all study cohorts, racial and ethnic minority patients had higher percentages of diagnosis of end-stage renal disease (ESRD) in the measurement year. In the hypertension-only cohort, the percentage of White patients with an ESRD diagnosis was 41.3%, compared with 66.9% of Black patients, 60.4% of Hispanic patients, 55.5% of Asian patients, and 62% of patients in other racial/ethnic groups ($P<.05$).

In chi-square analyses of patients with hypertension only and those with dyslipidemia only, all racial and ethnic minority groups were less likely to be included in assessments compared with White patients ($P<.0001$).

Among patients with any two conditions (diabetes, hypertension, and/or dyslipidemia), compared with White patients, all racial and ethnic minority groups were less likely to be included in assessment of one or two Star Ratings measures ($P<.0001$). Among kidney transplant recipients with three conditions, all racial and ethnic patients were less likely than White patients to be included in assessment of one, two, or three Star Ratings measures ($P<.05$).

In adjusted analysis, Black and Hispanic kidney transplant recipients in the diabetes-only cohort were less likely than White patients to be included in the assessment of the Star Ratings adherence measure for oral diabetes medications ($P<.0001$); there were no significant differences between White patients and Asian patietns and patients of other race/ethnicity. In the hypertension-only and dyslipidemia-only cohorts, all racial and ethnic minority groups were less likely than White patients to be included in assessments of the Star Ratings adherence measures for oral hypertension and dyslipidemia medications ($P<.002$).

The researchers cited some limitations to the study findings, including not directly examining who was and was not included in assessments of Star Ratings adherence measures across MAPDs, and the inability to definitively establish causality between criteria for inclusion in Star Ratings measure assessments and racial and ethnic disparities.

In conclusion, the authors said, "Racial and ethnic disparities exist among kidney transplant patients with diabetes, hypertension, and dyslipidemia regarding likelihood of inclusion in assessment of Star Ratings medication adherence measures. Future studies are needed to determine if not being included in assessment of Star Ratings measures contributes to disparities in assess to MAPD-provided services to support medication adherence and, ultimately, health outcomes among racial and ethnic minority patients who have received a kidney transplant." ■

TAKEAWAY POINTS

- Patients who have received a kidney transplant who are not included in assessment of Medicare Part D Star Ratings measures for medication adherence may face worse outcomes than those who are included.
- Researchers conducted a cross-sectional secondary analysis to examine whether criteria for inclusion in assessment of Medicare Part D Star Ratings medication adherence is associated with racial and ethnic disparities among kidney transplant recipients with diabetes, hypertension, and/or dyslipidemia.
- The findings suggest that kidney transplant recipients in racial and ethnic minority groups are less likely to be included in assessments of Star Ratings medication adherence measures.

Results of Studies of Fabry Disease Treatment Presented

In early September, Chiesi Global Rare Diseases sponsored multiple presentations at the Society for the Study of Inborn Errors of Metabolism Annual Symposium in Freiburg, Germany. The company presented five abstracts with data from a clinical development program evaluating pegunigalsidase alfa (PRX-102), an investigational enzyme replacement therapy (ERT) for the treatment of Fabry disease.

Currently, there are 350 million individuals who live with a rare disease. There are more than 7000 known rare diseases, with only 5% having an approved treatment or experimental therapy in development.

At the symposium Chiesi presented results for the phase 3 clinical development program sponsored by Protalix Ltd evaluating PRX-102. The presentation included data from the BRIGHT and BALANCE studies. Results from the BRIGHT study suggested that treatment with 2 mg/kg of PRX-102 administered via intravenous infusion every 2 weeks for 52 weeks was well tolerated and that Fabry disease remained stable throughout the study period. The BALANCE study is an active-control, randomized, double-blind, 24-month study in adults with Fabry disease with renal function impairment evaluating the safety and efficacy of 1 mg/kg of PRX-102 administered every 2 weeks versus agalsidase beta at the same dosing schedule. The study cohort included 78 patients who had been previously treated with agalsidase beta for a minimum of 1 year. Results met the predefined criteria of noninferiority for the primary end point of renal function.

Three-Way Merger Creates InterWell Health

In a recent press release, InterWell Health announced the completion of a three-way merger among Fresenius Health Partners, InterWell Health, and Cricket Health. The resulting independent company will operate under the InterWell Health brand and will partner with a patient's nephrologist to improve kidney disease care delivery. The new company aims to improve health outcomes for those with kidney disease and to reduce costs to public and private payers, health systems, and others involved in the care for that patient population. The merger has received regulatory clearance in the United States.

InterWell Health CEO, Robert Sepucha, said, "In a value-based world, it is no longer enough to just provide quality care—providers must help patients change behavior, and this requires a fundamental shift in how we engage patients. The new InterWell Health is bringing together cutting-edge data analytics capabilities that identify high-risk patients with the industry's leading patient engagement platform to deliver a rich in-person and virtual experience where they immerse themselves in information about their disease. At the same time, we offer real-time access to multidisciplinary care teams, patient peer mentors, as well as the largest network of nephrologists in the country to help patients live their best lives. Working closely with our physician partners, we will reduce hospital admissions and readmissions, increase transplant referrals and rates, accelerate the transition to home dialysis, and improve health equity."

The completed merger, first announced in March 2022, will position InterWell Health to engage and manage the care of more than 270,000 individuals in the United States living with kidney disease. The new company expects to have $11 billion in costs under management by 2025, and increase from 100,000 covered lives and $6 billion currently under management.

AOPO Announces 2022 Award Recipients

The Association of Organ Procurement Organizations (AOPO) held their annual meeting in Phoenix, Arizona. At the meeting, they announced the award winners who were recognized for their work to advance the AOPO's vision of a day when every donation opportunity results in lives saved.

The AOPO Lifetime Achievement Award is presented to individuals employed by or affiliated with an OPO who have contributed to the goals and ideals in the field of organ donation for at least 20 years. This year's honorees were **Anne Kowalczyk,** chief financial officer at Gift of Life Michigan; **Tracy Schmidt,** president/CEO of Donor Connect; and **Anthony D'Alessandro,** MD, medical director at UW Organ & Tissue Donation.

The AOPO/National Disease Research Interchange Empowering Research & Discovery Award that recognizes an OPO working to advance research, was presented to the Washington Regional Transplant Community.

AKF Responds to Senate Hearing on Transplant System

In a recent press release, **LaVarne A. Burton,** president and CEO of the American Kidney Fund (AKF) issued a statement in reaction to the US Senate Finance Committee's hearing on the US transplant system:

"A bipartisan investigation into the United Network of Organ Sharing and its oversight of the US Open Procurement and Transplantation Network has brought to light several deeply troubling findings, including issues related to patient safety, transport and care of organs from deceases patients, accountability of organ procurement organizations, and the organ transplant system's technological capabilities and security.

"The Senate Finance Committee's August 3 hearing on this matter comes less than 6 months after the National Academy of Sciences released a comprehensive report that included the US organ transplant system is 'demonstrably inequitable.'

"That study, sponsored by the National Institutes of Health, made a number of near- and long-term recommendations to create a fairer and more transparent and efficient system for deceased donor organs.

"According to this week's report from the Finance Committee, a series of disturbing failures in recent years have put patient safety at risk and left viable organs unrecovered. The 106,000 people in the United States fighting for their lives deserve better.

"The American Kidney Fund strongly supports the National Academy's recommendations to achieve equity in organ transplantation. We also call for immediate actions to implement Congressional recommendations that would improve safety and oversight within the organ procurement system as well as enhance technological capabilities."

Single-Use Bloodline Supports Fluid Management

In a press release, the Renal Therapies Group of Fresenius Medical Care North America announced the availability of the CombiSet SMARTECH™, a single-use bloodline with an integrated Crit-Line® blood chamber (CLIC®) that reduces the number of manual connections required. The chamber is built into the bloodline itself and is designed to provide optimal performance with the 2008 series hemodialysis machines.

Crit-Line technology provides continuous monitoring of the percent change in blood volume, plasma refill, and oxygen saturation as well as other key parameters during hemodialysis treatment. The data allow clinicians the option to intervene by adjusting the ultrafiltration rates during the dialysis session.

Mike Anger, MD, senior vice president and chief medical officer of the Renal Therapies Group, said, "By combining these two components into one bloodline, we are simplifying the set-up process which will hopefully encourage increased use of Crit-Line technology. This new bloodline is designed to make fluid management even easier, providing insights that can help better manage the fluid status of dialysis patients."

Pat McCarthy, senior vice president, Renal Therapies Group, said "This interdiction of this new bloodline is part of our commitment to bring innovations to market that improve patient care, making the dialysis process simpler and safer for our patients. This new integrated system is a step forward within our already trusted and reliable bloodline product offerings."

Diality Names New CFO

In an early fall press release, Diality, Inc, announced the appointment of **Pamela Wapnick** as chief financial officer. Diality is a medical technology company that is working on the development of a smart, mobile hemodialysis platform, with a commercial launch of the technology scheduled for 2023.

Ms. Wapnick has more than 30 years of financial experience, primarily in the biotech and pharmaceutical industries. Most recently, she served as CFO at Capsida Biotherapeutics where she built various functions of the company from startup to more than 100 employees. She holds a BA in economics from Wellesley College and an MBA from Columbia University.

The smart hemodialysis platform under development is a small, easy-to-use device, with a compact footprint and mobility intended to enable it to be integrated into any dialysis setting, including acute-care hospitals, dialysis clinics, transitional care units, and traditional home or skilled nursing facilities.

Osman Khawar, MD, chief executive office at Diality, said, "Pam is a proven leader with decades of financial and fundraising expertise, both in the private sector

and in the capital markets. Her extensive experience in the life sciences industry will be invaluable as we look to change the standard of care for dialysis patients."

Ms. Wapnick said, "I was immediately intrigued by Diality's elegant and innovative approach to mobile hemodialysis and plans to come to market in 2023. I share our team's dedication to the company's mission of developing solutions that improve lives impacted by kidney disease."

Funding for Know Your Kidneys Campaign

The American Kidney Fund's (AKF) education program, Know Your Kidneys™, has received renewed sponsorship from Otsuka American Pharmaceutical, Inc. and Boehringer Ingelheim and Eli Lilly and Company, according to a recent press release. The goal of the ongoing, nationwide program is to help individuals prevent or slow the progression of chronic kidney disease (CKD).

There are 37 million people with kidney disease in the United States; however, nine of 10 people are unaware they have kidney disease. The AKF campaign aims at helping Americans understand the vital role kidneys play in overall health and to take action to ensure early diagnosis and management of CKD, along with hypertension and diabetes, the primary causes of kidney disease.

LaVarne A. Burton, president and CEO, AKF, said, "We are grateful to Otsuka and Boehringer Ingelheim and Lilly for helping AKF continue and expand our Know Your Kidneys campaign. As the rates of kidney disease continue to rise in the US, we hope to increase access to educational tools that will help people receive an earlier diagnosis of kidney disease, and hopefully prevent it altogether."

The campaign includes educational content and downloadable discussion guides to encourage patients to initiate conversations with their health care teams before and after a diagnosis of kidney disease. With the additional support from Otsuka and Boehringer Ingelheim and Lilly, AKF will expand the program to include new material such as animated explainer videos and information highlighting stage 3 CKD prior to progression to kidney failure.

Renal Care 360° Expands Operations

Renal Care 360° has announced expansion to three new markets through transactions with Nephrology of the Golden Isles, South Carolina Nephrology and Hypertension Centers, and the Kidney Clinic. The new operation swill expand the clinical capabilities of Renal Care 360° in markets in Georgia and South Carolina.

In a recent press release, Renal Care 360° founder and CEO, **Joseph Cashia,** said, "We are thrilled to be partnering with experienced nephrologists who share our mission for bringing quality care to underserved communities. Becoming part of Renal Care 360° provides these practices with additional resources to continue to deliver critical patient care to some of the region's most vulnerable CKD and ESKD patients. Our experience across value-based care, physician practice management, and population health will enable our physician partners

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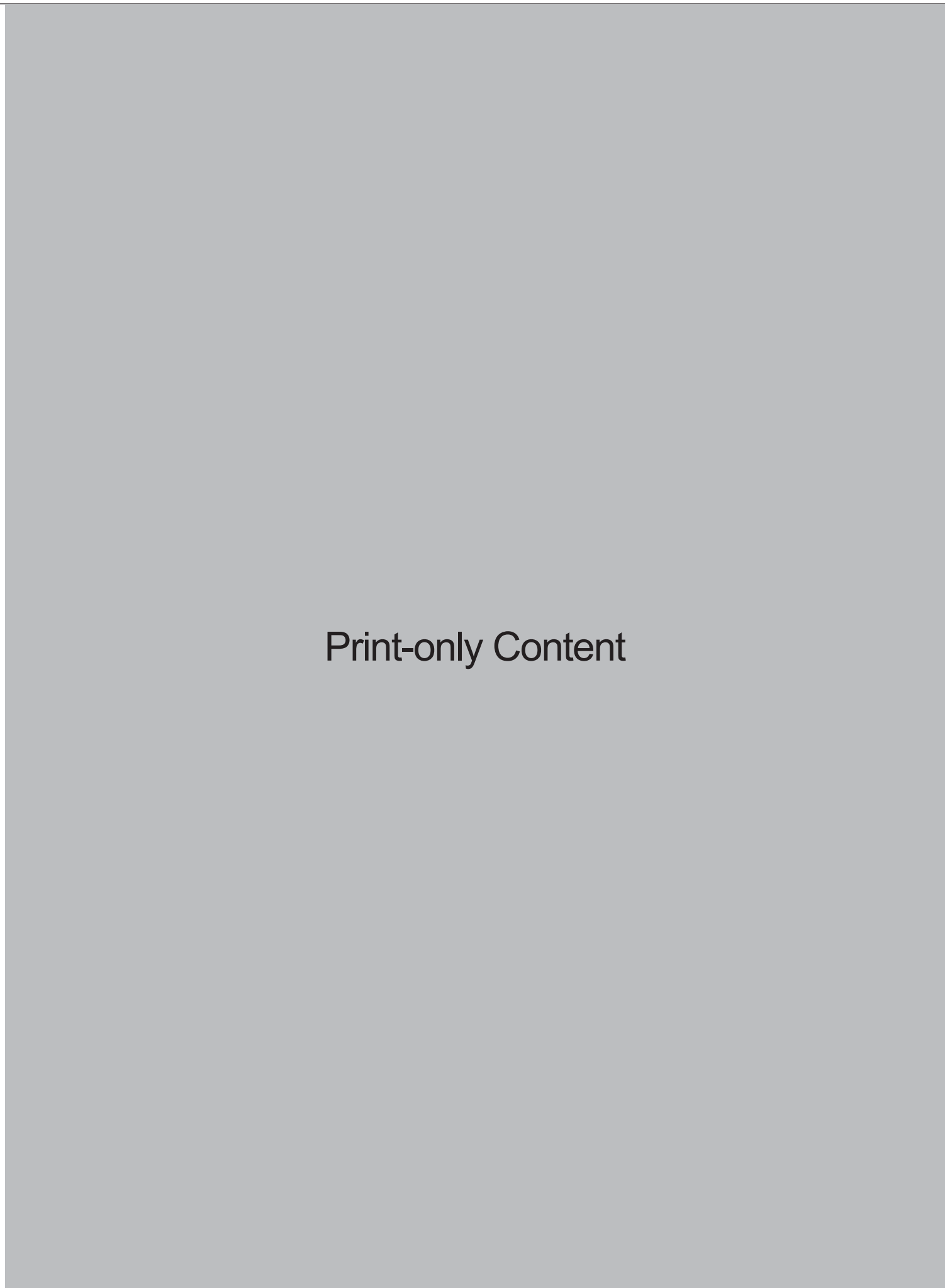
to provide individualized, preventative care to improve patient outcomes and increase access to care, and in doing so in alignment with health systems and payers, will generate transformation cost savings to the system."

Renal Care 360° utilizes a model focused on early detection of unidentified chronic conditions using proprietary data analytics and, once identified, offers early interventions with personalized education, real-time engagement, local and virtual clinic options, and dedicated care coordination to slow disease progression and improve outcomes for chronic kidney disease and end-stage kidney disease.

American Kidney Fund Announces UCKD Coalition

The American Kidney Fund (AKF) has announced the formation of the Unknown Causes of Kidney Disease (UCKD) Coalition that includes 14 organizations and individuals working to support policies and actions designed to identify kidney disease of unknown origin. The coalition grew out of AKF's UCKD Project that sought to improve understanding of how undiagnosed or misdiagnosed causes of kidney disease have direct impacts on patient care and outcomes.

In a recent press release, **LaVarne A. Burton,** president and CEO of AKF, said, "The UCKD Coalition is united in its commitment to advance policies



and legislation that will help people with kidney disease, in particular rare kidney diseases, get the answers and support that they need. Everyone with kidney disease should receive an early diagnosis in order to give them the opportunity to treat the disease and delay or prevent kidney care."

The UCKD Project has been working across three areas that are critical to improving diagnosis and treatment of kidney disease: (1) finding public policy solutions, such as improving access to genetic counseling and testing for people with kidney disease; (2) expanding provider education; and (3) educating patients about kidney disease testing. The coalition will strengthen efforts to educate and inform policy makers about rare kidney disease and recommend strategies to address and understand causes.

Sponsors of the UCKD Project are Sanofi, Otsuka American Pharmaceutical, Inc, Travere Therapeutics, Vertex Pharmaceuticals, Alexion, AstraZeneca Rare Disease, and Natera.

AHA Report Endorses Home Dialysis Therapies

The American Heart Association (AHA) has issued a report titled "Cardiovascular Effects of Home Dialysis Therapies," endorsing home dialysis therapies, including the more frequent hemodialysis (MFD) model of care. In a press release, Dialyze Direct noted that the AHA report encapsulated many of Dialyze's research findings that the MFD model offers more effective

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News Briefs

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and gentle treatments for residents of skilled nursing facilities. The AHA report was authored by 12 cardiologists and nephrologists and concluded that more physiologic dialysis, such as the MFD model, is associated with improved outcomes for patients with end-stage renal disease compared with traditional three times per week in-center dialysis treatment.

Alice Hellebrand, chief nursing officer and senior vice president of education at Dialyze Direct, said, "The ability to provide patient-centric care utilizing an MFD model provided dialysis patients the opportunity to live life to their optimal level. The need for innovative care is fundamental to the MFD treatment regimen, and our ability to provide MFD to this frail and largely unrecognized patient group brings professional satisfaction to the clinical staff and optimum outcomes for the patients we serve."

Allen Kaufman, MD, chief medical officer at Dialyze Direct, said, "MFD is at the core of Dialyze Direct's patient-centric approach to dialysis treatment when a patient exhibits comorbidities that deem it medically necessary. By applying one of the most advanced forms of more physiologic dialysis, MFD provides a more effective and gentler treatment for the very complex patient population residing in nursing homes. Patients receiving MFD in the nursing home setting experience longer life, fewer hospitalizations, gentler dialytic treatments and substantially faster postdialysis recovery times."

NKF Launches Educational Video Series

An educational initiative titled Kidney Numbers and the CKD Heat Map has been launched by the National Kidney Foundation (NKF). Kidney Numbers and the CKD Heat Map is an animated video series aiming to present complex health information to patients with varying levels of health literacy. The initative is supported by Bayer.

In a recent press release, **Joseph Vassalotti, MD,** chief medical officer for NKF, said, "Understanding the role of kidney numbers and how to read and interpret that data can be complex and difficult to convey to both patients and the general public. Our experts have developed three short and engaging animated videos and a series of CKD heat maps to help explain these complex topics in the simplest terms possible."

There are an estimated 37 million adults in the United States with chronic kidney disease (CKD), but ~90% do not know they have it. The videos, available on YouTube in English and Spanish and at www.kdiney.org, seek to explain how kidney measurements such as glomerular filtration rate and urine albumin-to-creatinine ratio are used to assess overall kidney health in addition to their associated risks for CKD and cardiovascular disease. Nearly one in three adults in the United States are at risk for CKD.

"Kidney disease is a public health issue," Dr. Vassalotti added. "We have developed similar public education programs, and they have been very well received. These animated educational videos will help us communicate complex medical terminology in lay terms to help improve patient understanding of risk ad well as promote awareness of CKD and the current treatment options available."

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Delaware SB 301 Provides Incentives for Living Donors

In October, **John Carney,** governor of Delaware, signed SB 301 into law. The law is designed to reduce barriers to organ donation through tax credit incentives for living organ and bone marrow donors and their employers.

In a press release, **LaVarne A. Burton,** president and CEO of the American Kidney Fund (AKF), said, "This new law significantly helps in efforts to encourage Delawareans to become living donors, removing potential hurdles that might otherwise keep them from saving someone's life. Deciding to donate an organ is one of the most altruistic choices a person can give, and they should not be financially deterred from making it."

AKF has been leading an effort to protect living donors through legislation at the state level. With the enactment of SB 301, Delaware joins the 28 other states that have provided protections and incentives for living organ donors. The Fund's State of the States: Living Donor Protection Report Card measures seven types of legislation to provide protections to living donors and encourage living organ donation. SB 301 is Delaware's third protection for living donors signed into law in that state, raising the state's grade from a C to a B. The average grade for a state is a C. ■

Abstract Roundup

ACUTE KIDNEY INJURY

Biomarkers to Predict AKI Progression

Nephrology Dialysis Transplantation. 2022;37(9):1668-1678

Hospitalized patients commonly develop acute kidney injury (AKI), putting them at increased risk for morbidity and mortality. **Stephen Duff, MD,** and colleagues at the University College Dublin, Ireland, conducted the prospective cohort study, Dublin Acute Biomarker Group Evaluation. The study of critically ill patients was designed to test the hypothesis that novel urinary biomarkers would predict progression of AKI as well as associated outcomes.

The primary analysis examined the ability of biomarker levels at the time of early stage 1 or 2 AKI to predict progression to higher AKI stage, the need for renal replacement therapy (RRT), or death within 7 days of admission to the intensive care unit. The secondary analysis examined the association between biomarker levels and RRT or death within 30 days.

A total of 186 patients had AKI within 7 days of admission. In the primary (diagnostic) analysis, there were independent associations between eight of the 14 biomarkers of interest and progression of AKI. The best predictors were cystatin C (adjusted odds ratio [aOR], 5.2; 95% CI, 1.3-23.6), interleukin-18 (IL-18) (aOR, 5.1; 95% CI, 1.8-15.7), albumin (aOR, 4.9; 95% CI, 1.5-18.3), and neutrophil gelatinase-associated lipocalin (NGAL) (aOR, 4.6; 95% CI, 1.4-17.9). Receiver-operating characteristics and new reclassification index analyses similarly demonstrated improved prediction by those biomarkers.

In the secondary (prognostic) analysis of patients with stage 1-3 AKI, there were independent associations between IL-18, NGAL, albumin, and monocyte chemotactic propgtein-1 and RRT or death within 30 days.

In summary, the researchers said, "Among 14 novel urinary biomarkers assessed, cystatin C, IL-18, albumin, and NGAL were the best predictors of stages 1-2 AKI progression. These biomarkers, after further validation, may have the utility to inform diagnostic and prognostic assessment and guide management of AKI in critically ill patients."

COVID-19

Outcomes in Kidney Transplant Recipients After COVID-19 Vaccine

Vaccines. doi.org/10.3390/vaccines10070990

Recipients of kidney transplantation who contract COVID-19 are at increased risk of mortality, with an incidence of death four times higher than in the general population. The availability of mRNA vaccines for COVID-19 infection have dramatically changed the impact of COVID-19, even within the vulnerable population of kidney transplant recipients; however, patients who have received a transplant have impaired immunological response to the mRNA vaccines.

Mariarosaria Campise, MD, and colleagues in Milan, Italy, initiated a vaccination campaign in March 2021. Preliminary results of the campaign indicate that the incidence of death dropped from 13% to 2.4% and the incidence of hospitalization dropped from 45% to 12.5%, compared with data prior to the vaccine campaign.

Results of univariate analysis revealed two variables associated with an increased risk of hospitalization: older age (P=.023) and dyspnea (P<.0001). In multivariate analysis, dyspnea and mycophenolate therapy were independently associated with the risk of hospitalization (P<.0001 and P=.003, respectively). When the two variables were combined, the association was even stronger (P<.0001).

In summary, the authors said, "Vaccinations did not reduce the incidence of COVID-19 infections among our transplanted patients, but provided certain protection that was associated with a significantly better outcome for this infection."

MIS-C and AKI in Pediatric COVID-19

Pediatric Nephrology. doi.org/10.1007/s00467- 022-05701-3

Multisystem inflammatory syndrome (MIS-C) is a rare pediatric hyperinflammatory disorder that may follow SARS-CoV-2 infection in children. Approximately 1/4 to 1/3 of patients with MIS-C develop acute kidney injury (AKI) and face increased risk for poor prognosis. **Anchal Kumar Tripathi, MBBS,** and colleagues performed a review to assess the incidence of AKI, mortality, and the need for renal replacement therapy (RRT) in patients with MIS-C.

The researchers searched databases from Medline, EMBASE, Cochrane Register, and Google Scholar from December 2019 to December 2021. Eligible studies included the following criteria: (1) articles on AKI in MIS-C; (2) studies that provided data on AKI in MIS-C and COVID-19 infection separately; (3) studies reporting outcomes related to mortality, RRT, serum creatinine level, and length of hospital and/or intensive care stay. The National Heart Lung and Blood Institute quality assessment tool was used to assess the quality of the cohort studies and case series included in the review.

Outcomes and their 95% CIs were reported if a meta-analysis of the outcomes of interest was conducted. Heterogeneity was reported using I^2 statistics, and heterogeneity ≥50% was considered high.

The review included 24 studies. Of those, 11 were included in the meta-analysis. The pooled proportion of patients with MIS-C developing AKI was 20% (95% CI, 14%-28%; I^2=80%). Pooled proportion of death in children with MIS-C was 4% (95% CI, 1%-14%; I^2=93%). The odds of death in patients with AKI were 4.68 times higher than in patients without AKI (95% CI, 1.06%-20.7%; I^2=17%). The overall proportion of patients with MIS-C who required RRT was 15% (95% CI, 4%-42%; I^2=91%).

In summary, the researchers said, "Approximately one-fifth of children with MIS-C develop AKI, which is associated with higher odds of death."

CHRONIC KIDNEY DISEASE

Self-care Health-Promoting Behaviors in Hypertension and CKD

Primary Health Care Research & Development. doi:10.1017/S1463423622000299

Oleksii Korzh, MD, PhD, and colleagues conducted a study designed to examine the relationships among health behaviors and quality of life (QoL) and to test a proposed model among people with hypertension and concomitant chronic kidney disease (CKD) in primary care. The researchers also sought to examine the mediation effect of modifiable risk factors between self-care health behaviors and QoL.

The prospective study was conducted in primary care centers from January 2018 to January 2020. A total of 170 patients who were diagnosed with hypertension and CKD at least 12 months prior to study enrollment were included in the study. The parameters of interest were self-efficacy, self-care health behaviors (including subscales of health responsibility, exercise, consumption of a healthy diet, stress management, and smoking cessation), modifiable risk score, and QoL (assessed using the 36-Item Short-Form Health Survey instrument).

Results of the analyses demonstrated a significantly positive direct effect of self-efficacy on self-care health behaviors, with a standardized regression coefficient of 0.87 (P=.007) a negative indirect effect on risk factors, with a standardized regression coefficient of 0.11 (P=.006); and a positive indirect effect on QoL, with a standardized regression coefficient of 0.62 (P=.008).

Self-care health behaviors had a significantly positive direct effect on QoL, with a standardized regression coefficient of 0.72 (P=.012); there was also an indirect effect of 0.053 (P=.004). The direct effect of risk factors on QoL was also significant (standardized regression coefficient, 0.44; P=.018). The direct effect of self-care health behaviors on QoL was 0.77 (P=.008); that was reduced to 0.72 (P=.012). The reduced effect of 0.05 was significant (P=.004), confirming the mediating role of modified risk factors.

"This study indicates health-promoting behaviors in hypertensive patients with CKD have a potential impact on their QoL in primary care," the researchers said. "Primary care physicians should focus on motivation strategies to encourage individuals to perform self-care health-promoting behaviors associated with the improved QoL in order to achieve better outcomes in risk factor management."

DIALYSIS

Inflammatory Demyelinating Polyneuropathy

Cureus. doi:10.7759/cureus.27095

Length-dependent demyelination and axonal degeneration are associated with uremic neuropathy, a sensorimotor polyneuropathy affecting lower extremities. Patients with end-stage renal disease (ESRD) are commonly treated with hemodialysis or peritoneal dialysis. Recent understanding of solute and water kinetics has led to consideration of peritoneal dialysis as equivalent to in-center hemodialysis. Chronic inflammatory demyelinating polyneuropathy (CIDP) manifests as symmetric, motor-predominant neuropathy resulting in both

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Abstract Roundup

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proximal and distal muscle weakness, and is treatable with immune modulatory therapies.

Kunal Bhuta, MD, and colleagues presented a case series of three patients who developed CIDP following initiation of peritoneal dialysis. Patient A is male, 39 years of age, with ESRD secondary to renal dysplasia; he presented with new onset neuropathy 4 months following initiation of peritoneal dialysis. Patient B is male, 30 years of age, with ESRD secondary to IgA nephropathy; he presented with a history of numbness in his feet that gradually progressed to his legs 12 months after peritoneal dialysis initiation. Patient C is female, 56 years of age, with ESRD and uncontrolled diabetes mellitus; she presented with progressive muscle weakness 4 months after peritoneal dialysis initiation.

The three patients, who were followed at three different dialysis centers, were receiving continuous cycling peritoneal dialysis, initiated at different times. They were all found to have CIDP on electromyography.

Patients A and B were treated with intravenous immunoglobulin and improved. Patient C received plasmapheresis and improved.

In conclusion, the authors said, "It has been recognized that peritoneal dialysis solution is not physiological and may lead to activation of the host immune system triggering an autoimmune demyelinating process. Immunologic pathogenesis is not clearly understood. Macrophage activation and cytokines may play a role in the demyelination proves. With the recent initiative to increase the use of peritoneal dialysis, more studies are warranted to understand this common complication."

TRANSPLANTATION

Kidney Transplantation in Patients With Obesity

Nephrology Dialysis Transplantation. 2022;37(9):1768-1776

While kidney transplantation is recognized as the optimal treatment for end-stage renal disease (ESRD), there are concerns about the benefit of transplant in obese patients with ESRD due to the increased incidence of posttransplant adverse events in that population. **Christel Castelli, MD, PhD,** and colleagues conducted a study designed to compare patients who underwent kidney transplant with patients on dialysis awaiting kidney transplant.

Matching on time-dependent propensity scores was used to estimate life expectancy (restricted mean survival time [RMST]) for a 10-year follow-up. The primary outcome of interest was time to death.

Among patients with a body mass index (BMI) ≥30 kg/m^2 (n=2155 patients per arm), the RMST was 8.23 years (95% CI, 8.05-8.40) in the kidney transplant group versus 8.00 years (95% CI, 7.82-8.18) in the group awaiting kidney transplant, a difference of 2.71 months (95% CI, –0.19 to 5.63).

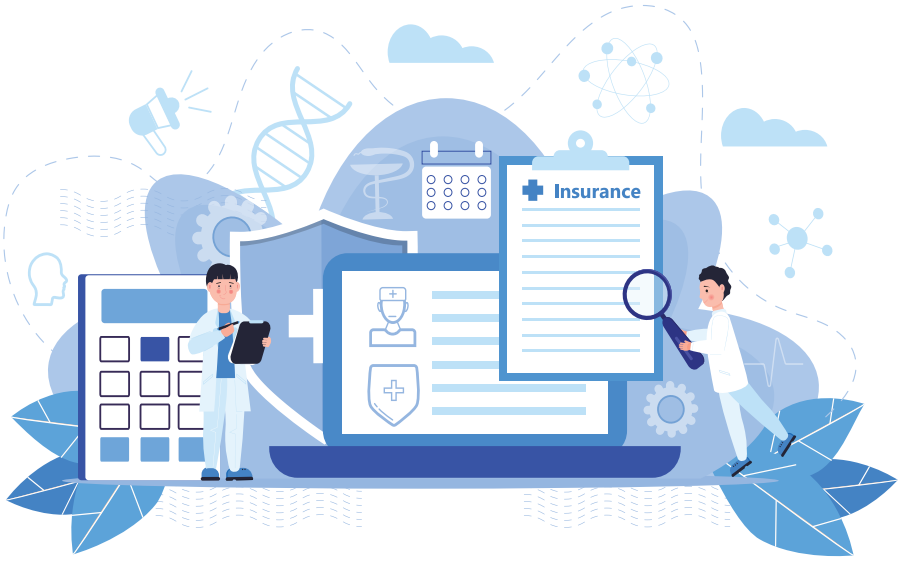
In patients with BMI ≥35 kg/m^2 (n=212 patients per arm), there was no significant difference (8.56 years [95% CI, 7.96-9.08] vs 8.66 [95% CI, 8.10-9.17]), leading the researchers to deduce that kidney transplant in patients with a BMI between 30 and 35 kg/m^2 was beneficial in terms of life expectancy.

"Regarding the organ shortage, kidney transplantation may be questionable for those with BMI ≥35 kg/m^2. These results do not mean that a BMI ≥35 kg/m^2 should be a barrier to kidney transplantation, but it should be accounted for in allocation systems to better assign grafts and maximize the overall life expectancy of ESRD patients," the researchers said. ■

Sarah Tolson

Taking a Closer Look at the 2023 ESRD Final Rule

Since the beginning of the Public Health Emergency (PHE) in early 2020, the economy, labor market, and health care landscape have changed dramatically. Staffing shortages and skyrocketing labor costs are common in most industries, but these struggles seem to have been amplified in dialysis programs nationwide. The labor costs in dialysis programs have continued to increase substantially each year since the beginning of the PHE. As CMS reviewed data for the 2023 ESRD PPS, the most recent data available for review purposes are for 2020. Since 2021 and 2022 have seen continued increases in labor costs, using 2020 data to determine the base rate for 2023 does not paint an accurate picture of the current costs associated with providing a dialysis treatment.



Dialysis programs of all sizes, dialysis patients, provider advocacy associations, and professional associations in the renal industry rallied to provide CMS with clear information about the gap between the proposed ESRD PPS base rate and the current cost of a dialysis treatment due to the increase in labor and supply costs. In addition to outlining the reimbursement gap, the renal community provided CMS with potential solutions to providing additional reimbursement within the regulatory confines CMS is subject to.

In the final rule, CMS finalized an increase to the base rate that it estimates will result in a 3.1% increase in dialysis facility payments from 2022. Additionally, CMS addressed comments it received from the renal community, specifically regarding the productivity adjustment and the market basket update. CMS responded that the "2020-based ESRD Bundled (ESRDB) market basket increase adequately reflects the average change in the price of goods and services ESRD facilities purchase to provide renal dialysis services and is technically appropriate to use as the ESRD PPS payment update factor."

FACILITY LEVEL IMPACT FILE

As I've been working with my company's dialysis facility clients to provide data for financial forecasting, I've analyzed the ESRD Facility Level Impact file associated with the ESRD PPS Final Rule and found our clients are looking at increases in their ESRD PPS base rate ranging from less than half a percent to just over four percent. While the 2023 increase in the base rate is less than the renal community had hoped for, it is still helpful to have an understanding of the increase your facility should see to help with budgeting and forecasting for the coming year.

I would encourage each facility administrator to take the time to review their facility's estimated increase for 2023. The Facility Level Impact file can be found a CMD.gov with the file name "Addendum B - CMS-1768-F CY 2023 ESRD PPS & AKI NPRM Facility Level Impact File." If you are unsure how to use the Facility Level Impact published by CMS, here is a brief outline that may assist you in determining the impact the final rule will have on Medicare reimbursement for your program(s).

- Look up your dialysis program using the Medicare provider number.
- The column labeled "Total Payment for Step 2 – Non-Outlier" shows the estimated 2022 payment from CMS based on 2022 payment information and 2021 treatment counts without factoring in outlier payments.
- The column labeled "Total Payment for Step 7 – Non-Outlier" shows the estimated 2023 payment from CMS based on 2023 payment information and 2021 treatment counts without factoring in outlier payments.
- Subtract the amount in the "Total Payment for Step 7 – Non-Outlier" column from the amount in the "Total Payment for Step 2 – Non-Outlier" to determine the difference between the 2022 and 2023 CMS reimbursement.
- Divide the result of the previous step by the amount in the "Total Payment for Step 2 – Non-Outlier" column to determine the percentage of the anticipated increase for the dialysis program.

When reviewing the data in the Facility Level Impact file, it is important to keep in mind that one of the factors in the increase is the facility treatment count for 2021. If your dialysis program has had a change in census, it may be beneficial to break the numbers down to a per treatment number and estimate Medicare reimbursement based on the updated treatment counts. ■

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

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