Nephrology Times

Practical News, Trends, and Analysis

March 2021

VOLUME 13, NUMBER 2

Disparities in Management of Kidney Disease Exposed by COVID-19 Pandemic

Patients of racial and ethnic minorities face a disproportionate and complex burden of medical, mental health, and social needs. Disparities in healthcare among marginalized patients with kidney disease have been exacerbated by the coronavirus disease 2019 (COVID-19) pandemic. Nearly 50% of patients with kidney failure are Latinx, Black, or Native American/Pacific Islander, and patients in those groups are more heavily impacted with COVID-19 compared with non-Latinx White patients.

In addition, patients with COVID-19 commonly develop multiorgan failure, including kidney failure, and subsequently require renal replacement therapy. **Tessa K. Novick, MD, MSW, Katherine Rizzolo, MD,** and **Lilia Cervantes, MD,** described the disparities and difficulties of patient populations with kidney disease in the face of the COVID-19 pandemic, including difficulties associated with aging and homelessness, and among racial and ethnic minorities, immigrants, and refugees. The report was published in *Advances in Chronic Kidney Disease* [2020;27(5):427-433].

ELDERLY POPULATION

Older patients have been disproportionately affected by COVID-19, with greater risk for infection, severe complications, and death. In a cohort of 393 patients

continued on page 4

FOCUS ON TRANSPLANTATION

Management and Outcomes of COVID-19 Infection in Kidney Transplant Recipients

Among patients with coronavirus disease 2019 (COVID-19), those who are older and those with medical comorbidities or compromised immune systems are at increased risk for adverse outcomes. COVID-19 is caused by the novel acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Bassam G. Abu Jawdeh, MD, FASN, FAST, provided a review of outcomes of COVID-19 in kidney transplant recipients. The review, published in *Advances in Chronic Kidney Disease* [2020;27(5):383-389], focused on clinical characteristics

continued on page 13

C-SNP Enrollment Improves Outcomes for Patients with ESKD

The Centers for Medicare & Medicaid Services chronic conditions special needs plans (C-SNPs) are a type of Medicare Advantage plan that include targeted or specialized services for Medicare beneficiaries who have a severe or disabling chronic condition. End-stage kidney disease (ESKD) is included among the chronic or disabling conditions eligible for enrollment in C-SNPs. The plan receives payments per member per month and is at risk for coordinating and managing the care of enrolled individuals. Specific benefits and healthcare networks for the beneficiaries may also be offered; these may vary based on the plan and may include access to preventive vision and dental services, nutrition support, and access to transportation.

Bryan N. Becker, MD, and colleagues conducted a multicenter cohort study designed to assess whether and to what extent enrollment in a C-SNP was associated with improved clinical outcomes and quality of life among patients with ESKD. Results were reported in *JAMA Network Open* [doi:10.1001/jamanetworkopen.2020.23663].

The primary outcomes were hospitalizations, mortality, laboratory values indicative of metabolic control, and Kidney Disease Quality of Life 36-item (KDQOL-36) survey scores. Eligible patients were newly enrolled in an ESKD C-SNP between January 1, 2013, and September 30, 2017, and receiving dialysis from DaVita Kidney Care. Follow-up continued until death, loss of follow-up, or end of study.

continued on page 3

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

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

Nephrology Times

Nephrology Times
Practical News, Trends, and Analysis

PUBLISHER
Gene Conselyea

NEPHROLOGY TIMES STAFF

EDITORIAL

MANAGING EDITOR
Victoria Socha

CONTRIBUTING EDITOR
Eric Raible

DIGITAL PROJECTS MANAGER
Chris Gedikli

ART DIRECTOR
Ari Mihos

ASSISTANT ART DIRECTOR
John Salesi

ADVERTISING

ACCOUNT MANAGERS

Jane Liss
jliss@amcmediagroup.com

Jen Callow
jcallow@amcmediagroup.com

Recruitment advertising orders can be sent to:
DIRECTOR, RECRUITMENT CLASSIFIEDS

Lauren Morgan
lmorgan@amcmediagroup.com

Visit us at www.nephtimes.com

AMC MEDIAGROUP

630 Madison Avenue
Manalapan, NJ 07726

Nephrology Times (ISSN 1940-5960) is published monthly by AMC Media Group, at Madison Avenue, Manalapan, NJ 07726. Printed in the U.S.A.

C-SNP Enrollment Improves Outcomes

continued from page 1

Patients with ESKD enrolled in a C-SNP were matched via multiple clinical and demographic characteristics with two different control populations: (1) those in the same facilities (n=2545); or (2) those in similar counties (n=1986). Exclusion criteria included enrollment in CareMore C-SNPs (n=206).

A total of 2718 C-SNP enrollees met inclusion criteria. Of those, 2545 were matched to patients in the facility-matched analysis. At baseline, characteristics of the C-SNP and control groups were similar in age (mean, 57.2 years vs 57.1 years), sex (38.0% women vs 39.2% women), distribution of race (21.7% Black vs 21.1% Black), and ethnicity (52.2% Hispanic vs 53.1% Hispanic), respectively. The two groups were also similar in body mass index (mean 27.7 vs 27.7), etiology of kidney disease (e.g., diabetes, 48.9% vs 48.2%), and vintage (mean 46.3 months vs 48.0 months) (standardized difference <10% for all characteristics). The study population included more than 50% Hispanic patients, and Hispanic and Black patients accounted for nearly 75% of the cohort. The ESKD etiology reflected the distribution in data from the United States Renal Data System.

In the county-matched analysis, 1986 C-SNP enrollees were matched to control patients. At baseline, mean age of C-SNP enrollees compared with controls was 57.8 years versus 58.1 years, 35.5% women versus 35.5% women, 54.6% Hispanic versus 54.6% Hispanic, and 23.8% Black versus 23.8%.

Compared with non-C-SNP enrollees, those enrolled in a C-SNP had lower rates of hospitalization: incidence rate ratios were 0.90 (95% confidence interval [CI], 0.84-0.97; *P*=.006) in the facility-matched analysis and 0.76 (95% CI, 0.70-0.83; *P*<.001) in the county-matched analysis.

In both analyses, most patients were receiving in-center hemodialysis. There were no significant differences between C-SNP enrollees and matched patients in frequent comorbid cardiovascular, respiratory, or vascular conditions.

In the facility-matched analysis, C-SNP enrollees had 6141 hospital admissions during 55,561 patient-months of follow-up, for a hospitalization rate of 11.05 per 100 patient-months. Among matched controls, there were 6551 hospital admissions in 53,408 patient-months of follow-up, for a hospitalization rate of 12.27 per 100 patient-months. The incidence rate ratio for hospitalization was 0.90 (95% CI, 0.84-0.97; *P*=.006).

In the county-matched analysis, C-SNP enrollees had 4625 admissions in 44,553 patient-months of follow-up, for a hospitalization rate of 10.38 per 100 patient-months. Matched patients experienced 6348 admissions in 46,704 patient-months of follow-up, for a hospitalization rate of 13.59 per 100 patient-months. The corresponding incidence rate ratio was 0.76 (95% CI, 0.70-0.83; *P*<.001), favoring C-SNP enrollees.

In mortality analyses, there were 440 deaths during 55,561 patient-months of follow-up among C-SNP enrollees in the facility-matched cohort (mortality rate, 0.79 per 100 patient-months). There were 543 deaths among matched patients during 53,408 patient-months of follow-up (mortality rate, 1.02 per 100 patient-months). The hazard ratio (HR) for mortality among C-SNP enrollees was significantly lower than for matched controls (0.77; 95% CI, 0.68-0.88; *P*<.001).

In the county-matched analysis, there were 337 deaths during 44,553 patient-months of follow-up among C-SNP enrollees, for a mortality rate of 0.76 per 100 patient-months. In the matched patient cohort, there were a total of 461 deaths during 46,704 patient-months of follow-up, for a mortality rate of 0.99 per 100 patient-months. The HR for mortality was significantly lower among C-SNP enrollees compared with controls in the same counties (0.77; 95% CI, 0.66-0.88; *P*<.001).

There were no significant differences between C-SNP enrollees and matched patients in the same facilities in calcium, potassium, or parathyroid levels. There was a small but significant difference in phosphate levels; C-SNP enrollees had lower mean phosphate levels than the matched patients (5.4 [95% CI, 5.3-5.4] vs 5.5 [95% CI, 5.4-5.5] mg/dL; *P*=.04). There were no significant differences in any laboratory parameters between C-SNP enrollees and matched patients in the same counties.

In analysis of KDQOL-36 scores, there were no significant differences between C-SNP enrollees and matched patients in the same facilities or in similar counties.

Limitations to the findings cited by the authors included potential confounding by the populations as well as facility-level differences in care and care team member complement, the inability to account for potential shifts in physician coverage of patients and hospital programs during the study's timeframe, and concentrating the study population in select geographies, possibly limiting the applicability of the findings beyond those geographies.

In conclusion, the researchers said, "The data in this analysis suggested that enrollment in a C-SNP was associated with lower rates of hospitalization and mortality compared with similar patients who received ESKD care within the same facilities or within the same geographies but were not enrolled in C-SNPs. This suggests that aspects of the care model, including access to the integrated care team, regular interactions between this team and the interdisciplinary dialysis team (e.g., the patient's nephrologist), and possible access to the additional services and benefits provided via C-SNPs, may improve patient outcomes beyond the standard of care for this high-risk, high-need population." ■

TAKEAWAY POINTS

- Researchers conducted a retrospective multicenter cohort study to assess whether enrollment in a chronic condition special needs plan (C-SNP) improved outcomes among patients with end-stage kidney disease (ESKD).
- Compared with non-enrollees, those who enrolled in a C-SNP had lower rates of hospitalization and mortality, in both facility-matched and county-matched analyses.
- The researchers said the findings suggest that the additional services and benefits of C-SNP enrollment may improve outcomes compared with standard of care of ESKD.

Disparities in Management of Kidney Disease
continued from page 1

with COVID-19 in New York City, median age was 62 years; compared with younger patients, elderly patients were more likely to require invasive mechanical intervention, kidney replacement therapy, and die. That pattern is consistent with reports worldwide.

The multifactoral drivers of the variability in infection risk and severity of disease among the elderly are not well understood. Older patients are more likely to have underlying medical conditions, including chronic kidney disease (CKD), which is associated with COVID-19 infection and complications. Approximately 44% of individuals more than 70 years of age have CKD, compared with 9.2% of adults 40 to 59 years of age.

Many older adults live in long-term care facilities, settings that are high risk for COVID-19 outbreaks. Among older adults who live alone, many rely on visiting caregivers. In addition, older adults often rely on public transportation, which was identified as a factor in the spread of COVID-19 early in the pandemic.

As the pandemic persisted, shelter-in-place orders forced older adults to stay indoors and remain inactive, often in solitary settings, conditions that exacerbate frailty and depression. Frailty is associated with increased risk of hospitalization and mortality among patients with CKD and kidney failure, and allograft loss among kidney transplant recipients. Finally, older adults may not have access to the technology required for telemedicine, and hearing loss and low health-literacy may also negatively affect communication during telephone medical visits.

TAKEAWAY POINTS

- The coronavirus disease 2019 (COVID-19) pandemic has exposed racial, ethnic, socioeconomic, age, and sex-related disparities in the healthcare system in the United States.
- In a recent study,, disparities associated with the additional burdens in the management of kidney disease in those populations imposed by the pandemic were explored.
- Risks for elderly, homeless, and underserved minorities have been compounded by the strains on the healthcare system associated with the pandemic; putting patients with kidney disease at increased risk for adverse outcomes.

UNSTABLE HOUSING

Among unstably housed populations, COVID-19 is particularly prominent. Living in shelters and making numerous moves prohibits social distancing and limits opportunities for frequent hand washing and other hygiene measures to prevent infection. Transmission of COVID-19 in shelters has resulted in clusters of the disease in large cities. Due to higher prevalence of comorbidities among the homeless population, mortality among unsheltered homeless adults is 10 times higher than in the general population.

Having kidney disease may increase the risk for COVID-19 among the unsheltered population. A San Francisco study found that patients with CKD utilize acute care at higher rates than stably housed counterparts, increasing the risk for exposure to COVID-19. Patients requiring dialysis treatment may have increased risk for exposure due to increased reliance on emergency departments for treatment.

SEX DIFFERENCES

While the prevalence of CKD is higher in women than in men, the rates of disease progression and kidney failure are higher in men. Early data on COVID-19 mortality rates show a similar trend: In New York City, 42.9 men per 100,000 died compared with 23.1 per 100,000 women. Trends were similar in China and Italy.

The socioeconomic effects of the pandemic is predicted to have an inequitable effect on women. One in three jobs held by women are considered essential, with the highest proportion in healthcare. Women account for 73% of COVID-19 infections among US healthcare workers. Further, women shoulder the majority of the needs of child care at home. Women with CKD are more likely to belong to a racial or ethnic minority, be a single parent, or have low income and low-level education, contributing to a higher risk of exposure to infection as well as a higher burden of economic challenges due to lost employment and child care needs.

RACE AND ETHNICITY

The incidence of kidney failure is 3.5 times higher for Blacks and 1.5 times greater for Latinx, and both communities have higher rates of progression to kidney failure. Limited data on the COVID-19 pandemic reveal similar trends. In the United States, Black, Latinx, and Native Americans make up a disproportionate number of COVID-19-related deaths. In New York City, the age-adjusted morality rate for COVID-19 for Blacks is double that of White and Asian adults, and the age-adjusted case rate is highest in the Black and Latinx communities.

REFUGEES, IMMIGRANTS, AND UNDOCUMENTED

Undocumented immigrants are disproportionately essential workers, facing daily exposure to COVID-19. Immigrants are often employed in low-paying jobs in the service and hotel industries and are among those who have been out of work since the start of the pandemic in the United States. The undocumented population does not benefit from economic relief packages, adding to financial strain. Many will face having to forego spending on medications, healthy food, and other healthcare needs.

There are an estimated 5500 to 8857 uninsured immigrants with kidney failure in the United States, a population that relies largely on hospitals for emergency-only dialysis. Such treatment is associated with worse morbidity and mortality, and presents an economic burden on the medical system.

In summary, the authors said, "The COVID-19 pandemic is re-exposing an underlying and long-standing set of critical weaknesses in our nation's healthcare system, especially relevant to the stark burdens already faced by many underserved populations. Numerous complications and struggles with kidney disease have unfortunately intensified in patient groups and have risen to the forefront during a time of great patient need and distress. The risk for the elderly, the homeless, differences between sexes, and overwhelming threats to racial, ethnic, and underserved minorities and immigrants are compounding. All together, the broad and complex set of interconnected disparities, both nationally and globally, will require a similarly broad and complex set of solutions. As the nation pulls together during these times of great uncertainty, it will be our continued responsibility to move the needle forward on the inequities faced by marginalized populations that have been unheeded far too long." ■

Japanese Study: Roxadustat Noninferior to Darbepoetin Alfa in Dialysis Patients with Anemia

Anemia, a complication of chronic kidney disease (CKD), results from a decreased synthesis of erythropoietin by the impaired kidneys and an altered iron metabolism. In the general population, the prevalence of anemia is 7.6%; among patients with CKD, the prevalence is 15.4%, increasing with severity of CKD.

Currently available treatments for CKD-associated anemia include erythropoiesis-stimulating agents (ESAs), including darbepoetin alfa (DA). However, safety concerns and adverse events associated with higher doses and hemoglobin goals in CKD patients with cancer, diabetes, and cardiovascular disease have resulted in a decrease in the doses of ESAs used. Further, the efficacy of ESAs is reduced in patients with inflammation.

Alternative therapeutic strategies for CKD-related anemia are being investigated. Roxadustat, an orally active hypoxia-inducible factor prolyl hydroxylase inhibitor, was approved in China in December 2018 for the treatment of dialysis-dependent CKD anemia; the drug is being investigated in Japan, the United States, and Europe.

Researchers in Japan, led by **Tadao Akizawa, MD, PhD,** conducted a phase 3, multicenter, randomized, double-blind study to evaluate the noninferiority of roxadustat to DA when both drugs are titrated to maintain hemoglobin levels of 10 to 12 g/dL in patients in Japan with renal anemia on hemodialysis. The study was conducted from November 2016 to March 2018 at 58 Japanese sites. Results were reported in the *Journal of the American Society of Nephrology* [2020;31(7):1628-1639].

Patients were randomized 1:1 to oral roxadustat three times weekly or DA injections once weekly for up to 24 weeks. There was no formal washout period; the treatment period began on the day of dialysis after the longest dialysis interval in the week when ESA had been administered.

Patients were ≥20 years of age with CKD anemia, receiving stable hemodialysis three times weekly for >12 weeks. Prior to randomization, patients were receiving intravenous (IV) short-acting recombinant human erythropoietin or DA for >8 weeks, had hemoglobin levels 10 to 12 g/dL, and transferrin saturation (TSAT) ≥20% or serum ferritin ≥100 ng/mL.

The primary end point was change of average hemoglobin from baseline to weeks 18 to 24. Secondary end points included average hemoglobin and proportion of patients with hemoglobin between 10 and 12 g/dL (maintenance rates) at weeks 18 to 24, and iron parameters. Safety assessments included treatment-emergent adverse events (TEAEs) and adjudicated ophthalmologic findings.

A total of 415 patients were screened; following application of inclusion and exclusion criteria, the final cohort included 303 patients who were randomized to receive roxadustat (n=151) or DA (n=152). Of those 303 patients, 250 completed the study (roxadustat, n=119; DA, n=131) and 53 discontinued (roxadustat, n-32; DA, n=21). Patient demographics and baseline characteristics were similar between the two groups.

In the safety analysis set, mean treatment compliance during the study period was 99.23% in the roxadustat group and 100% in the DA group. Mean duration of exposure was 146.7 days in the roxadustat group and 154.7 days in the DA group, and the mean dose per administration at week 23 was 67.1 mg in the roxadustat group and 31.4 mg in the DA group. The mean number of changes in study drug dosing was 2.8 in the roxadustat group and 2.3 in the DA group.

In the per protocol set, the difference between roxadustat and DA in change in average hemoglobin from baseline to weeks 18 to

continued on page 6

CONFERENCE COVERAGE KIDNEY WEEK 2020

Efficacy of Roxadustat in Subgroups of Phase 3 Trials

Data from three phase 3 trials of roxadustat were examined in recent subgroup analyses. Roxadustat is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor for the treatment of anemia in patients with chronic kidney disease (CKD). The agent stimulates erythropoiesis and improves iron metabolism in that patient population.

During a virtual poster session at ASN Kidney Week 2020, **Daniel W. Coyne, MD,** and colleagues reported results of the analyses. Data from the randomized, double-blind, placebo-controlled studies of roxadustat for the treatment of anemia in patients with non-dialysis dependent CKD (NDD-CKD) were examined. Results were reported in a poster titled *Subgroup Analyses of Efficacy of Roxadustat for Treatment of Anemia in Patients with Non-Dialysis-Dependent CKD.*

The data were from prespecified, clinically relevant patient subgroups. Data were analyzed for mean change from baseline in hemoglobin averaged over weeks 28 to 52 regardless of rescue therapy (primary US efficacy end point) and percentage of patients who received rescue therapy in the first 52 weeks.

There were 2391 patients in the roxadustat group and 1886 in the placebo group. Patients in the roxadustat group achieved a significantly larger mean change from baseline in hemoglobin level (1.85 vs 0.13), corresponding to a least-squares mean difference of 1.72 (95% confidence interval [CI], 1.65-1.79; $P<.0001$).

Results for all subgroup analyses were consistent with those for the US primary efficacy end point and the percentage of patients requiring rescue therapy in the overall NDD population. Compared with those in the placebo group, significantly fewer patients in the roxadustat group required rescue therapy during treatment (8.9% in the roxadustat group vs 31.1% in the placebo group), corresponding to a hazard ratio of 0.19, 95% CI, 0.16-0.23; $P<.0001$). In all subgroups, the effect was consistent and was particularly pronounced in patients with baseline hemoglobin <8.0 g/dL (18.1% in the roxadustat group vs 59.3% in the placebo group) and those with baseline eGFR <10.0 mL/min/1.73 m^2 (14.8% in the roxadustat group vs 48.3% in the placebo group).

In conclusion, the researchers said, "The efficacy of roxadustat versus placebo for a larger mean change from baseline in hemoglobin and fewer patients that received rescue therapy was consistent across a wide range of prespecified subgroups in the NDD-CKD population."

Source: Coyne DW, El-Shahawy MA, Pecoits-Filho R, et al. Subgroup analyses of efficacy of roxadustat for treatment of anemia in patients with non-dialysis-dependent CKD. Abstract of a poster presented at the American Society of Nephrology virtual Kidney Week 2020 (P00260), October 22, 2020. Funding for this poster was provided by Fibrogen, Inc; AstraZeneca plc; and Astellas Pharma, Inc.

continued from page 5

24 was –0.02 g/dL (95% confidence interval [CI], –0.18 to 0.15). The lower limit of the 95% CI was above the predefined noninferiority margin of –0.75 g/dL, confirming roxadustat's noninferiority to DA. In the roxadustat group, the mean of average hemoglobin levels during weeks 18 to 24 was 10.99 g/dL and its 95% CI (10.88 to 11.10 g/dl) was within the prespecified reference range of 10 to 12 g/dL, confirming the efficacy of roxadustat.

In a secondary analysis in the full analysis set, results were similar. The mean of average hemoglobin levels during weeks 18 to 24 was 11.0 g/dL (95% CI, 10.89 to 11.10 g/dL) in the roxadustat group. The least squares mean of the change in average hemoglobin from baseline to weeks 18 to 24 was –0.07 for the roxadustat group and –0.06 g/dL for the DA group, and the estimated difference between the least squares means of the two groups was –0.01 /dL (95% CI, –0.18 to 0.16 g/dL).

In the full analysis set, the mean of average hemoglobin levels during weeks 18 to 24 was 11.00 g/dL (95% CI, 10.89 to 11.10 g/dL) in the roxadustat group and 10.95 g/dL (95% CI, 10.84 to 11.05 g/dL) in the DA group. The mean difference between the two groups was 0.05 g/dL (95% CI, –0.10 to 0.20 g/dL).

Among patients with at least one hemoglobin value during weeks 18 to 24, the maintenance rates of the target hemoglobin level was 95.2% (95% CI, 89.8% to 98.2%) for the roxadustat group and 91.3% (95% CI, 85.3% to 95.4%) for the DA group. The difference between the two groups was 3.9% (95% CI, –2.9% to 10.7%).

Mean values of serum iron, soluble transferrin receptor, TSAT, reticulocyte hemoglobin content, and ferritin remained clinically stable in both treatment groups.

The two groups were similar in the proportion of patients who reported TEAEs: 129/150 (86.0%) in the roxadustat group and 126/152 (82.9%) in the DA group. The incidence of serious TEAEs was 20.7% (31/150) in the roxadustat group and 14.5% (22/152) in the DA group. Serious TEAEs potentially related to the study drug were reported in 3.3% (5/150) of the roxadustat group and 3.9% (6/152) of the DA group.

Retinal hemorrhage was reported as a TEAE in 3.3% (5/150) of the roxadustat group and 3.9% (6/152) in the DA group. The proportion of patients with new or worsening retinal hemorrhage was 32.4% in the roxadustat group and 36.6% in the DA group. There were no clinically meaningful changes in retinal thickness from week 0 through the end of treatment in either group.

The authors cited some limitations to the study findings, including not including a placebo group for comparison, the study being underpowered to provide a definitive conclusion regarding overall safety or cardiovascular outcomes, and the need for a longer study period.

In summary, the researchers said, "Overall, this study demonstrated the efficacy of orally administered roxadustat and its noninferiority to DA in maintaining the levels of hemoglobin within the target range in Japanese patients with anemia on hemodialysis. Roxadustat displayed a manageable safety profile with no increased risk of ophthalmologic abnormalities; however, further investigation will be required to firmly establish the safety profile of roxadustat in this population. Additional large, long-term phase 3 studies of roxadustat are currently underway to confirm and extend these efficacy- and safety-related findings to other CKD populations." ■

TAKEAWAY POINTS

- Researchers in Japan reported on a phase 3, active-comparator trial among patients with anemia on hemodialysis treated with either roxadustat or darbepoetin alfa (DA).
- The difference between the two groups in change in average hemoglobin levels at weeks 18 to 24 was -0.02 g/dL, confirming the noninferiority of roxadustat to DA.
- The safety profiles were similar in the two groups; with no increased risk of ophthalmologic abnormalities.

Cardiovascular Events and Mortality in Elderly CKD Patients on DOACs

There is no clear consensus on the optimal type of oral anticoagulation therapy for patients with chronic kidney disease (CKD). Options include vitamin K antagonists (VKAs) or direct oral anticoagulants (DOACs). There is long-established clinical experience with the use of VKAs; however, according to **Justin Ashley, MD,** and colleagues, those agents are associated with a narrow window of efficacy and safety, a tendency to accelerate vascular calcification, and a high number of drug interactions. There are also concerns associated with DOACs, including safety and efficacy in patients with lower estimated glomerular filtration rates (eGFRs) and those treated by dialysis as well as reversibility in emergencies. Both agents carry an increased risk for hemorrhage and have limited data for efficacy among patients with CKD.

Results of previous studies suggest potential promise associated with DOACs in reducing cardiovascular events in patients with CKD at risk. Dr. Ashley et al. conducted a study designed to examine the association of use of DOACs with cardiovascular events and hemorrhage in patients with and without reductions in eGFR compared with VKAs. The researchers sought to test the hypothesis that DOACs would reduce the risk for adverse cardiovascular events compared with VKAs in patients with reduced eGFRs. Results of the population-based retrospective cohort study were reported in the *American Journal of Kidney Diseases* [2020;76(3):311-320].

Participants included all individuals ≥66 years of age with an initial prescription for oral anticoagulants dispensed in Ontario, Canada, from 2009 to 2016. The study exposures were DOACs (apixaban, dabigatran, and rivaroxaban) compared with VKAs by eGFR group (≥60, 30-59, and ≤30 mL/min/1.73 m^2). The primary outcome of interest was a composite of a cardiovascular event (myocardial infarction [MI], revascularization, or ischemic stroke) or morality. Secondary outcomes included cardiovascular events alone, mortality, and hemorrhage requiring hospitalization.

The final analytic cohort included 210,539 individuals on anticoagulation therapy. During the study period, there were 65,335 new DOAC users; of those, 42% (n=27,552) were matched to 27,552 VKA users. Among the DOAC cohort, mean age was 78.5 years and 48.9% were women; 27.1% were receiving apixaban, 31.6% were receiving dabigatran, and 41.3% were receiving rivaroxaban. A total of 27.8% of those in the DOAC cohort had a history of atrial fibrillation (AF), 36.2% had a history of venous thromboembolism, and approximately one in six were receiving concurrent antiplatelet agents. Previous cardiovascular disease (MI, coronary artery bypass grafting, percutaneous coronary intervention, or ischemic stroke) was noted in 13.9% of the DOAC cohort; major hemorrhage was noted in 1.2% of the cohort. Thirty-seven point nine percent of the DOAC cohort had eGFRs of 30 to 59 mL/min/1.73 m^2 and 2.7% had eGFR <30 mL/min/1.73 m^2. Following high-dimensional propensity scores matching, with the exception of index year, there were no statistically significant differences between the DOAC group and the VKA group.

MI was the most common type of cardiovascular event outcome (25.8%), followed by ischemic stroke (15.2%), and revascular-

ization (5.3%). Of the patients receiving a DOAC, 12.05% (n=3321) had a cardiovascular event or mortality during the study period, compared with 9.19% (n=2531) of the patients in the VKA group. The researchers noted that the median follow-up time on DOAC therapy was nearly 3.5 times longer compared with VKA therapy (1.14 vs 0.33 years, respectively). The rate of events was lower with DOAC use (79.78 and 99.77 per 1000 person-years, hazard ratio [HR], 0.82; 95% confidence interval [CI], 0.75-0.90). The association was similar using an intention-to-treat approach, and when limited to those with AF only.

In the DOAC cohort, 5.84% (n=1608) of patients experienced a cardiovascular event alone, compared with 4.00% (n=1103) of patients in the VKA group. After accounting for the difference in follow-up time, the event rate was lower with DOAC use (DOAC, 38.63 events/1000 person years vs VKA, 43.48 events/1000 person years; adjusted HR, 0.87; 95% CI, 0.76-0.98). Using an intention-to-treat approach and limited to AF only, the point estimate was similar but the upper CI crossed unity.

One point sixty-one percent (n=443) of the patients in the DOAC group experienced a major hemorrhage, compared with 1.58% (n=436) of those in the VKA group: 10.35 events/person years versus 16.77 events per 1000 person-years, respectively; adjusted HR, 0.73; 95% CI, 0.58-0.91. Results were consistent in the intention-to-treat analysis, with no difference detectable in those with AF only.

In analyses stratified by eGFR, the risk for cardiovascular events or mortality was significantly lower among DOAC users with lower eGFRs: eGFR ≥60 mL/min/1.73 m^2, HR, 1.01 (95% CI, 0.92-1.12); eGFR 30 to <60 mL/min/1.73 m^2, HR, 0.83 (95% CI, 0.75-0.93); and eGFR <30 mL/min/1.73 m^2, HR, 0.75 (95% CI, 0.51-1.10); interaction *P*=.02. Adjusted HRs demonstrated a similar trend for cardiovascular events alone by eGFR (interaction *P*=.01); there was no difference for major hemorrhage. The association was similar in an intention-to-treat analysis for cardiovascular events or mortality; there was no difference for cardiovascular events alone or hemorrhage.

Limitations to the study cited by the authors included the observational design, the lack of data for international normalized ratios levels for VKA users, and lack of complete information for indications for anticoagulation therapy.

"In patients with an indication for anticoagulation therapy, the use of DOACs was associated with lower relative risk for cardiovascular events or mortality, cardiovascular events alone, and major hemorrhage compared with VKAs. A significant trend toward lower cardiovascular events or mortality risk was observed with lower eGFRs, suggesting the potential of DOACs as a preventative therapy in a high-risk population and warranting clinical trials," the researchers said. ■

Print-only Content

Renal Outcomes with Empagliflozin Treatment in Patients with Heart Failure

TAKEAWAY POINTS

- Researchers conducted a study to evaluate the use of empagliflozin in a population of patients with chronic heart failure and a reduced ejection fraction, with and without diabetes.
- The trial's secondary outcome was the rate of decline in estimated glomerular filtration rate (eGFR) during the double-blind treatment period. Serious renal outcomes of interest included the need for chronic dialysis or transplantation, or a sustained and profound reduction in eGFR.
- Patients in the empagliflozin group had slower annual rate of decline in eGFR compared with those in the placebo group; patients treated with empagliflozin had a lower risk of serious renal outcomes than those who received placebo.

In patients with type 2 diabetes, sodium-glucose cotransporter 2 (SGLT2) inhibitors reduce the risk of hospitalization for heart failure as well as the risk for serious adverse renal events; the risk reductions are not seen with other antihyperglycemic therapies. Results of large-scale, randomized, placebo-controlled trials found a 30% to 35% reduction in the risk of hospitalization for heart failure in patients who received SGLT2 compared with those who received placebo. The risk of progression of renal disease, including the occurrence of renal death or the need for dialysis or renal replacement, was 35% to 50% lower in patients in the SGLT2 group compared with those in placebo cohorts.

To examine the effects of SGLT2 inhibitors in patients across the spectrum of heart failure, including patients with a markedly reduced ejection fraction, **Milton Packer, MD,** and colleagues reported results of the EMPEROR-Reduced [Empagliflozin Outcome Trial in Patients with Chronic Heart Failure and a Reduced Ejection Fraction] study online in the *New England Journal of Medicine* [10.1056/NEJMoa2022190].

The randomized, double-blind, parallel-group, placebo-controlled, event-driven trial was conducted at 520 centers in 20 countries. The primary outcome of interest was a composite of adjudicated cardiovascular death or hospitalization for heart failure, analyzed as the time to the first event. The first secondary outcome was the occurrence of all adjudicated hospitalizations for heart failure, including first and recurrent events. The second secondary outcome was the rate of decline in estimated glomerular filtration rate (eGFR) during double-blind treatment.

A total of 7220 patients were screened for eligibility from April 2017 through November 2019. Of those, 3730 met inclusion criteria and were randomly assigned to receive either empagliflozin (n=1863) or placebo (n=1867). The two groups were similar in baseline characteristics. Half of the overall cohort had a history of diabetes, 73% had a left ventricular ejection fraction of ≤30%, 79% had a N-terminal prohormone of brain natriuretic peptide level of at least 1000 pg per milliliter, 48% had eGFR of <60 mL/min/1.73 m^2, and nearly 20% were receiving an angiotensin receptor-neprilysin inhibitor.

> The second secondary outcome was the rate of decline in estimated glomerular filtration rate (eGFR) during double-blind treatment.

The primary composite outcome of death from cardiovascular causes or hospitalization for heart failure occurred in 19.4% of the patients in the empagliflozin group (n=361) and in 24.7% of the patients in the placebo group (n=462); hazard ratio (HR), 0.75; 95% confidence interval (CI), 0.65-0.86; *P*<.001. HRs for the effect of empagliflozin on cardiovascular death and on the first hospitalization for heart failure were 0.92 (95% CI, 0.75-1.12) and 0.69 (95% CI, 0.59-0.81), respectively. The number of patients who would need to have been treated with empagliflozin to prevent one primary event was 19 (95% CI, 13-37).

In analyses in prespecified subgroups, the effect of empagliflozin in the primary outcome was consistent, including in patients with diabetes and those without diabetes at baseline. Among patients who were receiving sacubitril-valsartan at baseline, the HR for the comparison between empagliflozin and placebo for the primary outcome was 0.64 (95% CI, 0.45-0.89), compared with 0.77 (95% CI, 0.66-0.90) among patients who were not receiving sacubitril-valsartan.

The rate of decline in eGFR over the treatment period was slower in the empagliflozin group compared with the placebo group (–0.55 mL/min/1.73 m^2 per year vs –2.28 m:/min/1.73 m^2 per year). The between-group difference was 1.73 mL/min/1.73 m^2 per year (95% CI, 1l10-2.37; *P*<.001).

The risks of serious renal outcomes were lower in the empagliflozin group compared with the placebo group. A composite renal outcome (chronic dialysis or transplantation or a profound, sustained reduction in eGFR) occurred in 1.6% of patients in the empagliflozin group (n=30) and in 3.1% of patients in the placebo group (n=58) (HR, 0.50; 95% CI, 0.32-0.77). In 966 patients with paired measurements prior to study participation and 23 to 45 days following the discontinuation of the trial regimens, enabling assessment of the effects of empagliflozin independent of the presence of the drug, eGFR declined by –0.93 mL/min/1.73 m^2 in the empagliflozin group (95% CI, –1.97 to 0.11) and by –4.21 mL/min/1.73 m^2 in the placebo group (95% CI, –5.16 to 3.17).

"Overall, in this trial, empagliflozin was associated with a lower combined risk of cardiovascular death or hospitalization for heart failure than placebo and with a slower progressive decline in renal function in patients with chronic heart failure and a reduced ejection fraction, regardless of the presence or absence of diabetes," the researchers said. ■

Cardiovascular Disease Risk in Overweight and Obese Children with CKD

Chronic kidney disease (CKD) is a leading risk factor for cardiovascular disease among children and young adults. Cardiovascular disease risk factors, both traditional and nontraditional, are highly prevalent in youth with CKD and are associated with a significant burden of intermediate cardiovascular outcomes that include left ventricular hypertrophy (LVH), increased arterial stiffness, and increased carotid intima media thickness.

Identification of the modifiable cardiovascular disease risk factors commonly associated with intermediate outcomes in youth with CKD may aid in the prevention and treatment in that patient population. There are associations between overweight and obesity and traditional cardiovascular disease risk factors among children with mild to moderate CKD. However, there are few data on the impact of adiposity on target-organ damage among children with CKD.

Tammy M. Brady, MD, PhD, and colleagues recently conducted a prospective cohort study to examine the longitudinal association of adiposity with cardiac damage among children with CKD. The study was also designed to examine whether the association was modified by sex. Results of the study were reported in the *American Journal of Kidney Diseases* [2020;76(2):166-173].

The cohort included children with moderate-to-mild CKD who were enrolled in the CKiD (Chronic Kidney Disease in Children) study at 49 pediatric nephrology centers across North America. The outcome of interest was age- and sex-specific left ventricular mass index (LVMI) z score and LVH. Mixed-effects models were used in longitudinal analyses to estimate sex-specific associations of body mass index (BMI) z scores with LVMI z score and with LVH, accounting for repeated measurements over time.

The analyses included 725 children for a total of 1483 study visits over 2829 person-years; median follow-up from study entry was 3.3 years. Forty percent (n=286) of the 725 children contributed one visit, 31% (n=228) contributed two visits, 18% (n=127) contributed three visits, 8% (n=60) contributed four visits, and 3% (n=24) contributed five visits.

Of the 725 children in the study, 38% were female and 21% were African American. Echocardiography and BMI were measured concurrently at the first visit. Median age at first visit was 11.0 years, median CKD duration was 8.0 years, and median estimated glomerular filtration rate was 52.6 mL/min/1.73 m^2. Average blood pressure was in the hypertensive range in 10% of the study population. Nearly one-third of the study cohort was overweight or obese: 13% (n=93) had BMI in the overweight category, in the 85th to <95th age- and sex-specific percentile range; and 16% (n=116) had BMI in the obese category, ≥95th age- and sex-specific percentile. There was no significant difference in the prevalence of overweight or obesity by sex. Median LVMI was 30.5 g/$m^{2.7}$ and median LVMI z score was 0.18. Eleven percent of the study cohort had LVH.

The prevalence of LVH across 1483 study visits by sex in 725 participants across three BMI categories (normal [BMI <85th age- and sex-specific percentile], overweight, and obese), was measured. In girls, the prevalence of LVH was 8.4% among those in the normal BMI group, 16.0% among those in the overweight group, and 33.7% among those in the obese group. The relationship between BMI and LVH was not as pronounced among boys; the prevalence in each category of BMI was close to 7.0%, which was similar to the overall prevalence of LVH across all visits among boys.

There was an association between each additional year from baseline and both a decrease in LVMI z score (–0.10; 95% confidence interval [CI], –0.12 to –0.08 in unadjusted analysis) and lower odds of LVH (–20%; 95% CI, –11% to –30%) per year.

In multivariable longitudinal analyses, there were significant differences by sex in the association of BMI z score and LVMI z score (*P*=.01). Among girls, there was an association between each 1-unit greater BMI z score and a 0.38 (95% CI, 0.29-0.47) greater LVMI z score. That association was significantly greater (*P*=.02) than the 0.24 (95% CI, 0.17-0.31) greater LVMI z score among boys. There was also a significant difference in the association of BMI z score with LVH in girls and boys: for each 1-unit greater BMI z score, girls had a 3.1 (95% CI, 1.8-4.4) times greater odds of LVH, while boys had a 1.5 (95% CI, 1.12-2.1) times greater odds of LVH with each 1-unit greater BMI z score.

Limitations to the study cited by the authors included not all children having repeated measurements, the observational design of the study, and, while LVH is a clinical biomarker for CKD risk, it is a surrogate and not a hard cardiac outcome.

"In children, adiposity is independently associated with the markers of cardiac damage, LVMI z score and LVH. This association is stronger among girls than boys. Pediatric overweight and obesity may therefore have a substantial impact on cardiovascular risk among children with CKD.

"Future studies that focus on enhanced risk stratification strategies and targeted treatment approaches among this at-risk population are needed. Determining the effect of tailored interventions on children with CKD and comorbid obesity will provide more insight into these sex-related differences and establish the effect of weight loss on CV risk," the researchers said. ■

TAKEAWAY POINTS

- Researchers conducted a prospective cohort study to examine the longitudinal association of adiposity with cardiac damage in children with chronic kidney disease, as well whether the association was modified by sex.
- The outcome of interest was age- and sex-specific left ventricular mass index (LVMI) z score and left ventricular hypertrophy ((LVH).
- There was an independent association between adiposity in children and LVMI z score and LVH; the association was stronger in girls than in boys.

AMERICAN SOCIETY OF TRANSPLANT SURGEONS

At the virtual American Society of Transplant Surgeons 21st Annual Winter Symposium, researchers from Natera, Inc. (San Carlos, California) presented recent case studies detailing the use of the Prospera™ test to detect active rejection and injury of kidney transplants. The test utilizes donor-derived cell-free DNA to monitor allograft health in situations where access to rapid biopsy results is challenging.

Incorporation of dd-cfDNA Testing in Clinical Practice

The treatment of choice for patients with end-stage kidney disease is kidney transplantation. Renal allograft failure occurs in 20% to 30% of kidney transplant recipients within 5 years. The current gold standard for diagnosing allograft rejection is biopsy, which is costly, invasive, and may be associated with post-procedural complications. Donor-derived cell-free DNA (dd-cfDNA) is a noninvasive biomarker for renal allograft injury including rejection.

Researchers at Natera, Inc., San Carlos, California, led by **Mark Fajardo, MHA, BSN, RN,** recently conducted a retrospective analysis on 1347 dd-cfDNA tests from 879 renal allograft recipients at 33 sites. Results of the analysis were reported during a virtual poster session at the American Society of Transplant Surgeons 21st Annual State of the Art Winter Symposium in a poster titled *Assessment of Donor-Derived Cell-Free DNA for Allograft Rejection in Kidney Transplant Patients and Its Incorporation into Clinical Practice*.

Blood samples were collected as part of routine clinical care, and the quality assurance team at Natera obtained data on biopsy and clinical follow-up. Prospera,™ a single-nucleotide polymorphism-based massively multiplexed-PCR test was used to identify dd-cfDNA in the 879 patients.

Of the 879 patients, 28 defined as high risk (dd-cfDNA fraction ≥1%) had definite biopsy results within 2 weeks of dd-cfDNA rejection test. Active rejection was diagnosed in 18 of those 28 high risk patients. Six of 10 biopsies with non-rejection showed other pathologic changes.

Median dd-cfDNA was higher in patients with T-Cell-mediated rejection (TCMR) than in those with antibody-mediated rejection (ABMR). Time to dd-cfDNA was longer for patients with ABMR rejection than for patients with TCMR, mixed rejection, or non-rejection.

In conclusion, the researchers said, "Analysis of real-world data revealed dd-cfDNA testing provided a 64% rejection rate among biopsies ordered by physicians in patients with a positive dd-cfDNA test. Abnormal pathological findings were noted in six of 10 biopsies with non-rejection consistent with allograft injury. dd-cfDNA identified TCMR, ABMR, and mixed rejection types, and dd-cfDNA detected active rejection both within the first year following transplant as well as after 1 year. Widespread adoption of routine dd-cfDNA testing may lead to a more judicious use of allograft biopsies and may detect rejection at an earlier, more treatable stage. Clinical follow-up provides vital information that is used to monitor test performance, identifies areas for additional research and development, and supports patient monitoring by providing longitudinal trend analysis."

Source: Fajardo M, McCormick S, Ahmed E, et al. Assessment of donor-derived cell-free DNA for allograft rejection in kidney transplant patients and its incorporation into clinical practice. Poster presented at the American Society of Transplant Surgeons virtual 21st Annual State of the Art Winter Symposium (E-poster 52), January 14, 2021. Support for this study was provided by Natera, Inc.

Anti-Rejection Therapies May Influence Total cfDNA Levels

To prevent rejection, recipients of organ transplants initiate a regimen of immunosuppressive medications. Modulation of immunosuppressants to prevent rejection is enabled via early detection of allograft injury. Kidney allograft rejection is indicated by elevated levels of donor-derived cell-free DNA (dd-cfDNA). Multiple factors, including therapy, surgical trauma, and comorbidities, can influence total levels of dd-cfDNA.

Prince Mohan, MD, at Geisinger Commonwealth Medical Hospital, Danville, Pennsylvania, and colleagues conducted a retrospective analysis of data from a patient with a biopsy confirmed antibody-mediated rejection who underwent serial blood draws for the assessment of dd-cfDNA. Results of the analysis were reported during a virtual poster session at the American Society of Transplant Surgeons 21st Annual State of the Art Winter Symposium. The poster was titled *Anti-Rejection Therapies in Renal Transplant Patients May Influence Total Cell-Free DNA, Impacting Relative Quantification of Donor-Derived Cell-Free DNA*.

The patient, a 52-year-old male, received a deceased donor kidney transplant in 2016. He was maintained on a triple immunosuppressive therapy regimen. His serum creatinine levels were stable, ranging from 1.4 to 1.6 mg/dL. At 4 years post-transplant, the patient presented with increased serum creatinine (2 mg/dL). Biopsy confirmed antibody-mediated rejection with moderate transplant glomerulopathy, and the patient was treated with plasmapheresis (1 gm/kg) and rituximab (1 gm). Following treatment, rejection was monitored with dd-cfDNA analysis on blood samples.

Five months after the biopsy confirmed active rejection, the initial blood test showed elevated dd-cfDNA level of 4.67%. Total cfDNA level was within the normal range. One month later, a second blood test demonstrated a drop in dd-cfDNA fraction of 0.64%, with a total cfDNA level elevated 11.2 times above the median. Subsequent blood tests demonstrated increases in dd-cfDNA and decreases in total cfDNA levels.

In conclusion, the researchers said, "These findings suggest that increases in total cfDNA levels may confound interpretation of dd-cfDNA test results. This case suggests that antirejection therapies may influence total cfDNA levels. The findings highlight the importance of continued monitoring of both dd-cfDNA and total cfDNA levels in identifying a true response to therapy."

Source: Mohan P, McCormick S, Wade H, et al. Anti-Rejection Therapies in Renal Transplant Patients May Influence Total Cell-Free DNA, Impacting the Relative Quantification of Donor-Derived Cell-Free DNA. Poster presented at the American Society of Transplant Surgeons virtual 21st Annual State of the Art Winter Symposium (E-poster 92), January 14, 2021. Support for this study was provided by Natera, Inc.

Monitoring Dual and en Bloc Kidney Transplant Patients for Allograft Rejection

End-stage kidney disease is commonly treated with kidney transplantation. However, the number of patients on the waitlist for transplant is significantly higher than the number of available donor organs; in 2019, there were approximately 95,000 patients on the waitlist to receive a kidney allograft.

According to **Obi Davies-Ekwenna, MD,** of the University of Toledo Medical Center, Toledo, Ohio, the donor pool could be increased with the use of high Kidney Door Profile Index (KDPI) organs as well as kidneys from small pediatric donors (en bloc). In those situations, dual kidney transplant may be associated with the best outcomes.

High KDPI organs have shorter graft survival times compared with low KDPI allografts. By identifying early signs of rejection, injury, and graft dysfunction, close monitoring may improve 1-year outcomes in patients receiving high KDPI organs. Donor derived cell-free DNA (dd-cfDNA) is an established biomarker for monitoring allograft rejection in kidney transplant recipients.

Dr. Ekwenna et al. conducted a retrospective analysis on data from nine patients who received dual or en bloc kidney transplants. Results of the analysis were reported during a virtual poster session at the American Society of Transplant Surgeons 21st Annual State of the Art Winter Symposium in a poster titled *Serial Testing with Donor-Derived Cell-Free DNA Test to Monitor Dual and en Bloc Kidney Transplants for signs of Rejection*.

In each patient, dd-cfDNA fractions were measured 2 to 3 weeks post-transplant using Prospera,™ a single nucleotide polymorphism (SNP)-based massively multiplexed PCR (mmPCr) assay. Four of the nine patients had elevated levels of dd-cfDNA.

Of those four, one patient experienced delayed graft function requiring dialysis, and one experienced thrombotic complications that required resection of one allograft. There was no clinical reason found for increased dd-cfDNA in the third patient; at a subsequent test 10 days later, dd-cfDNA decreased 1.7 times. The patient's dd-cfDNA levels are being monitored. The fourth patient experienced an increase in dd-cfDNA level. Biopsy revealed acute cellular rejection; the patient was treated with thymoglobulin and steroids and ultimately had rejection of the allograft.

All other patients are stable and undergoing serial monitoring.

"Dual and en bloc kidney transplants present unique situations where increased allograft volume or other factors not yet defined may contribute to increased basal levels of dd-cfDNA. Our early experience using dd-cfDNA to monitor dual/en bloc transplant recipients suggests that serial tests, starting early, can indicate allograft health," the researchers said.

Source: Davies-Ekwenna O, Brown ML, McCormick S, et al. Serial testing with donor-derived cell-free DNA test to monitor dual and en bloc kidney transplants for signs of rejection. Poster presented at the American Society of Transplant Surgeons virtual 21st Annual State of the Art Winter Symposium (E-poster 118), January 14, 2021. Support for this study was provided by Natera, Inc.

Elevated dd-cfDNA Levels to Monitor Patients with Delayed Graft Function

Among recipients of deceased donor kidney transplants, approximately 31% are affected by delayed graft function; in 2% of those cases, delayed graft function remains unsolved beyond 2 weeks. Biomarkers that predict the time to resolution of delayed graft function would allow optimal immunosuppression levels in the period immediately post-transplant.

Noninvasive assessment of kidney allograft injury and rejection can be achieved via measurement of donor-derived cell-free DNA (dd-cfDNA). Patients with dd-cfDNA levels elevated ≥1% are at risk for kidney rejection.

There are few data on the ability of dd-cfDNA to predict resolution in delayed graft function. **Obi Davies-Ekwenna, MD,** of the University of Toledo Medical Center, Toledo, Ohio, and colleagues conducted a retrospective analysis of data on 16 patients who underwent deceased-donor kidney transplantation and subsequently developed delayed graft function. Results of the analysis were reported during a virtual poster session at the American Society of Transplant Surgeons 21st Annual State of the Art Winter Symposium in a poster titled *Elevated Donor-Derived Cell-Free DNA in Patients with Delayed Graft Function.*

At an average of 2 weeks post-transplant, Prospera,™ a clinically validated dd-cfDNA assay was used to detect active rejection in each patient. At 4 to 9 weeks post-transplant, 13 of the 16 patients had one or more follow-up blood draws. Seven of the 16 had a biopsy accompanying one of the dd-cfDNA tests.

Mean dd-cfDNA level at the first blood draw was 1.32% (range 0.03% to 4.98%). Average time from transplant to first test was 15.57 days (range 5 to 28 days). Seven of the 16 patients had for-cause biopsies, and two had rejection. Both patients who had rejection had initial dd-cfDNA readings ≥1% threshold.

At the time of the first blood draw, nine patients had elevated dd-cfDNA levels (≥1%). Six of seven patients whose dd-cfDNA levels were <1% had resolution of delayed graft function within 2 weeks. Of the nine patients with elevated dd-cfDNA levels, six had resolution of delayed graft function within 2 weeks. One patient who had consistently elevated dd-cfDNA levels had persistent delayed graft function. At the follow-up blood draw, there was a mean decline of 30% in dd-cfDNA levels among those with elevated levels at the first draw.

"In this cohort, dd-cfDNA readings <1% were consistent with resolution of delayed graft function. Persistently elevated dd-cfDNA levels were associated with delayed graft function. Serial dd-cfDNA testing can be beneficial in monitoring kidney transplant patients with delayed graft function," the researchers said.

Source: Davies-Ekwenna O, Brown ML, McCormick S, et al. Elevated donor-derived cell-free DNA in patients with delayed graft function. Poster presented at the American Society of Transplant Surgeons virtual 21st Annual State of the Art Winter Symposium (E-poster 50), January 14, 2021. Support for this study was provided by Natera, Inc.

Monitoring Allograft Rejection with dd-cfDNA Testing

The current gold standard for diagnosis of allograft rejection is biopsy. However, access to biopsy services is limited in some areas. Donor-derived cell-free DNA (dd-cfDNA), a novel biomarker for monitoring transplant recipients for allograft rejection, provides an easily accessible tool for monitoring allograft health, and is particularly useful in locations where access to rapid biopsy results is difficult.

During a virtual poster session at the American Society of Transplant Surgeons 21st Annual State of the Art Winter Symposium, **David Ono, MD,** Hawaii Kidney Specialists, Honolulu, Hawaii, and colleagues reported on results from a retrospective analysis of data from four kidney allograft patients who underwent serial dd-cfDNA testing to monitor for graft rejection. The poster was titled *Clinical Utility of Donor-Derived Cell-Free DNA Testing for Allograft Rejection in Patients with Limited Access to Biopsy.*

The researchers examined levels of dd-cfDNA with patient blood draws by Natera (San Carlos, CA) using a single nucleotide polymorphism (SNP)-based massively multiplexed PCR (mmPCR) methodology.

Case Presentations

I. *Female, 67 years of age*. Recipient of a living non-related donor kidney transplant in 2009. Donor-specific antibodies developed in the absence of humoral rejection and patient was initiated on intravenous immunoglobulin therapy. Results of serial testing between March and October 2020 revealed transient increases in dd-cfDNA above the 1% threshold. Patient continually monitored for persistent changes in dd-cfDNA.

II. *Male, 66 years of age*. Recipient of a deceased donor kidney allograft in 2009. History of biopsy-proven antibody-mediated rejection, cytomegalovirus, viremia, and acute kidney injury. Results of serial testing between June and October 2020 showed persistently elevated dd-CFDNA levels, suggesting ongoing injury.

III. F*emale, 31 years of age*. Received a second kidney transplant in 2015. In 2016, had elevated levels of serum creatinine and a biopsy-confirmed Banff stage-1 B mixed rejection, necessitating anti-rejection treatment. Results of serial testing between June and December 2020 demonstrated consistently elevated dd-cfDNA levels.

IV. *Female, 32 years of age*. Recipient of a living, related donor kidney transplant in 2017. History of BK viremia required reduced mycophenolate mofetil dosing; patient was stable with negative donor-specific antibodies results. Results of serial testing between July and December 2020 revealed consistently elevated dd-cfDNA levels and a mild elevation in serum creatinine.

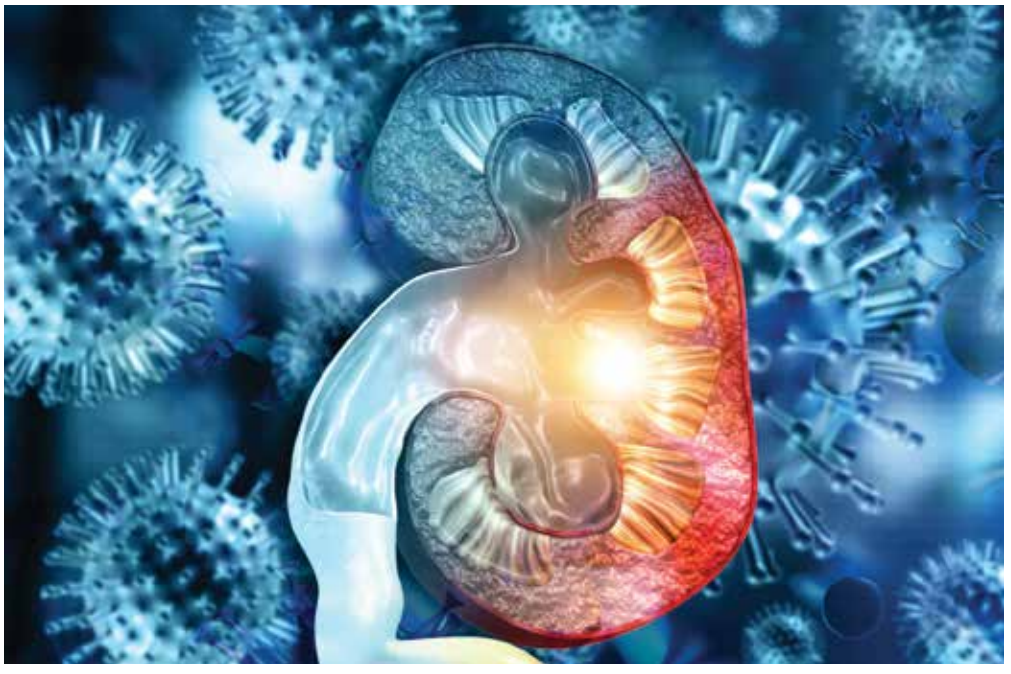
In conclusion, the researchers said, "dd-cfDNA test results for these kidney transplant recipients reflected patient histories of allograft injury and rejection. In these cases, dd-cfDNA testing was able to provide ongoing monitoring of allograft health. In locations with limited access to rapid biopsy reads, such as Hawaii, dd-cfDNA testing through serial draws can provide valuable information about allograft health and identify when a more in-depth investigation is required."

Source: Ono D, Hayashi R, McCormick S, et al. Clinical utility of donor-derived cell-free DNA testing for allograft rejection in patients with limited access to biopsy. Poster presented at the American Society of Transplant Surgeons virtual 21st Annual State of the Art Winter Symposium (E-poster 139), January 14, 2021. Support for this study was provided by Natera, Inc.

continued from page 1

and outcomes, immunosuppression management, and operational challenges facing transplant programs during the pandemic. To date, six retrospective studies from New York and Europe have reported on COVID-19 in kidney transplant recipients.

In one study of 36 patients, median age was 60 years, 72% were male, 39% were Black, and 75% received a deceased-donor transplant. The most common comorbidities were hypertension (94%), diabetes (69%), smoking (36%), and cardiovascular disease (17%). More than 85% were on mycophenolate/tacrolimus/prednisone maintenance immunosuppression and 42% received lymphocyte depleting induction. Twenty-eight patients were hospitalized; of those, all but one had radiologic evidence of a viral pneumonia. Of the patients with pneumonia, 11 required mechanical ventilation and six developed AKI that required renal replacement therapy. Of the 10 patients who died (median, 21 days), two were being monitored at home. Both were recent transplant recipients who received antithymocyte globulin within 5 weeks of presentation.



In a study at Columbia University of 15 kidney transplant recipients hospitalized with COVID-19, median age was 51 years, 65% were male, and 80% received a deceased-donor kidney transplant. Maintenance immunosuppression was primarily a regimen of an antimetabolite/tacrolimus/prednisone. The transplant program at Columbia adopts an early steroid-withdrawal strategy; however, the sample was enriched with patients on prednisone maintenance (67%), confirming the possible role of enhanced immunosuppression as a susceptibility factor.

Results of the early studies suggest that COVID-19 may present in an atypical manner in kidney transplant patients, with no fever, respiratory symptoms, or radiologic findings of pneumonia.

The optimal strategy for management of immunosuppression in transplant recipients with COVID-19 is unclear. Results of a study in cancer patients found that cancer patients with neutropenia have adverse outcomes, underscoring the role of the immune system in fighting the virus that causes COVID-19. Those results suggest the possibility of immunosuppression reduction to help alleviate the progression of SARS-CoV-2. However, that strategy may result in loss of the potential beneficial effect of immunosuppressive drugs in mitigating the systemic inflammatory response mediated by cytokine storm. In addition to antivirals, other strategies being investigated for the treatment of COVID-19 are adjunctive medications that target the inflammatory response, including glucocorticoids, interleukin-6 (IL-6) receptor antagonists, anticomplement-5 inhibitors, intravenous immunoglobulins, and mammalian target of rapamycin inhibitors that have been used for primary prevention and treatment of allograft rejection.

The role of diminished T-cell and B-cell immunity as a predisposing factor for severe infection is highlighted in the increased mortality among transplant recipients with COVID-19. However, to date, there is no level 1 evidence-based strategy to inform management of immunosuppression in that patient population. In patients with moderate disease, it may be reasonable to hold the antimetabolite and continue low-dose calcineurin inhibitor with or without glucocorticoids. In patients with severe disease and those who are critically ill, it may be justifiable to hold all maintenance immunosuppression and initiate remdesivir in addition to steroids.

Inflammatory biomarkers such as C-reactive protein, IL-6 levels, and ferritin have been shown to correlate with disease severity; albeit with substantial overlap and variability among patients. However, trending biomarkers in individual patients may play a role in guiding an immunosuppression reduction plan in those patients.

CHALLENGES FOR TRANSPLANT PROGRAMS

Many kidney transplant programs suspended or limited operations during the COVID-19 pandemic. Concerns and challenges facing kidney transplant programs and practices are multifaceted.

There is consensus that kidneys from deceased or living donors with confirmed infection of high risk of exposure to COVID-19 should not be used. While there are no data confirming donor to recipient viral transmission, the premise is plausible. There are three areas of concern: (1) the receptor that binds the spike protein of SARS-CoV-2 and facilitates its entry into targeted cells is angiotensin-converting enzyme 2; kidneys show the highest level of expression of the enzyme; (2) kidneys can be directly infected by SARS-CoV-2; and (3) SARS-CoV-2 viremia and viruria have been reported in 15% and 7% of COVID-19 patients, respectively.

Concerns are also related to the possibility of transplant team members as vectors of the virus. To date, 16% of all COVID-19 patients are healthcare workers; 29% of those had hospital-acquired infections. The possibility extends to organ procurement teams as well as transplant physicians and stresses the importance for appropriate physical distancing, hygiene, handwashing, and personal protective equipment for all team members.

In a survey of kidney transplant centers in the United States, 72% reported complete suspension of living donor transplant programs and 24% reported partial suspension of activities. Among deceased-donor programs, only 20% continued with no restrictions.

Most programs have adopted universal donor and recipient screening by nasopharyngeal nucleic acid testing (NAT) prior to transplantation. Only 17% of programs had blood NAT available to rule out viremia. For post-transplant care, 98% of centers limited in-person clinic visits and 97% reported adding telemedicine options.

In summary, the author said, "The COVID-19 pandemic has impacted transplantation and is associated with increased mortality among infected kidney transplant recipients. Without the availability of high-level evidence, most programs developed internal protocols to deal with new transplants and manage immunosuppression. Until effective therapies and a vaccine become available, we have to deal with this 'new normal' while taking care of our susceptible patient population. It is imperative for transplant providers to have a low threshold for suspecting SARS-CoV-2 infection and promptly initiate appropriate evaluation and immunosuppression reduction." ■

TAKEAWAY POINTS

- Coronavirus disease 2019 (COVID-19) is associated with adverse outcomes in kidney transplant recipients and has placed significant burden on kidney transplantation programs.
- Bassam G. Abu Jawdeh, MD, presented a review of COVID-19 and its impact in this patient population as well as challenges facing transplantation programs.
- Transplant providers should have a low threshold for suspected COVID-19 infections and steps in place for appropriate evaluation and reduction in immunosuppression in infected kidney transplant recipients.

Patients with CKD and Type 2 Diabetes and Comorbidities Face Higher Costs

TAKEAWAY POINTS

- Researchers conducted a retrospective cohort study to describe patients with type 2 diabetes and chronic kidney disease (CKD) and estimate the annual healthcare resource utilization and costs in that patient population, overall and stratified by disease severity and comorbidity subgroup.
- The rate of hospitalization was 7-fold higher among patients with type 2 diabetes and advanced CKD compared with those with an early stage of CKD.
- Patients with type 2 diabetes with CKD and anemia or heart failure had higher use of healthcare resources and higher healthcare-related costs, compared with patients with type 2 diabetes with CKD and no comorbidities.

Chronic kidney disease (CKD) is a common complication of type 2 diabetes mellitus, and is associated with considerable economic burden. CKD occurs in 20% of 40% of patients with diabetes, and costs incurred by patients with kidney disease and type 2 diabetes accounted for more than 50% of all Medicare costs in 2015. In addition, common comorbidities that include anemia, heart failure, and resistant hypertension are associated with worse health outcomes related to CKD. Annual spending for patients with CKD, type 2 diabetes, and heart failure was more than twice that for patients with CKD alone.

According to **Kerstin Folkerts, MS**, and colleagues, there are few real-world data available regarding costs and utilization of healthcare resources among patients with type 2 diabetes and CKD. Evidence that accounts for disease severity and additional comorbidities is even more scarce.

The researchers conducted a retrospective cohort study designed to describe patients with type 2 diabetes and CKD identified in US administrative claims data; the gold standard criteria for the diagnosis of kidney disease, results of specific laboratory tests for kidney function, were used to identify the patient population. A second study objective was an estimate of the annual healthcare resource use and costs among the patient population, both overall and stratified by disease severity and comorbidity subgroup. Results of the study were reported in the *Journal of Managed Care & Specialty Pharmacy* [2020;26(12):1506-1516].

The study period extended from January 1, 2008, through December 31, 2017. Patients ≥18 years of age with type 2 diabetes and newly recognized CKD were eligible. CKD was defined as at least two laboratory results for estimated glomerular filtration rate of <60 mL/min/1.73 m^2 or at least two results for urine albumin-to-creatinine ratio (UACR) of values between ≥30 mg/g between 90 to 365 days apart. The index date was the date of the second laboratory result confirming CKD; CKD stage was defined on the index date according to Kidney Disease: Improving Global Outcomes (KDIGO) CKD stage criteria

Additional inclusion criteria were a baseline diagnosis of type 2 diabetes, defined as at least one inpatient or two outpatient *International Classification of Diseases, Ninth/Tenth Revision, Clinical Modification* codes for type 2 diabetes at least 30 to 365 days apart; patients were also required to have a minimum of 365 days of baseline enrollment in a commercial or Medicare Advantage health plan prior to cohort entry date.

During the study period, there were 106,369 patients with type 2 diabetes and newly recognized CKD identified. Mean age was 70.6 years, 56.5% were female, 57.7% were White, and approximately 73% were Medicare Advantage patients.

Among patients with commercial health coverage, the mean and median number of days of follow-up were 300 days and 365 days, respectively. Among the Medicare Advantage patients, mean and median follow-up was 317 days and 365 days, respectively. In the commercial health plan group, 35.1% had fewer than 365 days of follow-up; in the Medicare Advantage group, 28.8% had fewer than 365 days of follow-up.

In the overall cohort, the most common comorbidities were hypertension (89.4%), hyperlipidemia (83.2%), and pain disorders (69.1%). Common comorbidities related to cardiovascular disease included angina pectoris (24.2%), resistant hypertension (15.9%), coronary artery disease (13.5%), heart failure (11.1%), and atrial fibrillation (10.2%). Seventy-four percent were classified as CKD stage 3.

Average inpatient, emergency department (ED), and outpatient visits per person per year (PPPY) among patients with type 2 diabetes and newly recognized CKD were 0.3, 0.7, and 12.6, respectively. Mean duration of all in-patient stays per patient during follow-up was 3.2 days.

Patients with type 2 diabetes with newly recognized CKD and comorbid heart failure had nearly three times higher mean count

of inpatient visits PPPY, three times longer average duration of inpatient stay, and twice the count of ED visits compared with patients without heart failure. Patients with type 2 diabetes and newly recognized CKD and comorbid anemia had double the mean number of hospital admissions PPPY and two times longer duration of inpatient stay compared with patients without anemia.

Among patients with type 2 diabetes and newly recognized CKD, those with advanced CKD had a seven-fold higher rate of hospitalization compared with those with an early disease stage. The mean duration of all inpatient visits was 10 times higher among patients with CKD stage 5 compared with patients with CKD stage 1.

For the overall cohort, mean annualized total cost was $24,029 PPPY. Mean costs for inpatient visits were $7223 PPPY, $5087 PPPY for outpatient visits, $1073 PPPY for ED visits, and $4672 PPPY for pharmacy costs.

Among patients with type 2 diabetes with newly recognized CKD and heart failure, total annualized costs were $41,951 PPPY; among those with anemia, total annualized costs were $33,127 PPPY. In all categories of care, mean annualized costs among patients with heart failure were higher than for those without heart failure: 2.6 times higher for inpatient visits, 1.8 times higher for outpatient visits, and 2.2 times higher for ED visits. Among patients with anemia, mean annualized cost was nearly double that of those without anemia ($11,338 PPPY vs $6292 PPPY, respectively).

Across worsening stages of CKD, annualized total cost was consistently higher; the higher costs were driven primarily by inpatient costs. Among patients with CKD stage 5, the total annualized cost was $17,432 PPPY among patients with normal UACR levels of <30 mg/g and $110,210 PPPY among patients with microalbuminuria (30-300 mg/g).

Among patients with type 2 diabetes and newly recognized CKD, those with advanced CKD had a seven-fold higher rate of hospitalization compared with those with an early disease stage.

Study limitations cited by the authors included laboratory results being available in only 30% of patients in the overall Optum Clinformatics Data Mart database, the potential for misclassification of diagnoses due to use of claims data, the possible imprecision of laboratory measurements of kidney function, the inability to assess the degree of variation of cost estimates at the population level, and the possibility that the results are not generalizable to non-US-based patients and noncommercially insured populations in the United States.

In conclusion, the researchers said, "While CKD typically develops many years after the initial diagnosis of diabetes, it may also be present at the time of the type 2 diabetes diagnosis. Despite the high burden of CKD among patients with type 2 diabetes, many patients are unaware of their condition and face delays in CKD diagnosis and proper treatments. This study indicates that CKD patients with more advanced disease and other comorbidities have much higher healthcare resource use and cost. Given these findings, it is possible that earlier diagnosis of CKD and its complications in patients with type 2 diabetes, as well as interventions that are effective in halting or slowing the progression of CKD and treating other comorbid conditions, could result in substantial cost savings. The net cost benefit of such interventions will need to be assessed in future studies." ■

Renal-Focused Genomic Registry Launched

Fresenius Medical Care has announced an initiative to develop the world's largest renal-focused genomic registry brand. The company's Frenova division enrolled the first participants early in 2021. In a press release, Fresenius also announced that **Ali Gharavi, MD,** chief of the division of nephrology at Columbia University Irving Medical Center and professor of nephrology at Columbia University Vagelos College of Physician and Surgeons, will lead the project and act as principal investigator.

Frenova oversees studies within the clinical footprint of Fresenius Medical Care, a leading provider of products and services for people with chronic kidney failure including dialysis treatments for ~350,000 patients worldwide. The renal-based genomic registry is a new business line within Frenova, and is based in Fresenius Medical Care's Global Medical Office.

The registry will contain genetic sequencing data from patients with CKD and will be used by researchers to improve understanding of kidney disease. The registry was created to address the lack of large-scale, renal-focused registry of genomic and clinical data.

Franklin W. Maddux, MD, global chief medical office at Fresenius Medical Care, said, "The new Frenova registry will close this gap by generating data that add a clinical and genetic backbone to help support and fuel scientific innovation. The evidence for genetic drivers in kidney diseases is substantial, but much larger data sets will be needed to untangle the complex interactions that lead to kidney injury. By combining clinical and genetic sequencing data from ethnically and pathologically diverse participants, this genomic and phenotypic research resource will help scientists better understand how genetic variations in patients can lead to more precise diagnoses and therapies that help improve outcomes by individualizing care."

Kurt Mussina, president of Frenova, said, "Our renal-focused genomic registry will be a sustainable and comprehensive tool for kidney-focused research. It will bring patients, their families, patient advocacy groups, physicians, and researchers together in the common cause of improving the lives of people living with kidney disease."

Partnership Aims for Early Identification of CKD Progression Risk

In a press release, RenalytixAI and DaVita announced a partnership in a program aimed at slowing progression of kidney disease and improving health outcomes among the estimated 37 million adults in the United States living with chronic kidney disease. The program is designed to improve patient outcomes and realize cost reductions for healthcare providers and payers by enabling earlier intervention for patients with early-stage kidney disease (stage 1, 2, and 3) via actionable risk assessments and end-to-end care management. The program will launch in three major markets in 2021.

Javier Rodriguez, CEO of DaVita, said, "Almost 50% of people whose kidneys fail find out after it is too late, and we are on a mission to change that. Our partnership with RenalytixAI could allow us to help slow disease progression for the millions of people living with kidney disease.

The program will utilize the RenalytixAI's KidneyIntelX in vitro diagnostic platform that uses a machine learning algorithm to assess a combination of biomarkers from a simple blood draw with features from the electronic health record to generate a patient-specific risk score. The integrated program may also help to reduce misclassification of kidney disease.

James McCullough, CEO at RenalytixAI, said, "This is the first clinical-grade program that delivers advanced early-stage prognosis and risk stratification, combined with actionable care management right to the primary care level where the majority of kidney disease patients are being seen. Making fundamental change in kidney disease economics and outcomes must begin with providing a clear, actionable understanding of disease progression risk."

Following risk stratification, patients identified as intermediate and high risk will receive care management support through DaVita's integrated kidney care program. Among patients whose disease progresses, earlier intervention can result in more time for the patient and nephrologist to make an informed decision about treatment options, including pre-emptive transplantation, home dialysis, or in-center dialysis. For patients who opt to initiate dialysis, the extra time will increase the chance for an out-patient dialysis start, avoiding initiation of dialysis with a costly hospitalization.

RenalytixAI Applauds CMS Finalization of MCIT Rule

Early in 2021, the Centers for Medicare & Medicaid Services (CMS) announced the establishment of the Medicare Coverage of Innovative Technology (MCIT) pathway. The pathway was established to provide a coverage mechanism for Medicare beneficiaries to have faster access to innovative medical devices and diagnostic tests designated under the Breakthrough Device review program and with market authorization by the FDA.

Under the MCIT, national Medicare coverage can become effective on the date of FDA approval or clearance of a breakthrough designated device and will continue for 4 years. At the end of the 4-year period, continued coverage for Medicare beneficiaries will be based on one of three methods: (1) case-by-case coverage; (2) local coverage determination; or (3) a national coverage determination.

MAJOR MEETINGS 2021

National Kidney Foundation Spring Clinical Meetings 2021

April 6-10, 2021

Virtual

www.kidney.org/spring-clinical

American Nephrology Nurses Association 2021 National Symposium

May 2-5, 2021

Virtual

www.annanurse.org/events/2021-national-symposium

American Transplant Congress 2021

June 5-9, 2021

Virtual

atcmeeting.org

American Society of Nephrology Kidney Week 2021

November 2-7, 2021

San Diego, California

www.asn-online.org/education/kidneyweek/archives/future.aspx

In a press release, **Tom McLain,** president of RenalytixAI, said, "Having a clear path to national Medicare coverage for innovative products like KidneyIntelX provides a major catalyst to drive the robust research and clinical development programs necessary to address major unmet medical needs such as kidney disease. MCIT will also encourage early engagement with FDA in developing new diagnostic tests and leverage the many benefits of Breakthrough Designation including priority review of needed technology. We appreciate the opportunity to work with the FDA and CMS to tackle the critical issue of early stage prognosis to help slow or prevent kidney disease progression. This new coverage pathway will facilitate accelerated access to KidneyIntelX for Medicare beneficiaries and their primary care doctors to help assure a better quality of life and save lives."

KidneyIntelX, RenalytixAI's lead product, was granted FDA breakthrough designation in May 2019. In August 2020, RenalytixAI submitted its DeNovo 510K application for clearance. When FDA clearance is received in 2021, RenalytixAI will opt in for the automatic 4-year national Medicare coverage period. In addition to the MCIT coverage pathway for the test, RenalytixAI has designed a prospective utility and outcome study to further demonstrate the clinical value of KidneyIntelX testing in delaying or preventing the progression of early-stage diabetic kidney disease.

Last Mile Delivery Solution Improves Distribution of Home Dialysis Equipment

In a recent press release, Fresenius Medical Care North American (FMCNA) and Descartes Systems Group announced the rollout of Descartes' last mile delivery solution to improve the distribution of equipment and services to home dialysis patients and centers across the United States. FMCNA is a leading provider of kidney care products and services and Descartes Systems Group is a leader in uniting logistics-intensive businesses in commerce.

Scott McLean, director of transportation at FMCNA, said, "We take great pride in the superior care we give to our patients and the best-in-class service we provide to our customers. Our distribution operations are fundamental to this commitment and the Descartes solution allows us to realize greater efficiencies managing over 400 vehicles on a daily basis to support people who are relying on our critical medical supplies."

The last mile delivery solution provides an end-to-end platform for home and last mile delivery operations. The enhancements support efforts to increase adoption of home dialysis treatment for patients with kidney failure, an FMCNA priority and a goal of the federal government's Advancing American Kidney Health Initiative.

continued on page 18

Print-only Content

continued from page 17

"We are pleased to help Fresenius Medical Care North American make the distribution of its services and equipment more responsive and efficient," **James Wee,** vice president at Descartes said. "By optimizing the entire delivery process from appointment booking to post-delivery, Descartes' proven last mile delivery solution changes how companies engage with their customers, elevating the customer experience while minimizing delivery costs."

The solution was rolled out beginning in February in select markets within TruBlu Logistics®, the supply chain division of FMCNA. The full nationwide rollout, including patient scheduling and notification, is expected later this year.

Print-only Content

AKF and GSK Launch Resource for Lupus Nephritis Patients

Lupus nephritis is the subject of a new patient-focused education and awareness campaign launched by the American Kidney Fund (AKF). Lupus nephritis is a form of kidney disease caused by lupus. The new campaign will provide information about the signs, symptoms, and treatment of lupus nephritis. The campaign has been developed with grant support from GSK.

LaVarne A. Burton, president and CEO of AKF, said, "Lupus nephritis is challenging to diagnose because it does not always have major symptoms and it can look like so many other conditions, which is why many patients do not get the timely, accurate diagnoses they so desperately need. We are grateful to GSK for working with us to support the lupus community with educational resources that are aimed at early detection and careful management of lupus nephritis so that fewer patients will experience kidney failure from this condition."

The campaign will include a suite of resources, beginning with a doctor discussion guide to help patients manage the range of specialists that they should consult, including a primary care physician, nephrologist, cardiologist, renal dietitian, as well as a therapist, counselor, or social worker. The campaign will continue throughout 2021 and will release additional educational resources as the year progresses.

Bernie Rubin, MD, US medical affairs director, GSK, said, "Kidney damage is one of the most serious complications of lupus, and GSK is passionate about making a positive impact in the lives of people at risk for, or living with, lupus nephritis. Patient-facing educational resources and outreach can help improve the lives of people with lupus, and we are proud to support this initiative led by the American Kidney Fund." ■

COVID-19

Glomerular Disease Associated with COVID-19

Journal of the American Society of Nephrology. 2021;32(1):33-40

Patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection may develop acute kidney injury (AKI) with high-grade proteinuria, as documented by recent studies. In some patients, biopsies have revealed collapsing glomerulopathy, a distinct form of glomerular injury that has been associated with other viruses, such as HIV. Patient reports have described patients of African ancestry who developed nephrotic-range proteinuria and AKI early in the course of SARS-CoV-2 infection.

Researchers from the division of nephrology and hypertension, Northwestern University Feinberg School of Medicine, Chicago, Illinois, led by **Aneesha A. Shetty, MD,** reported a patient series of six patients with coronavirus disease 2019 (COVID-19), AKI, and nephrotic-range proteinuria. COVID-19 was diagnosed by a positive nasopharyngeal swab RT-PCR for SARS-CoV-2 infection.

Biopsy specimens from one transplanted kidney and five native kidneys were examined. Three of the six patients underwent genetic analysis of *APOL1*, the gene encoding the APOL1 protein, from DNA extracted from peripheral blood. The researchers also purified genomic DNA from paraffin-embedded tissue and performed *APOL1* genotype analysis of one of the native biopsies and the donor kidney graft.

All of the six patients were of African ancestry, and developed AKI associated with COVID-19 with podocytopathy, collapsing glomerulopathy, or both. The patients experienced generally mild respiratory symptoms and none required ventilator support.

High-risk *APOL1* genotypes were confirmed by genetic testing in three patients. One of those three patients developed collapsing glomerulopathy in the engrafted kidney. The kidney had been transplanted from a donor who carried a low-risk *APOL1* genotype, contradicting models of APOL1-mediated kidney injury, and suggests that intrinsic renal expression of APOL1 may not be the driver of nephrotoxicity and specifically, of podocyte injury.

"Glomerular disease presenting as proteinuria with or without AKI is an important presentation of COVID-19 infection and may be associated with a high-risk *APOL1* genotype," the researchers said.

Risk Factors for RRT Dependence in Patients with COVID-19 Related AKI

Journal of the American Society of Nephrology. 2021;32(1):161-176

Patients with coronavirus disease 2019 (COVID-19) may develop acute kidney injury (AKI). However, there are few data available regarding COVID-19 patients with AKI requiring renal replacement therapy (AKI-RRT). **Shruti Gupta, MD,** of the division of renal medicine, Brigham and Women's Hospital, Boston, Massachusetts, and colleagues conducted a study to identify risk factors for AKI-RRT, as well as risk factors for 28-day mortality among patients with AKI-RRT.

The multicenter cohort study included 3099 critically ill patients with COVID-19 who were admitted to intensive care units (ICUs) at 67 hospitals in the United States. Identification of patient- and hospital-level risk factors for AKI-RRT and risk factors of 28-day mortality in that patient population utilized multivariable logistic regression.

Of the 3099 patients, 20.6% (n=637) developed AKI-RRT within 14 days of ICU admission; of those, 54.9% (n=350) died within 28 days of ICU admission. Patient-level risk factors for AKI-RRT included chronic kidney disease, male sex, non-White race, hypertension, diabetes mellitus, higher body mass index, higher D-dimer, and greater severity of hypoxemia on admission to the ICU. Predictors of 28-day mortality were older age, severe oliguria, and admission to a hospital with fewer ICU beds or one with greater regional density of COVID-19.

At the end of a median follow-up of 17 days (range, 1-123 days), 63.3% (403/637) of the cohort had died, 33.9% (n=216) were discharged, and 2.8% (n=18) remained hospitalized. Of the 216 discharged patients, 33.8% (n=73) were RRT-dependent at discharge; 18.1% (n=39) remained RRT dependent 60 days following ICU admission.

In conclusion, the researchers said, "AKI-RRT is common among critically ill patients with COVID-19 and is associated with a hospital mortality rate of >60%. Among those who survive to discharge, one in three still depends on RRT at discharge, and one in six remains RRT dependent 60 days after ICU admission."

CHRONIC KIDNEY DISEASE

Slopes in eGFR Decline Associated with Mortality Risk

Journal of the American Society of Nephrology. 2020;31(12):2912-2923

Slopes of estimated glomerular filtration rate (eGFR) are associated with increased risk of death and cardiovascular disease in a U-shaped fashion. Poor outcomes in patients with rising eGFR may be attributable to sarcopenia, hemodilution, and other indications of clinical deterioration.

Paula F. Orlandi, MD, Center for Clinical Epidemiology and Biostatistics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, and colleagues conducted an analysis of data from the multicenter Chronic Renal Insufficiency Cohort (CRIC) study. The researchers sought to examine the association between eGFR slopes and risks of death or cardiovascular events, accounting for multiple confounders.

The analysis used linear, mixed-effects models to estimate slopes with up to four annual assessments of eGFR and Cox proportional hazards models to examine the association between slopes and the risks of death and cardiovascular events. The cohort included 2738 individuals with moderate to severe chronic kidney disease.

Slopes of eGFR had a bell-shaped distribution (mean, –1.5 mL/min/1.73 m^2 per year). There was an association between declines of eGFR that were steeper than the average decline and progressively increasing risk of death: hazard ratio (HR), 1.23; 95% confidence interval (CI), 1.09-1.39; for a slope 1 standard deviation below the average. There was also an association between steeper than average eGFR declines and increasing risk of cardiovascular events: HR, 1.19; 95% CI, 1.03-1.38. There were no associations between rises or declines in eGFR lower than the average decline and the risk of death or cardiovascular events.

In conclusion, the researchers said, "In a cohort of individuals with moderate to severe CKD, we observed steep declines of eGFR were associated with progressively increasing risks of death and cardiovascular events; however, we found no increased risks associated with eGFR improvement. These findings support the potential value of eGFR slopes in clinical assessment of adults with CKD."

Short-Duration Sleep Behaviors Associated with Adverse Effect on Kidney Function

Journal of the American Society of Nephrology. 2020; 31(12):2937-2947

Results of earlier studies have shown an association between sleeping behaviors, such as sleep duration, and kidney function and risk of cardiovascular disease. There are few data available on whether short or long sleep duration is a causative factor for impairment of kidney function. **Sehoon Park, MD,** and colleagues in South Korea conducted an analysis of data from participants 40 to 69 years of age in the UK Biobank prospective cohort, including 25,605 who self-reported short duration sleep (<6 hours per 24 hours), 404,550

continued on page 20

continued from page 19

who self-reported intermediate-duration sleep (6 to 8 hours), and 35,659 who self-reported long-duration sleep (≥9 hours).

The researchers used logistic regression analysis to examine the association between the sleep duration group and prevalent chronic kidney disease (CKD) stages 3-5. They performed Mendelian randomization (MR) analysis involving 321,260 White British individuals using genetic instruments (genetic variants linked with a short- or long-duration sleep behavior as instrumental variables), as well as genetic risk score analysis as a one-sample MR and extended the finding with a two-sample MR analysis with CKD outcome information from the independent CKDGen Consortium genome-wide association study meta-analysis.

Compared with intermediate-duration sleep, short or long sleep duration was clinically associated with higher prevalence of CKD. The genetic risk score for short (but not long) sleep duration was significantly related to CKD (per unit reflecting a two-fold increase in the odds of the phenotype; adjusted odds ratio, 1.80; 95% confidence interval, 1.25-2.60). In two-sample MR analysis, there were causal effects of short duration on CKD by the inverse variance weighted method, supported by causal estimates from MR-Egger regression.

"These findings support an adverse effect of a short sleep duration on kidney function. Clinicians may encourage patients to avoid short-duration sleeping behavior to reduce CKD risk," the researchers said.

Early Change in Albuminuria with Canagliflozin Predicts Renal Outcomes

Journal of the American Society of Nephrology. 2020;31(12):2925-2936

Results of previous studies have suggested an association between early changes in albuminuria and kidney and cardiovascular events; those results were primarily in studies of renin-angiotensin blockade. There are few data available on whether the association occurs with sodium-glucose cotransporter 2 inhibition.

Megumi Oshima, MD, and colleagues conducted a post hoc analysis of data from the CREDENCE (Canagliflozin and Renal Events in Diabetes with Established Nephrology Clinical Evaluation) trial to assess canagliflozin's effect on albuminuria and the association between early change in albuminuria (from baseline to week 26) and the primary kidney outcome (end-stage kidney disease, doubling of serum creatinine, or kidney death), major adverse cardiovascular events, and hospitalization for heart failure or cardiovascular death.

The CREDENCE trial enrolled 4401 patients with type 2 diabetes and chronic kidney disease (CKD), defined as urinary albumin-creatinine ratio (UACR) >300 mg/g. Of the 4401 patients, 87.2% (n=3836) had complete data for early change in albuminuria and other covariates. Compared with placebo, canagliflozin lowered UACR by 31% (95% confidence interval [CI], 27%-36%) at week 26, and significantly increased the likelihood of achieving a 30% reduction in UACR (odds ratio, 2.69; 95% CI, 2.35-3.07).

Over the 26 weeks, there was an independent association between each 30% decrease in UACR and a lower hazard for the primary kidney outcome (hazard ratio [HR], 0.71; 95% CI, 0.67-0.76; $P<.001$), major adverse cardiovascular events (HR, 0.92; 95% CI, 0.88-0.96; $P<.001$), and hospitalization for heart failure or cardiovascular death (HR, 0.86; 95% CI, 0.81-0.90; $P<.001$). At week 26, residual albuminuria levels remained a strong independent risk factor for kidney and cardiovascular events, overall and in each treatment arm.

In conclusion, the researchers said, "In people with type 2 diabetes and CKD, use of canagliflozin results in early, sustained reductions in albuminuria, which were independently associated with long-term kidney and cardiovascular outcomes."

DIALYSIS

Diet Therapy Efficacious for Management of Hyperphosphatemia

Clinical Journal of the American Society of Nephrology. 2021;16(1):107-120

Individuals undergoing maintenance hemodialysis commonly experience hyperphosphatemia, a risk factor for vascular and bone complications. Some dialysis centers have dietitians who work with patients to help them manage their serum phosphate level. **David E. St-Jules, PhD,** at the University of Nevada, Reno, and colleagues conducted a systematic review and meta-analysis of clinical trials to evaluate the evidence for that practice.

The review included MEDLINE, Embase, CINAHL, Web of Science, Cochrane Central Register of Controlled Trials, and other databases. The researchers searched for trials published in English from January 2000 through November 2019. Inclusion criteria were studies designed to examine the effect of phosphate-specific diet therapy provided by a dietitian on serum phosphate levels in individuals on hemodialysis. The Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) method was used to assess the risk of bias and certainty of evidence.

The search included 8054 titles/abstracts. Of those, 168 articles were reviewed and 12 clinical trials were included in the final review. Of the 12 trials, 11 were randomized and one was nonrandomized.

In all 12 studies, diet therapy reduced serum phosphate compared with controls; the reduction reached statistical significance in eight of the 12 studies, although overall certainty of the evidence was low, due to randomization issues and deviations from protocol.

CONFERENCE COVERAGE **KIDNEY WEEK 2020**

Metabolic Acidosis Associated with Increased Mortality Risk

Patients with metabolic acidosis may develop wide-ranging complications consistent with the fact that many critical cell functions require physiologic pH. However, according to **Navdeep Tangri, MD, PhD, FRCP,** and colleagues, there are few data available on the extent to which metabolic acidosis is associated with mortality in patients with chronic kidney disease (CKD). The researchers conducted an analysis of a de-identified Electronic Health Records dataset (Optum®) from 2007 to 2017. Results of the analysis were reported during a virtual poster session at ASN Kidney Week 2020 in a poster titled *Metabolic Acidosis Is a Predictive Factor for All-Cause Mortality in Patients with CKD.*

The dataset was utilized to identify patients with non-dialysis-dependent CKD stages 3-5 with two or more consistent serum bicarbonate tests 28 to 365 days apart, three or more estimated glomerular filtration rate (eGFR) values <60 mL/min/1.73 m^2, and two or more years of post-index data, or mortality during the study period. Patients were stratified into two groups based on baseline serum bicarbonate level: (1) metabolic acidosis, serum bicarbonate 12 to 22 mEq/L or (2) normal serum bicarbonate, 22 to 29 mEq/L.

All-cause mortality was measured at 2 years in patients with metabolic acidosis versus normal serum bicarbonate at baseline. Logistic regression models were used to assess the impact of baseline serum bicarbonate on 2-year mortality, adjusted for age, sex, race, diabetes, hypertension, heart failure, Charlson Comorbidity Index score, baseline eGFR, and log albumin-to-creatinine ratio (ACR).

The analysis included 51,558 patients; of those, 17,350 had metabolic acidosis and 34,208 had normal serum bicarbonate at baseline. The unadjusted rates of mortality within 2 years were higher in the metabolic acidosis group than in the normal serum bicarbonate group (30.9% vs 10.2%, respectively; $P<.0001$) and within all stages of CKD ($P<.001$). There was an independent association between each 1 mEq/L lower serum bicarbonate value and a 15% higher risk of all-cause mortality (odds ratio, 0.853; 95% confidence interval, 0.846-0.861). Findings were consistent in subgroup and sensitivity analyses.

"The presence of metabolic acidosis was associated with a high 2-year risk of all-cause death in patients with CKD. This finding was independent of age, sex, race, pre-existing comorbidities, and baseline eGFR and ACR," the researchers said.

Source: Tangri N, Reaven NL, Funk SE, Mathur VS. Metabolic acidosis is a predictive factor for all-cause mortality in patients with CKD. Abstract of a poster presented at the American Society of Nephrology virtual Kidney Week 2020 (P01483), October 22, 2020.

Funding for this poster was provided by Tricida, Inc.

In patients with persistent hyperphosphatemia, monthly diet therapy of 20 to 30 minutes per session significantly lowered serum phosphate for 4 to 6 months, without compromising nutrition status; however, the intervention appeared unlikely to maintain the effects if discontinued. The trials were too varied in design, setting, and approach to appropriately pool in meta-analysis, and were too limited in number to assess the timing, dose, and strategy of phosphate-specific diet therapy.

In conclusion, the researchers said, "There is low-quality evidence that monthly diet therapy by a dietitian appears to be a safe and efficacious treatment for persistent hyperphosphatemia in patients on hemodialysis."

TRANSPLANTATION

Pulmonary HT in Patients Screened for Kidney Transplantation

Transplantation. 2020;104(10):2113-2119

Patients with advanced chronic kidney disease frequently present with pulmonary hypertension, a risk factor for early allograft failure and death. The causes of pulmonary hypertension are heterogeneous and, according to **Melissa C. Caughey, PhD,** and colleagues, patient prognosis may vary by etiologic subtype.

The researchers utilized data from the University of North Carolina Cardiorenal Registry to examine associations between pulmonary hypertension, with or without elevated left atrial pressure (eLAP), and mortality in candidates for kidney transplantation. Pulmonary hypertension was determined by Doppler echocardiography; eLAP was determined by tissue Doppler imaging.

The registry preoperatively screened 778 patients by echocardiology from 2006 to 2013. Of those, mean age was 56 years, 64% were Black, and 56% were male. Pulmonary hypertension was identified in 12% (n=97); eLAP was prevalent in half of those patients.

Median follow-up was 4.4 years. During follow-up, 23% (n=179) of patients received a kidney transplant and 25% (n=195) died. Following adjustment for demographics, comorbidities, dialysis vintage, and kidney transplantation, there was an association between pulmonary hypertension and twice the 5-year mortality (hazard ratio [HR], 2.11; 95% confidence interval [CI], 1.48-3.03). The associations were stronger in the absence of eLAP (HR, 2.87; 95% CI, 1.83-4.49) than with eLAP (HR, 1.11; 95% CI, 0.57-2.17), *P* for interaction .01.

In conclusion, the researchers said, "The mortality risk associated with pulmonary hypertension among patients with advanced chronic kidney disease appears to differ by etiology. Patients with pulmonary hypertension in the absence of eLAP are at high risk of death and in need of focused attention. Future research efforts should investigate potential strategies to improve outcomes for these patients." ■

Print-only Content

Conversation with an Expert

Joseph Vassalotti, MD
Chief Medical Officer of the
National Kidney Foundation

Nephrology Times recently spoke with **Joseph Vassalotti, MD,** chief medical officer of the National Kidney Foundation, to discuss a recent partnership with Healthy.io, the category creator of smartphone urinalysis, to offer free at-home testing to Americans at risk for kidney disease.

NEPHROLOGY TIMES: The National Kidney Foundation recently partnered with Healthy.io. Can you talk to us a little bit about who they are, what this partnership is about, and the significance of this partnership?

DR. VASSALOTTI: This partnership really is about understanding that there are people with kidney disease and people at risk for kidney disease, and the National Kidney Foundation has a risk campaign that is targeted to people with conditions like diabetes to help them understand that they need to partner with their clinicians for blood and urine testing to find out if they have kidney disease.

The blood and urine testing will also tell them if they have kidney disease, how severe it is, and help them work with their clinicians to determine the best treatments, which may involve medications, and also the best ways that they can become engaged in their care with lifestyle changes, maybe with diet and physical activity, and also to understand what kind of targets they need for their diabetes, how to control their diabetes, to help reduce the risk of worsening kidney disease and other diabetes complications.

NT: How prevalent is kidney disease in the US?

DR. VASSALOTTI: According to the CDC, about 15% of the US population, or 37 million American adults, have chronic kidney disease, and diabetes is the most common cause [of death] in the United States.

NT: How important is early diagnosis?

DR. VASSALOTTI: It's been estimated that one in three Americans is at risk for kidney disease, with conditions like diabetes and high blood pressure, obesity, cardiovascular disease, and also a family history of kidney disease. Kidney disease can run in families, so it's important to talk to your family about health history and particularly kidney disease.

NT: Can you talk to us about the uACR [urine albumin-to-creatine ratio] test? Where can people go to access the Kidney Risk Assessment Quiz?

DR. VASSALOTTI: The Kidney Risk Assessment Quiz is available on the National Kidney Foundation website. If you go to the main page, kidney.org, there's a very simple quiz. It's just a number of questions about your health status, with things like the risk conditions I mentioned before, particularly diabetes, to see if you're at risk, and then also to partner with your clinicians for testing.

The Healthy.io product is a type of urine testing that can be offered to a patient with a clinician or can be offered in the patient's home. So, it's a convenient way to do one of the tests for kidney disease, and that's the urine albumin-to-creatinine ratio. It's a urine test of kidney damage, and there's another test that we call a test of kidney function that comes from the blood, and that's the estimated glomerular filtration rate [eGFR].

NT: Closing thoughts?

DR. VASSALOTTI: Well, for primary care clinicians it's so important to test individuals with the risk conditions. Diabetes, I think, is the most important one that I've mentioned several times today. Do your patients with diabetes have these tests annually, the eGFR and the urine albumin-to-creatinine ratio? Are you acting on those tests? Those test results should help you inform how you control the blood pressure, how you control the diabetes. If patients have elevated albumin in the urine, that's a sign that they will benefit from angiotensin converting enzyme inhibitors and angiotensin receptor blockers for blood pressure control. That's also a sign, if they have diabetes, that they may benefit from a new class of medicines called SGLT2 [sodium-glucose cotransporter 2 inhibitors] or flozins.

These are kidney- and cardioprotective, so we should certainly encourage use of those. If the patient has a high level of albumin in the urine, there may be another condition going on and you may want to consult with a nephrologist. You may want to consult with a dietician. You may want to consult with a pharmacist to help you manage your patient. And, of course, the level of kidney function by the eGFR is important for you to think about what kind of interventions you apply and also when to refer to a nephrologist. In general, the opinion-based recommendation is that when the eGFR is less than 30 [mL/min/1.73 m^2], a nephrologist should be consulted. And that would also follow care coordination so that you work with a nephrologist to determine what stays in the primary care space and what the nephrologist will address. ■

Sarah Tolson

Clarifications and Further Changes to 2021 ESRD PPS

Shortly after I submitted last month's edition of From the Field, the Centers for Medicare & Medicaid Services (CMS) released an updated change request in which they rescinded the requirement for reporting the total monthly minutes of dialysis provided to a patient (see Change request 12011 for details). On the one hand, I am relieved these data will not be required on claims; however, I am not looking forward to updating training documents to remove the short-lived condition code D6.

As we discussed in the last edition of From the Field, the other substantial change to the ESRD PPS for 2021 is the reimbursement and billing requirements for calcimimetics. Effective with January 2021 dates of service, CMS will no longer reimburse calcimimetics under the Transitional Drug Add-On Payment Adjustment (TDAPA). Rather, oral and injectable calcimimetics will be eligible for an outlier adjustment, and reimbursement will be included in the ESRD PPS base rate just like oral vitamin D and erythropoietin stimulating agents.

At the time of this writing, one point that seems to be unclear is the exact billing requirements for reporting oral calcimimetics on a ESRD facility claim now that they are no longer reimbursed under TDAPA. During the time that calcimimetics were reimbursed under TDAPA, CMS required oral cinacalcet to be reported with revenue code 0636, HCPCS (Healthcare Common Procedure Coding System) code J0604 and modifier AX. In late 2020 and early 2021, Medicare released some guidance to dialysis facilities that indicates cinacalcet should be billed similarly to other oral medications that have been eligible for outlier payment for many years now. Additionally, there was guidance issued to Medicare Administrative Contractors to "Discontinue processing the TDAPA for J0604 and J0606 when billed with modifier AX" for date of service on or after January 1, 2021. While the exact requirements are unclear at the time of this writing, I am confident that the ambiguity will be resolved quickly.

2021 ESRD PPS CALCIMIMETICS REIMBURSEMENT

The biggest reimbursement changes in the 2021 ESRD PPS were the terminating reimbursement for oral and injectable calcimimetics under TDAPA and adding calcimimetics to the list of items that qualifies for an outlier adjustment. Under TDAPA, CMS reimbursed dialysis facilities for the number of units of calcimimetics they administered to their patients. In lieu of reimbursing calcimimetics under TDAPA, CMS increased the 2021 ESRD PPS base rate amount by $14, $10 of which was earmarked for calcimimetics.

In conjunction with adding calcimimetics to the list of items that qualify for an outlier adjustment, CMS significantly increased the Fixed Dollar Loss (FDL) amount for 2021. For an adult dialysis claim to be eligible for an outlier payment, the average per treatment allowed amount for the drugs, labs, and supplies eligible for an outlier included on the claim must exceed approximately $174 per treatment (this number is comprised of the adult 2021 MAP of $50.92 and FDL of $122.49).

When CMS released the proposed rule for the 2021 ESRD PPS, my company completed analyses of our clients' calcimimetics utilization and reimbursement so they would have an idea what the fiscal impact of incorporating calcimimetics reimbursement into the ESRD PPS would be. The common theme was that all the dialysis programs that were utilizing calcimimetics in their Medicare patient populations were receiving, on average, more than the additional $9.93 per treatment allotted in the 2021 base rate—but less than the amount needed to qualify for an outlier payment adjustment.

Of the dialysis programs that my company bills for, there are several programs that have not incorporated calcimimetics. For dialysis programs such as these, the increase in the ESRD PPS will be a very welcome increase in revenue. However, in dialysis programs that have incorporated calcimimetics into their patient's medications, it will be important to the facility's fiscal well-being to monitor the cost, utilization, and reimbursement of calcimimetics. ■

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 vascular access. Your questions are welcome and she can be reached at stolson@sceptremanagement.com, 801.775.8010, or via Sceptre's website, www.sceptremanagement.com.

Print-only Content