Nephrology Times

Practical News, Trends, and Analysis

March 2020

VOLUME 12, NUMBER 2

Kidney Function after RAAS Inhibition in Patients with HFrEF

In patients with heart failure with reduced ejection fraction (HFrEF), blockage of the renin-angiotensin-aldosterone system with either angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) is beneficial in reducing the risk for cardiovascular events. RAAS inhibition is considered an integral part of the management of patients with HFrEF. Therapy with ACE inhibitors or ARBs lead to dilation of the efferent arteriole in the kidney and can be associated with short-term declines in estimated glomerular filtration rate (eGFR). Previous studies in patients with diabetes have shown that early declines in eGFR following ACE inhibitor/ARB initiation are associated with slower long-term declines; it is unclear whether that trend applies to HFrEF.

A reduced level of kidney function in patients with HFrEF is a strong predictor of poor outcomes, and the mortality risk is increased in patients with eGFR <60 mL/min/1.73 m^2. As eGFR declines, the mortality risk increases. However, there are few available data on longitudinal trends in patients with HFrEF. Declines in eGFR of 30% to 40% or greater as well as progression to chronic kidney disease (CKD) stage 4 are associated with increased risk for mortality and hospitalizations in the general population; the incidence of those kidney function end points are unclear in patients with HFrEF.

Wendy McCallum, MD, MS, and colleagues recently conducted a post hoc analysis of trial data to describe

continued on page 3

High-Dose versus Standard-Dose Influenza Vaccine in Patients on Hemodialysis

Patients with end-stage renal disease (ESRD) are at increased risk of morbidity and mortality associated with influenza compared with individuals in the general population. Patients with ESRD have an impaired innate and adaptive immune system, including defects in complement activation and B- and T-cell function, adding to the increased risks for complications from influenza, mortality, and increased healthcare costs. The recommendation from the Centers for Disease Control and Prevention (CDC) strongly recommend annual influenza

continued on page 4

Sex Differences in CKD Progression

Implementing individualized treatment in the era of precision medicine calls for examining sex-specific data. Previous studies have established the importance of sexual dimorphisms for hypertension and cardiovascular complications regarding disease presentation, likelihood of disease progression, and response to treatment. There are few data available on the impact of sex on chronic kidney disease (CKD); the mechanisms underlying the observed sex disparity in the epidemiology of kidney diseases.

Researchers in Italy, led by **Roberto Minutolo, MD, PhD,** recently conducted a pooled analysis of four Italian observational cohort studies to examine the association between sex and CKD. Results of the analysis were reported in the *American Journal of Kidney Diseases* [2020;75(1):30-38].

The researchers sought to evaluate the potential effect of sex on CKD progression in analyses of data on men and women with moderate to advanced CKD in a multicohort study group regularly followed up in renal clinics in Italy. The four studies in the analysis were conducted in 40 nephrology clinics in Italy. The primary aim of the four studies differed but they shared similar inclusion and exclusion criteria. Each cohort enrolled consecutive patients with CKD under stable nephrology care for at least 6 months.

In all four cohorts, participating nephrologists collected demographic information and clinical history. Physical examinations were performed, including assessment of height, body weight, blood pressure, and medication profile. Data

continued on page 5

Print-only Content

Kidney Function after RAAS Inhibition

continued from page 1

longitudinal trends in eGFR in HFrEF and how those changes are influenced by ACE-inhibitor therapy. Results of the analysis were reported in the *American Journal of Kidney Diseases* [2020;75(1):21-29].

The researchers utilized data from SOLVD (Studies of Left Ventricular Dysfunction), two multicenter, double-blind, randomized controlled trials sponsored by the National Heart, Lung, and Blood Institute. The two studies (Treatment Trial and Prevention Trial) were designed to assess the effects of the ACE inhibitor enalapril versus placebo on mortality in patients with HFrEF (ejection faction <35%).

The outcomes of interest of the current analysis were annual rate of decline in eGFR as well as four kidney function end points: (1) increase in serum creatinine level ≥0.3 mg/dL; (2) decline in eGFR >30% from baseline; (3) decline of eGFR >40%; and (4) incident eGFR <30 mL/min/1.73 m^2.

A total of 2423 patients from the Treatment Trial and 4094 from the Prevention Trial were included in the analysis. Mean age was 60 years in the Treatment Trial and 59 years in the Prevention Trial; the Treatment Trial had a slightly higher percentage of women (19% vs 11% in the Prevention Trial). Baseline characteristics were generally similar across randomly assigned groups within each trial. There was a greater prevalence of diabetes, hypertension, and use of a diuretic in Treatment Trial participants; baseline eGFR was also worse in Treatment Trial participants (eGFR 69.5 mL/min/1.73 m^2 vs 76.2 mL/min/1.73 m^2 in the Prevention Trial).

Median follow-up was 34 months (range, 0.5 to 62.3 months). Among patients who were alive and reached each follow-up visit, there was no substantial difference in missing eGFR data by randomization arm in either trial.

There were early declines in eGFRs that were more pronounced in the enalapril arms of both trials, followed by parallel progressive declines in eGFRs over the remaining course of follow-up. There were no statistical differences in slopes during the median 3-year follow-up in either the Treatment Trial: –0.84 mL/min/1.73 m^2 in the enalapril arm versus –1.36 mL/min/1.73 m^2 in the placebo arm (P=.08) or the Prevention Trial: –1.27 mL/min/1.73 m^2 in the enalapril arm versus –1.36 mL/min/1.73 m^2 in the placebo arm (P=.7).

In the first 6-week period of the Treatment Trial, random assignment to the enalapril arm increased the risk for all four outcomes of interest: hazard ratio [HR], 1.48 (95% confidence interval [CI], 1.10-1.99) for creatinine increase by ≥0.3 mg/dL; HR, 1.38 (95% CI, 0.98-1.94) for eGFR decline >30%; HR, 2.60 (95% CI, 1.30-5.21) for eGFR decline >40%; and HR, 4.71 (95% CI, 1.78-12.50) for eGFR <30 mL/min/1.73 m^2. After the first year, there was no significant association between treatment with enalapril and increased risk.

In the Prevention Trial, there was a similar, but less pronounced, pattern, with risks present only in the early period.

Limitations to the study cited by the authors included the exclusion of patients with serum creatinine levels >2.5 mg/dL from the original trial, and not collecting urinalyses as part of the trial.

In conclusion, the researchers said, "On average, decline in eGFR was relatively slow in both symptomatic and asymptomatic patients with HFrEF and only a small percentage reached incident CKD stages 4 to 5 during a median follow-up of 3 years. Random assignment to enalapril treatment only minimally hastened the progression of decline in kidney function. Despite a slightly increased risk for reaching several kidney function surrogate end points, the overall incidence of these end points was low and occurred early. Renin-angiotensin-aldosterone system inhibitors have been shown to have a clear mortality benefit for patients with HFrEF, as demonstrated in multiple landmark trials including SOLVS, and it is encouraging that their use appears to have minimal added risk for detriment to kidney function, although admittedly also no kidney benefit." ■

High-Dose versus Standard-Dose Influenza Vaccine continued from page 1

vaccinations for patients with ESRD.

At present, there are several types of influenza vaccines in the United States, including the standard-dose vaccine (SDV) and the high-dose vaccine (HDV). Standard practice in dialysis clinics is administration of the trivalent, and more recently quadrivalent, inactivated seasonal SDVs. In 2009, a trivalent HDV was licensed by the US FDA for use among adults ≥65 years of age; the HDV contains the same three strains as the SDV, but has more antigen than standard vaccines (60 vs 15 mg per strain). Over time, use of the HDV among patients receiving maintenance dialysis has increased.

A small observational study conducted among the dialysis population demonstrated that the HDV was more effective in preventing all-cause hospitalization during the 2016 to 2017 influenza season. However, the results were limited by the small sample size, adjustment for a small set of confounders, and the lack of outcomes related to influenza. **Anne M. Butler, PhD,** and colleagues recently conducted a cohort study to examine the effectiveness of standard-dose versus high dose influenza vaccine among patients on dialysis. Results were reported in the *American Journal of Kidney Diseases* [2020;75(1):72-83].

Patients with chronic kidney disease receiving in-center maintenance dialysis during 2009 to 2015 were identified using data from the US Renal Data System. The researchers constructed yearly cohorts for five individual influenza seasons: 2010 to 2011, 2011 to 2012, 2012 to 2013, 2013 to 2014, and 2014 to 2015. Eligible patients were ≥18 years of age with ESRD who had initiated hemodialysis at least 9 months prior to the index date. Additional inclusion criteria were receipt of continuous hemodialysis for 3 months immediately prior to vaccination and Medicare as a primary insurance payer.

There were three primary clinical outcomes of interest: (1) all-cause mortality; (2) the first occurrence of hospitalization for influenza or pneumonia; and (3) the first occurrence of influenza-like illness (ILI).

Patients were eligible for inclusion in multiple yearly cohorts. The unit of analysis was the influenza patient-season. Propensity score weighting of Kaplan-Meier functions were used to estimate risk differences and risk ratios. A wide range of covariates were identified during the 6-month baseline period, including demographic characteristics (age, sex, race, dual-eligible for Medicaid, region, and year), clinical characteristics (cause of ESRD and duration of dialysis), dialysis facility characteristics (affiliation, type, profit status, and size), and comorbid conditions and procedures. Other covariates included preventive health services (other vaccinations and health screenings), health care utilization, and frailty. Timing of administration of the influenza vaccine was categorized as August or September versus October through the start of the influenza season.

Following application of inclusion and exclusion criteria, the researchers identified 255,281 eligible adults who contributed 507,552 unique influenza patient-seasons. The primary analysis included 225,215 adults ≥65 years of age; of those, 97.4% (n=219,439) of eligible vaccinations were SDV, and the remaining 2.6% (n=5776) received HDV. All HDV were trivalent; 76.7% of SDV were trivalent and 23.3% were quadrivalent.

TAKEAWAY POINTS

- Researchers conducted a cohort study to compare the effectiveness of standard-dose influenza vaccine (SDV) with high-dose influenza vaccine (HDV) in patients on maintenance hemodialysis.
- Outcomes of interest were all-cause mortality, hospitalization for influenza or pneumonia, and influenza-like illness during the influenza season.
- The findings suggested that the HDV does not provide additional protection beyond that of the SDV for adults on maintenance hemodialysis.

After accounting for the competing risk of death for nonmortality outcomes, for each outcome of interest the weighted risks for HDV and SDV were similar.

Mean age was slightly older among those who received the HDV compared with those who received SDV (75.8 years vs 74.6 years). HDV administration was less common among patients who were black or other race, were dual-eligible for Medicaid, were on dialysis for >3 years, or resided outside of the Midwest. The prevalence of comorbid conditions was higher in recipients of HDV; frailty indicators were similar between those who received SDV and those who received HDV. Recipients of HDV were more likely to receive preventive healthcare such as diabetic eye examinations, lipid testing, and cancer screenings.

After accounting for the competing risk of death for nonmortality outcomes, for each outcome of interest the weighted risks for HDV and SDV were similar. In the weighted analyses, there were similar associations between vaccine dose and risk for mortality (risk difference, –0.08%; 95% confidence interval [CI], –0.85% to 0.80%), hospitalization due to influenza or pneumonia (risk difference, 0.15%; 95% CI, –0.69% to 0.93%), and ILI (risk difference, 0.00%; 95% CI, –1.50% to 1.08%).

Risks for mortality, hospitalization for influenza or pneumonia, and ILI within subgroups defined by influenza season, age group, dialysis vintage, month of influenza vaccination, and vaccine valence were generally similar between HDV and SDV recipients throughout the influenza season, with a few exceptions. In the 2010 to 2011 season, there was a higher risk for hospitalization among patients who received the HDV compared with patients who received the SDV (risk difference, 2.85%; 95% CI, 0.59% to 5.86%). There were no differences in risk in any of the other four seasons.

For both hospitalization and ILI outcomes, the risk among HDV versus SDV recipients ≥65 years of age was higher; the risk was lower among HDV versus SDV recipients 75 to 84 years of age. There was no difference in risk among those <65 years of age or ≥85 years of age.

There were some limitations to the findings cited by the authors, including the observational design of the study that did not involve randomization of the exposure, only accounting for baseline characteristics measured prior to vaccination, the requirement of survival until 9 months following initiation of dialysis, and basing the study primarily on administrative billing claims data.

In summary, the researchers said, "Our large comparative study failed to demonstrate that HDV has superior effectiveness compared to SDV for preventing all-cause mortality and influenza-related outcomes among patients receiving maintenance hemodialysis. Given the findings of our population-level study, along with the substantially higher cost and side-effect profile of HDV compared to SDV, it appears that HDV should not conclusively be considered the standard of care at the present time for influenza immunization of patients treated by maintenance hemodialysis. The findings of our population-level study should not be interpreted to discourage influenza vaccination in the dialysis population. Rather, dialysis patients should continue to receive annual influenza immunization per CDC guidelines. In addition, future studies of alternative strategies (eg, booster doses) and alternative vaccine production technologies (eg, adjuvanted or cell-based vaccines) are warranted because there remains a need for improved influenza prevention efforts in this population." ■

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@nephtimes.com

Jen Callow
jcallow@nephtimes.com

Recruitment advertising orders can be sent to:

DIRECTOR, RECRUITMENT CLASSIFIEDS

Lauren Morgan
lmorgan@americanmedicalcomm.com

Visit us at www.nephtimes.com

AMC MEDIA GROUP

630 Madison Avenue
Manalapan, NJ 07726

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

Sex Differences in CKD Progression
continued from page 1

were collected in anonymous electronic case reports and subsequently sent to the coordinating centers for quality assessment, storage, and analyses.

For the current analysis, the primary outcome of interest was time to end-stage renal disease (ESRD), defined as maintenance dialysis or kidney transplantation. For time to ESRD, death before ESRD was a competing event. Secondary end points included time to all-cause mortality and the slope of change in estimated glomerular filtration rate (eGFR).

The initial pooled cohorts included 3212 individuals. Of those 148 were duplicate patients, 13 had missing information, and 716 had eGFR >45 mL/min/1.73 m^2, resulting in an analysis cohort of 2335 individuals (1311 men and 1024 women). In the four cohorts, sex distribution as similar. There were no differences in age and the prevalence of diabetes between men and women; the prevalence of smokers, left ventricular hypertrophy, and history of cardiovascular disease was higher in men than in women.

On average, eGFR was 1.6 mL/min/1.73 m^2 lower in women, and women had a different prevalence of CKD stage. Mean eGFR was similar in men and women in stage 3B and stage 4 CKD; it was slightly higher in women in stage 5 CKD. Proteinuria was higher in men compared with women: 56.3% of men and 46.2% of women had protein excretion >0.5 g/d (P<.001).

Blood pressures were similar in men and women; achievement of blood pressure <130/80 mm Hg was also similar between the two groups. In terms of number of antihypertensive drugs and use of renin-angiotensin system inhibitors, calcium channel blockers, and beta-blockers, the two groups were similar; women used diuretics more frequently compared with men. Prescription of statins and antiplatelet drugs was similar between the two groups; women received erythropoiesis-stimulating agents more frequently than men (20.8% vs 15.0%; P<.001). Women adhered more frequently to nonpharmacological recommendations for CKD; intensity of nephrology care was similar between the groups.

During a median follow-up of 4.21 years, there were 727 ESRD events (295 in women and 432 in men); the overall incidence rate was 7.92 per 10 person-years (7.19/100 person-years in women and 8.53/100 person-years in men). When taking into account the competing risk for death prior to development of ESRD, the analysis of cumulative incidence of ESRD was higher in men overall and by CKD stage subgroup. In the entire cohort, the adjusted risk for ESRD was 50% greater in men than in women. The higher risk for men persisted across CKD stages (range, 52% in stage 3b to 41% in stage 5).

Results of multivariable survival analysis demonstrated a significant interaction between sex and proteinuria (P=.02) in predicting risk of ESRD. The relative risk for ESRD for men versus women was dependent on proteinuria levels, with the rate becoming significantly greater in men at protein excretion of ~0.5 g/d or greater. The results suggested that a male patient with CKD with protein excretion of 1 g/d has a 50% higher risk for progressing to ESRD than a female patient with the same level of proteinuria.

> When taking into account the competing risk for death prior to development of ESRD, the analysis of cumulative incidence of ESRD was higher in men overall and by CKD stage subgroup.

In secondary outcome analysis, 471 patients died during follow-up (196 women and 275 men); the incidence rate was similar in the two groups (4.77/100 person-years in women and 5.43/100 person-years in men). In the entire cohort, the adjusted risk for death was higher in men than in women; the difference was not statistically significant but was consistent across CKD stage.

Decline in eGFR over time was assessed in patients who had at least one eGFR post-baseline assessment: 98.2% of the cohort (n=2292). In mixed-regression analysis, there was a significant difference in eGFR reduction between men and women. Adjusted eGFR change was –1.79 mL/min/1.73 m^2 in women and –2.09 mL/min/1.73 m^2 in men. Sex differences in the rate of eGFR decline were not different across CKD stages.

There were some limitations to the analysis cited by the authors, including the relatively large sample size in the context of the study setting; persistence of results following stratification for the four cohorts; and simultaneous evaluation of ESRD and mortality.

The researchers said, "In conclusion, in elderly patients with moderate to advanced CKD under nephrology care, the risk for progression to ESRD is 50% higher in men than in women, irrespective of CKD stage, and men experience a steeper eGFR decline compared with women. Proteinuria levels may modify the association between sex and renal risk." ■

TAKEAWAY POINTS

- Researchers in Italy conducted a pooled analysis from four cohort studies to examine the association between sex and progression of chronic kidney disease (CKD); the cohorts included elderly patients treated at nephrology clinics in Italy.
- The primary outcome of interest was end-stage renal disease (ESRD) (defined as requiring maintenance dialysis or kidney transplant); secondary outcomes were all-cause mortality and decline in estimated glomerular filtration rate.
- The adjusted risks for ESRD and mortality were higher in men; the finding was consistent across stages of CKD.

Alterations in Kidney Function in Overweight and Obese Children and Adolescents

TAKEAWAY POINTS

- Researchers in Mexico conducted a cross-sectional study to examine the frequency of renal damage in overweight/obese children and adolescents.
- Compared with subjects with normal weight, those with overweight/obesity had significantly higher abdominal obesity, hypertension, hypertriglyceridemia, high low-density lipoprotein cholesterol, low high-density lipoprotein cholesterol, hyperuricemia, and hyperinsulinemia.
- In multivariable analyses, kidney alterations were significantly predicted by higher body mass index and lower high-density lipoprotein cholesterol.

Worldwide, the public health problem of obesity is increasing. The prevalence of overweight and obesity is extremely high in Mexico in both the adult and pediatric population (72% and 35%). Among adults, there are strong associations between obesity and kidney disease; however, there are few data available regarding such associations in adolescents and children.

Researchers in Guadalajara, Mexico, led by **Fabiola Martin-del-Campo, LN, MSc,** recently conducted a cross-sectional analysis designed to compare the frequency of renal damage according to the presence of overweight-obesity in the pediatric population. The study also sought to compare nutritional and biochemical risk factors according to the presence of kidney alterations. Results of the analysis were reported in the *Journal of Renal Nutrition* [2019;29(5):370-376].

The study cohort included 172 children and adolescents; 27% (n=42) were classified as normal weight, 32% (n=55) as overweight, and 41% (n=71) as obese. Participants in the obesity group had significantly higher proportion of family history of obesity and higher systolic blood pressure compared with the other two groups. In the group with obesity, there was a nonsignificant trend to higher birth weight, higher diastolic blood pressure, and more sedentary activities. There were no other differences observed regarding age, sex, and family history of diabetes, hypertension, or kidney disease.

BIOCHEMICAL CHARACTERISTICS

Compared with controls, participants in the overweight and obesity groups had significantly higher prevalence of abdominal obesity (0% vs 69%), hypertension (19% vs 26%), hyperuricemia (11% vs 28%), hypertriglyceridemia (11% vs 47%), high low-density lipoprotein cholesterol (2% vs 8%), and low high-density lipoprotein cholesterol (2% vs 28%).

Those in the overweight and obesity groups had higher prevalence of risk factors for kidney disease than those in the normal weight group. Individual prevalence of risk factors such as dyslipidemia, hyperinsulinemia, and abdominal obesity was >60% in children and adolescents in the overweight and obesity groups.

There were no significant differences in serum creatinine, glomerular filtration rate (GFR), and albuminuria between the groups. However, the researchers did note that there was one case of decreased GFR as well as four cases of hyperfiltration in the obesity group, and one case of hyperfiltration in the overweight group. Microalbuminuria was present in four cases (none with hypertension); one case was in the overweight group and the other three were in the obesity group. Including both alterations in GFR and microalbuminuria, the frequency of kidney alterations was ~10% in the obesity group, 4% in the overweight group, and 0% in the normal weight group.

In multivariable analysis, there was a negative correlation between GFR and age, uric acid, and intake of monounsaturated fatty acid. Age and uric acid levels were also negatively correlated with albuminuria; sodium intake and protein intake had a positive correlation ($P<.05$ for all). In multivariant analysis, significant predictors of kidney alterations were higher body mass index and lower HDL cholesterol.

> Those in the overweight and obesity groups had higher prevalence of risk factors for kidney disease than those in the normal weight group.

The researchers said, "In conclusion, kidney alterations were observed in 5.3% of the whole sample of children and adolescents of this sample. Such alterations were present only in subjects with overweight (3.6%) and obesity (9.9%), who additionally displayed several cardiometabolic and kidney disease risk factors more frequently than those with normal weight. Screening for kidney alterations in high-risk children and adolescents with overweight/obesity may be an excellent opportunity in helping to prevent the burden of kidney failure in adulthood." ■

Diabetes Remission and Kidney Disease in Bariatric Surgery Patients

Worldwide, the leading cause of chronic kidney disease and kidney failure is type 2 diabetes. Only modest benefits are seen with current recommended treatment options for CKD in patients with type 2 diabetes. There is a strong link between obesity and type 2 diabetes, suggesting that intentional weight loss should be explored as an additional treatment option for CKD in that patient population.

There are few data available on whether remission of diabetes mitigates CKD in patients with type 2 diabetes. Because bariatric surgery has been shown to induce remission in a substantial proportion of patients, it provides a model in which to evaluate this concept. The bariatric surgery model also allows researchers to examine whether remission of diabetes is influenced by the presence of CKD. There is a link between kidney disease and insulin resistance, but it is not known whether patients with type 2 diabetes are less likely to achieve remission following bariatric surgery due to underlying insulin resistance or other factors related to CKD.

Allon N. Friedman, MD, and colleagues conducted a study designed to examine whether remission of diabetes following bariatric surgery influences estimated glomerular filtration rate (eGFR), proteinuria, and prognostic risk for CKD. The researchers also sought to determine if the presence of baseline CKD influences the likelihood of diabetes remission following bariatric surgery. Results of the study were reported in the *American Journal of Kidney Diseases* [2019;74(6):761-770].

The study included a large prospective multicenter cohort of patients with obesity and type 2 diabetes who underwent bariatric surgery and had regular follow-up over 5 years ; the participants were part of the LABS-2 (Longitudinal Assessment of Bariatric Surgery-2) study.

Of the 737 study participants, 71% were women, 85% were white, and 75% had some postsecondary school education. Median hemoglobin A1c level was 6.9%. More than 78% of the cohort used two or more noninsulin diabetes medications, and 28% required insulin. Median eGFR was 94 mL/min/1.73 m^2; 12% of participants had eGFR <60 mL/min/1.73 m^2. Median urinary albumin-creatinine ratio (UACR) was 8.9 mg/g; 22% of participants had moderately/severely increased albuminuria. As a measure of prognosis, 18.8%, 8%, and 3.3% of participants were in the moderately increased, high, and very high Kidney Disease Improving Global Outcomes CKD risk categories, respectively

By the end of year 5, median percent weight loss was 24%, change in eGFR was negligible, 34% had regression of their moderately/severely increased albuminuria, and 47% achieved remission of diabetes.

The researchers examined the relationship between post-bariatric surgery diabetes remission and eGFR and UACR during follow-up in separate adjusted analyses. There was no significant association between remission of diabetes and eGFR after surgery; this observation remained true even following exclusion of patients with hyperfiltration. There were associations between higher eGFR after surgery and shorter time elapsed since surgery, younger age at the time of surgery, higher household income, lower baseline systolic blood pressure, higher baseline eGFR, and Roux-en-Y gastric bypass (vs laparoscopic adjustable gastric banding) as surgery type.

Compared with patients with no remission of diabetes, those with partial or complete remission had lower odds of moderately/severely increased albuminuria following surgery (risk ratio [RR], 0.66; 95% confidence interval [CI], 0.48-0.90) following adjustment for baseline characteristics. In sensitivity analysis that excluded three patients with baseline UACRs >2000 mg/g, results were similar (RR, 0.70; 95% CI, 0.50-0.97). There were also significant associations between lower odds of moderately/severely increased albuminuria and younger age at the time of surgery, female sex, white race, lower baseline UACR and insulin sensitivity by homeostatic model assessment, and no use of renin-angiotensin-aldosterone-blocking agents.

There was a significant association between complete or partial remission of diabetes at 5 years and greater likelihood of stabilization in the prognostic risk for CKD, compared with no remission. The association was dependent on baseline ghrelin levels (P=.02 for interaction between baseline ghrelin level and diabetes remission). Other baseline characteristics associated with stabilization of prognostic risk were private

medical insurance, lower baseline systolic blood pressure, no use of renin-angiotensin-aldosterone-blocking agents, and being in a moderately increased or high versus low CKD risk category.

There was an association between increased odds of partial or complete diabetes remission and higher baseline eGFR (P<.001); this effect was amplified at higher C-peptide levels. Conversely, there was no association between baseline UACR and diabetes remission (odds ratio, 1.004; 95% CI, 0.999-1.01).

Limitations to the findings cited by the authors included lack of a sufficient number of patients with established or advanced kidney disease or long enough follow-up to assess outcomes such as death or kidney failure; lack of a comparison group, preventing the researchers from determining the relative effects of bariatric surgery; not including episodes of hospitalizations and acute kidney injury in the analyses; and lack of kidney biopsies to determine the precise cause of kidney disease in the study participants.

"In summary, we report that partial or complete remission of type 2 diabetes at 5 years after bariatric surgery is associated with improvement in moderately/severely increased albuminuria and stabilization of prognostic risk for CKD. Additionally, worse kidney function or risk at time of bariatric surgery was linked to a lower likelihood of diabetes remission. Finally, ghrelin was associated with salutary effects on prognostic risk for CKD. These intriguing findings warrant further study to determine whether and through what mechanisms bariatric surgery can prevent or delay the progression to kidney failure in this population and identify which patients would most benefit," the researchers said. ■

TAKEAWAY POINTS

- Researchers conducted a prospective observational study to assess whether remission of diabetes after bariatric surgery influences estimated glomerular filtration rate (eGFR), proteinuria, and prognostic risk for chronic kidney disease (CKD) in patients with type 2 diabetes.
- There was no independent association between diabetes remission at 5 years post-surgery and eGFR; there was an association with lower risk for moderate/severe increase in albuminuria.
- There was also an association between diabetes remission and stabilization in prognostic risk for CKD.

Equations Predict Development of Chronic Kidney Disease

The worldwide prevalence of chronic kidney disease (CKD) is on the rise. The Global Burden of Disease study estimated that nearly 697 million individuals worldwide had reduced estimated glomerular filtration rate (eGFR) or increased albuminuria in 2016, an increase of 70% since 1990. During the same time period, the years of life lost to CKD increased by 53%; CKD is the 16th most common cause of years of life lost. The aging of the population and the increase in the prevalence of diabetes, hypertension, and obesity are the primary factors associated with the increase in CKD prevalence.

Identification of patients at risk for CKD may prevent the adverse health outcomes associated with the disease; in addition, management of patients with CKD may be hindered by lack of CKD awareness. **Robert G. Nelson, MD, PhD**, and colleagues conducted a study utilizing data from multinational cohorts to develop and evaluate risk prediction equations for CKD defined by reduced eGFR. Results were reported online in *JAMA* [doi:10.1001/jama2019/17379].

The study included data on 5,222,711 individuals in 34 multinational cohorts from the CKD Prognosis Consortium from 28 countries. Within cohorts, eligible participants were ≥18 years of age with an eGFR of less than 60 mL/min/1.73 m^2 at baseline. Inclusion criteria were no prior end-stage kidney disease and at least one serum creatinine value recorded during follow-up. Most cohorts used self-report to define race/ethnicity. The data were collected from 1970 through 2017.

Of the total cohort, 15.0% (n=781,627) had diabetes. Mean age in the population without diabetes was 54 years and 38% were women. Among the population with diabetes, mean age was 62 years and 13% were women. The low percentage of women was due primarily to the Veterans Administration cohort, which was 97% male.

During a mean follow-up of 4.2 years, in the 4,441,084 participants without diabetes, there were 660,856 incident cases (14.9%) with an eGFR less than 60 mL/min/1.73 m^2; 56.7% (n=374,513) were confirmed by subsequent eGFR measurements. In the cohort with diabetes, the percentage of incident cases of reduced eGFR was 40.1% (n=313,646) during a mean follow-up of 3.9 years; 67.7% of those (n=212,246) were confirmed by subsequent eGFR measurements.

In cohorts with and without diabetes, there was a significant association between incident eGFR less than 60 mL/min/1.73 m^2 and older age, female sex, black race, hypertension, history of cardiovascular disease, lower eGFR values, and higher urine albumin:creatinine ratio. In the cohorts without diabetes, there was also a significant association between smoking and an incident eGFR less than 60 mL/min/1.73 m^2. In cohorts with diabetes, elevated hemoglobin A1c and the presence and type of diabetes medication were significantly associated with an incident eGFR of less than 60 mL/min/1.73 m^2.

In the cohorts without diabetes, the median C statistic for the 5-year predicted probability of all eGFR events of less than 60 mL/min/1.73 m^2 was .0845; in the cohorts with diabetes, it was 0.801, reflecting good discrimination. For confirmed eGFR events of less than 60 mL/min/1.73 m^2, the median C statistic was 0.869 in the cohorts without diabetes and 0.808 in the cohorts with diabetes.

Model calibration was assessed visually by plotting observed versus predicted risk per decile of predicted risk at 5 years in the cohorts with frequent measures of creatinine. In calibration analyses, nine of 13 study populations (69%) had a slope of observed to predicted risk between 0.80 and 1.25. Calibration was generally better for the eGFR of less than 60 mL/min/1.73 m^2 end point than for the lower eGFR end points, where calibration was poor in some cohorts.

Discrimination was similar in 18 study populations in nine external validation cohorts (n=2,253,540); calibration showed that 16 of 18 (89%) had a slope of observed to predicted risk between 0.80 and 1.25.

The researchers cited some limitations to the study, including the absence of data on albuminuria in most cohorts of patients without diabetes, necessitating that a statistical patch derived from cohorts without diabetes, but with albuminuria data, be applied to the remaining cohorts in order to estimate how including albuminuria altered the models. The risk equations developed incorporated routinely collected demographic, clinical, and laboratory data, but not genotype data or newly identified biomarkers of early CKD. The equations developed were intended to identify individuals at increased risk of an intermediate health outcome; the equations did not identify risk of progression of CKD, cardiovascular events, or death. Calibration varied across setting, with particularly poor performance in some of the cohorts.

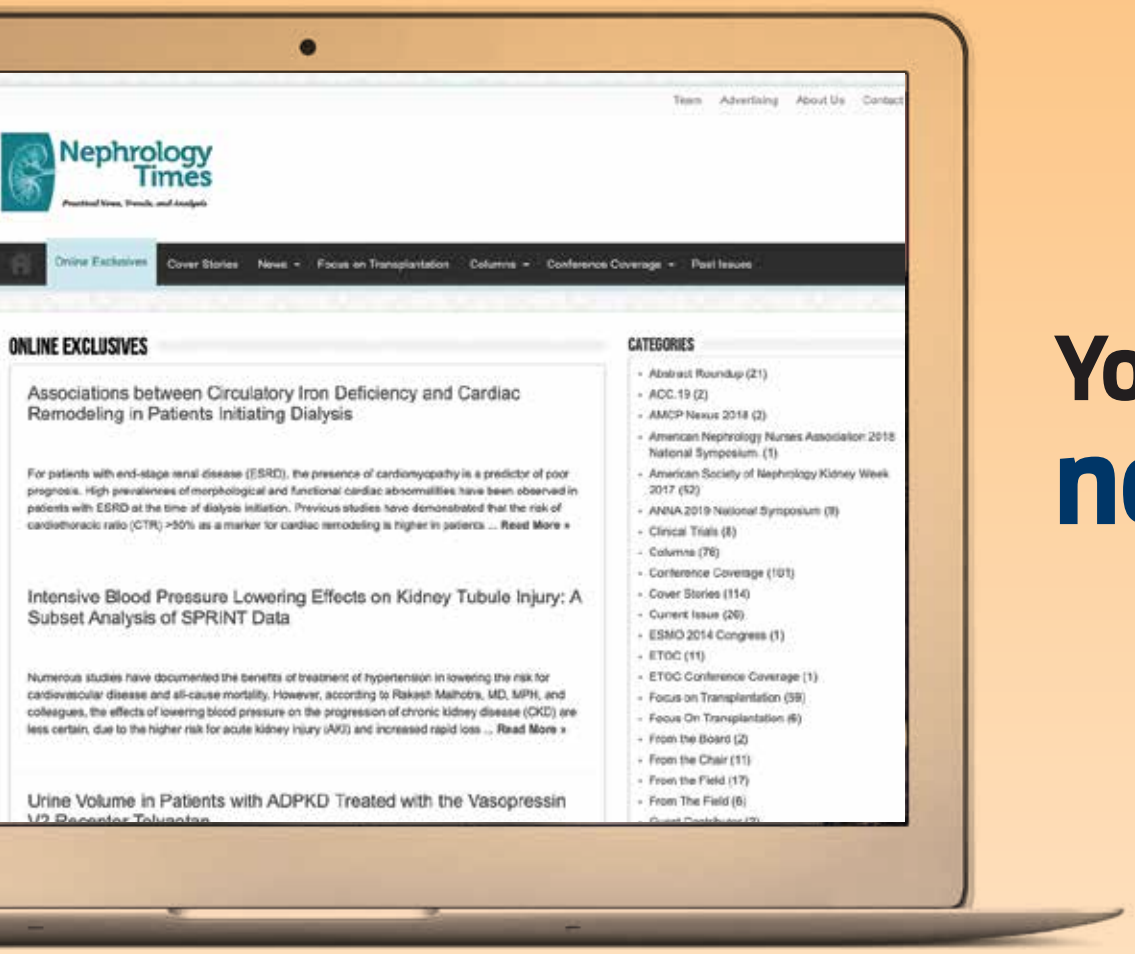
In conclusion, the researchers said, "Equations for predicting risk of incident chronic kidney disease were developed from more than five million individuals from 34 multinational cohorts and demonstrated high discrimination and variable calibration in diverse populations. Further study is needed to determine whether use of these equations to identify individuals at risk of developing chronic kidney disease will improve clinical care and patient outcomes." ■

TAKEAWAY POINTS

- Researchers conducted a study of data from multinational cohorts to develop and evaluate risk prediction equations for chronic kidney disease defined by reduced estimated glomerular filtration rate (eGFR).
- Equations for 5-year risk of reduced eGFR included age, sex, race/ethnicity, eGFR, history of cardiovascular disease, ever smoker, hypertension, body mass index, and albuminuria concentration. For patients with diabetes, the model also includes diabetes medication and hemoglobin A1c.
- The developed equations demonstrated high discrimination and variable calibration in diverse populations.

Nephrology Times Gives You

- Analysis of Key Journal Studies
- Focus on Transplantation
- News Briefs
- Abstract Roundup
- From the Field



You get even more at nephtimes.com

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

Nephrology Times
Practical News, Trends, and Analysis

No Change in Vascular Function with Aldosterone Antagonism in Patients with ADPKD

Autosomal dominant polycystic kidney disease (ADPKD) occurs worldwide and affects all races. It is characterized by the development and continued growth of multiple kidney cysts, leading to end-stage renal disease in the majority of patients. However, the leading cause of death in patients with ADPKD is cardiovascular complications and disorders. Hypertension occurs early in the progression of the ADPKD and is associated with the increased risk for cardiovascular disease in the patient population with the disease.

Impaired vascular endothelial function is often assessed as reduced endothelium-dependent dilation. Increased large-elastic artery stiffness also occurs early in the course of ADPKD, even in the presence of preserved estimated glomerular filtration rate (eGFR). Vascular dysfunction is an important predictor of cardiovascular events and mortality in patients with ADPKD.

In this patient population, activation of the renin-angiotensin-aldosterone system is the result of expansion of renal cysts and compression of the renal vasculature. Treatment for hypertension commonly includes use of angiotensin-converting enzyme (ACE) inhibitors; however, aldosterone breakthrough may occur. Increased oxidative stress and inflammation has been shown to be associated with aldosterone excess, which has been implicated in the development of endothelial dysfunction.

Kristen L. Nowak, PhD, MPH, and colleagues conducted a prospective, randomized, controlled, double-blind clinical trial to test the hypothesis that aldosterone antagonism would improve brachial artery flow-mediated dilation (FMD_{BA}) and reduce carotid-femoral pulse-wave velocity (CFP-WV) in patients with ADPKD. Results were reported in the *American Journal of Kidney Diseases* [2019;74(2):213-223].

The primary end point was the efficacy of an aldosterone antagonist for improving vascular function; the secondary end point was the reduction of large-elastic artery stiffness in patients with early-stage ADPKD who were being treated with the maximal tolerable dose of an ACE inhibitor or angiotensin receptor blocker (ARB).

Eligible patients were enrolled at the University of Colorado Denver Anschutz Medical Campus between July 2014 and

> There was no significant difference between the intervention group and the placebo group in the primary end point (change in FMD_{BA}, expressed as percent change) after 24 weeks.

Kidney Week

CKD Prevalence in Military Health System Database by Laboratory versus ICD-9 Codes

Washington, DC–Varying definitions of chronic kidney disease (CKD) and diagnosis accuracy in medical records contribute to limitations in analyses of the epidemiology of CKD. **James D. Oliver, MD,** and colleagues utilized laboratory and coding data in the US Military Health System (MHS) Repository to examine the prevalence of CKD as measured by *International Classification of Diseases, Ninth Revision (ICD-9)* codes compared with laboratory test results. The MHS is a large database for a universal system of health coverage for US active-duty military, retirees, and family members. Demographics are similar to those in the general population in the United States.

Results of the analysis were reported during a poster session at the American Society of Nephrology Kidney Week 2019. The poster was titled *CKD Prevalence in the US Military Health System (MHS) by Laboratory vs* ICD-9 *Coding.*

Data on patients ≥18 years of age were extracted from fiscal year (FY) 2015. Diagnosis of CKD was based on either *ICD-9* codes or from laboratory tests. CKD from laboratory testing was defined by the CKD-EPI (Chronic Kidney Disease-Epidemiology Collaboration) equation as estimated glomerular filtration rate <60 mL/min/1.73 m^2, urine protein-to-creatinine ratio ≥15 g/g, or urine albumin-to-creatinine ratio ≥30 mg/g.

CKD diagnoses from *ICD-9* codes were defined as one or more inpatient or two or more outpatient CKD codes during the FY. Two definitions of laboratory testing were used: 2Lab+, the most recent laboratory tests in the study period being persistently abnormal over ≥3 months (gold standard); or 1Lab+, any abnormal lab during the FY. Sensitivity/specificity, chi-square, Cohen's kappa, and McNemar's test were used to compare *ICD-9* code and 1Lab+ to 2Lab+.

Data on 3,360,305 patients were analyzed for FY 2015. Mean age was 37.6 years, and 28.9% (n=969,873) had laboratory results. Among the patients with laboratory results, 2Lab+ CKD prevalence was 2.5% overall, increasing to 9.7% for patients ≥60 years of age, compared with 1Lab+ CKD prevalence of 9.9% overall, increasing to 31.5% for age ≥60 years.

Overall, Code+ CKD prevalence was 2.8% compared with 4.8% in patients with laboratory results. Only 54.8% of 2Lab+ patients were also Code+. In the 1Lab+ group, the positive predictive value (PPV) was 0.25 and the negative predictive value (NPV) was 1.0 for the 2Lab+ group. Patients in the code group had a PPV of 0.28 and a NPV of 0.99 for 2Lab. PPVs were higher for both 1Lab and Code in patients >60 years of age (0.31 and 0.47, respectively).

In conclusion, the researchers said, "Based on *ICD-9* codes, provider awareness of CKD in the MHS is low. Use of a single lab value significantly overestimates CKD prevalence and has a poor PPV compared to repeat measures. The views expressed in this abstract are those of the authors and do not reflect the official policy of the Departments of Army/Navy/Air Force, Department of Defense, Department of Health and Human Services, or the US Government."

Source: Oliver JD, Nee, RW, Grunwald L, et al. CKD prevalence in the US military health system (MHS) by laboratory vs. *ICD-9* coding. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2019 (Abstract TH-P0397), November 7, 2019, Washington, DC.

June 2016. Inclusion criteria were adults 22 to 55 years of age with a diagnosis of ADPKD, total kidney volume between 500 and 2500 mL, eGFR ≥60 mL/min/1.73 m^2, and a history of hypertension treated with an ACE inhibitor or an ARB.

A total of 66 patients were screened for participation; of those, 61 were randomly assigned to receive either the aldosterone antagonist spironolactone or placebo. One participant in the spironolactone group discontinued the intervention prior to the final study visit. Mean age of the participants was 34 years, 54% were women, and 84% were non-Hispanic white. There were no significant differences between the intervention and placebo group in baseline characteristics, including sex, race/ethnicity, body mass index, blood pressure, lipids, eGFR, and medications.

There was no significant difference between the intervention group and the placebo group in the primary end point (change in FMD_{BA}, expressed as percent change) after 24 weeks. When FMD was expressed as absolute change, results were similar. There was also no change in the secondary end point (CFPWV) after 24 weeks in the intervention group compared with the placebo group.

There was a reduction in brachial systolic blood pressure with spironolactone compared with placebo: median change –6 mm Hg versus –2 mm Hg, respectively. There was no change in the majority of circulating and/or endothelial cell markers of oxidative stress or inflammation with spironolactone. In addition, there was no change in vascular oxidative stress with the intervention.

The relatively small sample size was cited by the researchers as a potential limitation to the study, as was the difficulty in separating the effects of blood pressure lowering from potential reductions in CFPWV because regulation of blood pressure and arterial stiffness are closely related. A third limitation was the lack of measurements of plasma or urinary aldosterone.

The researchers said, "In conclusion, in individuals with early-stage ADPKD, mineralocorticoid antagonism does not improve FMD_{BA} or reduce CFPWV despite reducing blood pressure. This is consistent with the general lack of evidence for a reduction in oxidative stress and inflammation and associated pathways. Alternative interventions targeting an improvement in vascular endothelial function and reduced arterial stiffness in early ADPKD should be evaluated." ■

Kidney Week

Long-Term Safety and Efficacy of Veverimer for Metabolic Acidosis

Washington, DC–Patients with chronic kidney disease (CKD) who develop metabolic acidosis are at risk for accelerated decline in estimated glomerular filtration rate (eGFR), augmented muscle catabolism, and increased mortality. Veverimer is an oral, non-absorbed, counterion-free, polymeric drug candidate; the drug selectively binds and removes hydrochloric acid from the gastrointestinal lumen.

During a poster session at Kidney Week 2019, **Donald E. Wesson, MD, MBA, FACP, FASN,** and colleagues reported results of a multicenter, blinded, placebo-controlled, 40-week extension (n=196) of a 12-week parent study (n=217) of veverimer. The poster was titled *Randomized Controlled Trial of Long-Term Safety and Efficacy of Veverimer for Treatment of Metabolic Acidosis*. Patients with CKD and metabolic acidosis were randomly assigned in a 4:3 ratio to veverimer or placebo. CKD was defined as eGFR 20 to 40 mL/min/1.73 m^2 and metabolic acidosis was defined as serum bicarbonate level 12 to 20 mEq/L.

The primary end point of the extension study was safety; secondary end points included effect on bicarbonate level, and patient-reported physical function. Physical function was measured using Kidney Disease and Quality of Life Physical Functioning Domain (KDQOL-PFD) and objectively measured physical function using the repeated chair stand (RCS) test. The researchers also performed a pre-specified time-to-event analysis for the composite outcome of death, renal replacement therapy, or decline in eGFR ≥50%.

Premature treatment discontinuation was less common among patients in the veverimer group compared with those in the placebo group (2.6% vs 9.8%); serious adverse events were also less common in the veverimer group (1.8% vs 4.9%). No patients in the veverimer group died versus two in the placebo group. No patients in the veverimer group discontinued due to an adverse event compared with one in the placebo group; the frequencies of adverse events were similar.

At week 52, more patients in the veverimer group had an increase in bicarbonate (>4 mEq/L or normalization) compared with patients in the placebo group (62.7% vs 37.8%; P=.001). Higher bicarbonate levels were seen in the veverimer group at all time points (P<.001).

Patients in the veverimer group improved on the KDQOL-PFD score versus patients on placebo; mean placebo-subtracted change at the end of treatment was 12.1 points (P<.001). Specifically, veverimer improved the ability to climb one flight of stairs (P<.001) and all measures of walking (P<.01) on the KDQOL-PFD. In the veverimer group, the time to perform the RCS test decreased by 4.3 seconds versus 1.4 seconds in the placebo group.

There was an association between veverimer and longer time to the kidney composite end point (annualized incidence rate 4.2% [veverimer] vs 12.0% [placebo]; P=.022).

In conclusion, the researchers said, "Veverimer safely and effectively improved metabolic acidosis in patients with CKD. Our multicenter, randomized, controlled trial adds to the evidence that treating metabolic acidosis slows progression of CKD and improves physical function."

Source: Wesson DE, Mathur VS, Tangri N, et al. Randomized controlled trial of long-term safety and efficacy of veverimer for treatment of metabolic acidosis. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2019 (Abstract TH-P0448), November 7, 2019, Washington, DC.

Care Gaps in Patients with Incident Abnormal Test Results

To avoid errors in diagnosis and treatment, abnormal laboratory test results require timely follow-up. Increasing use of electronic health records (EHRs) can facilitate follow-up of abnormal results; however, studies have shown that EHRs alone do not contribute to improvements in care quality. Follow-up is similar in systems that do and do not depend on EHRs for electronically acknowledged and unacknowledged result alerts. Even with alerts labeled high priority, delays longer than 30 days can occur. In addition, the high volume or alerts and notifications sent to physicians may create new challenges for managing test results.

There are particular challenges associated with the diagnosis of chronic kidney disease (CKD) due to the recommended 90 days for retesting creatinine following an incident abnormal laboratory result to establish chronicity. Researchers, led by **Kim N. Danforth, ScD, MPH,** conducted a mixed-methods study designed to identify patient, provider, and system-level factors associated with care gaps in the follow-up of abnormal test results. The study utilized retrospective analyses of EHRs as well as physician interviews. Results were reported in the *American Journal of Kidney Diseases* [2019; 74(5):598-600].

The study was conducted within Kaiser Permanente Southern California (KPSC), an integrated healthcare delivery system that serves more than 4.5 million members in 230 medical offices. KPSC adopted EHRs in 2006 and approximately half of its members are registered for KPSC's online patient portal.

The study used a convergent design with both quantitative and qualitative analyses. The retrospective cohort included KPSC members ≥21 years of age who had a creatinine laboratory result in the period 2010 to 2015 corresponding to an incident abnormal estimated glomerular filtration rate (eGFR). Abnormal eGFR was defined as <60 mL/min/1.73 m^2 using the Modification of Diet in Renal Disease (MDRD) Study equation ($eGFR_{MDRD}$). Incident cases were defined as those without abnormal eGFR results in the prior 2 years. Exclusion criteria were prior diagnosis of CKD or kidney cancer, or unknown or multiple race/ethnicity.

Primary care physicians (PCPs) selected for interviews were categorized by distribution of eGFR follow-up: (1) high-care-gap PCPs, ≥60% of patients with care gaps and (2) low-care-gap PCPs, <40% of patients with care gaps. The PCPs were unaware which care-gap group they belonged to.

The outcome of interest was timely follow-up of incident abnormal eGFRs, defined as repeat eGFR obtained within 60 to 150 days, follow-up testing before 60 days that indicated normal kidney function, or diagnosis before 60 days of CKD or kidney cancer.

The study included a total of 244,540 patients with an incident $eGFR_{MDRD}$ <60 mL/min/1.73 m^2, ordered by 7164 providers. Of the total cohort, 141,630 (58%) did not receive timely follow-up. Retesting in 48% of patients with a care gap was late (151-365 days; n=68,057), 49% had no repeat creatinine test within a year (n=69,209), and 3% were retested early (30-59 days; n=4364). Of the patients with an incident $eGFR_{MDRD}$ <45 mL/min/1.73 m^2 (n=21,888), 6139 (28%) experienced a care gap in follow-up. Of those, 2991 (49%) were retested late, 2290 (37%) had no repeat test within a year, and 858 (14%) were retested early.

Across providers, care gaps in follow-up of incident abnormal eGFR results were common: 5925 (83%) had at least one patient with a care gap. Those who had no patients with care gaps were more likely to be non–full time, have small panel sizes, or were specialists.

Compared with patients with no care gap, those who had a care gap were younger, more likely to be women, more likely to be non-Hispanic white, and more likely to have a Charlson Comorbidity Index score of zero. They were less likely to have diabetes or hypertension or to be obese. Those with care gaps also tended to have higher eGFRs on their incident abnormal laboratory results, and an association between their test results and creatinine results flagged as abnormal was less likely: only 18.8% (n=26,570) of patients with a care gap had a creatinine result flagged as abnormal compared with 43.7% (n=44,991) of those without a care gap. When a physician other than the patient's PCP ordered the test, care gaps in follow-up were less likely.

Multivariable analyses were conducted among three subcohorts: patients with incident $eGFR_{MDRD}$ <45 mL/min/1.73 m^2 as well as those with eGFRs calculated using the CKD Epidemiology Collaboration (CKD-EPI) equation ($eGFR_{CKD-EPI}$) <60 or <45 mL/min/1.73 m^2. Results of the multivariable analyses were generally similar for the main cohort ($eGFR_{MDRD}$ <60 mL/min/1.73 m^2) and the subcohort ($eGFR_{MDRD}$ <45 mL/min/1.73 m^2). Care gaps were more common among women and non-Hispanic white patients, an association that was stronger using the $eGFR_{MDRD}$ <45 mL/min/1.73 m^2 cutpoint. Patients who had higher eGFRs on the incident abnormal laboratory result were less likely to receive timely follow-up; this association was also stronger in the subcohort.

When the abnormal laboratory result was flagged in the EHR, there was an association between the flag and a reduced risk for a care gap (risk ratio [RR], 0.65 for $eGFR_{MDRD}$ <60 mL/min/1.73 m^2; RR, 0.68 for $eGFR_{CKD-EPI}$ <60 mL/min/1.73 m^2; and RR, 0.87 for $eGFR_{CKD-EPI}$ <45 mL/min/1.73 m^2). When a provider other than the patient's PCP ordered the laboratory test, the risk of a care gap was lower.

Patients registered for an online portal who checked results within 14 days were less likely to experience care gaps (RR, 0.90-0.98 across models). There were no differences between those who registered for an online portal and those who did not when results were not checked within 14 days.

Physician interviews revealed both system-level and provider-level factors that influence management of laboratory results. Factors identified included panel size and assistance in managing laboratory results and provider-level proficiency in using EHR tools.

The inability to capture intentional delays in follow-up testing was cited by the authors as a limitation to the study findings.

In conclusion, the researchers said, "Timely follow-up of abnormal results remains challenging in an EHR-based integrated healthcare delivery system. Strategies improving provider EHR message box management and leveraging health information technology (e.g., flagging abnormal eGFR results), making organizational/staffing changes (e.g., increasing the role of nurses in managing laboratory results), and boosting patient engagement through better patient portals may improve test follow-up." ■

TAKEAWAY POINTS

- A mixed-methods study that included retrospective electronic health record analysis and physician interviews sought to identify risk factors, facilitators, and barriers to timely follow-up of incident abnormal laboratory results.
- Lack of timely follow-up was evident in 58% of patients with incident abnormal estimated glomerular filtration rate testing, creating a gap in care.
- There were weak associations between timely follow-up and patient online portal use and physician panel size.

Increasing the Rate of Appropriate CRRT Dosing: A Quality Improvement Initiative

Acute kidney injury (AKI) is reported in up to 20% of all hospitalized patients and in 30% to 50% of hospitalized patients admitted to the intensive care unit (ICU). Even in mild disease, AKI is linked to increased rates of in-hospital mortality. Among hospitalized patients with severe AKI requiring renal replacement therapy (RRT), the mortality rate is an estimated 33% overall, and can be as high as >50% in patients in the ICU. The only FDA-approved therapy for AKI is RRT and continuous RRT (CRRT) is the preferred modality in the ICU due to an association with less hemodynamic instability compared with intermittent therapy.

The optimal dose in CRRT is based on urea clearance. In the 2012 Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guidelines, the recommendations call for patients treated with CRRT to receive an effluent flow rate of 20 to 25 mL/kg/hour; the recommendation had a 1A rating. In 2013, the National Kidney Foundation Kidney Disease Outcomes Quality Initiative endorsed the recommendation for a CRRT dose of 20 to 25 mL/kg/hour.

However, according to **Benjamin R. Griffin, MD,** and colleagues, despite clear recommendations, dosing of CRRT remains highly variable. Results of national surveys reveal that <50% of practitioners target a specific dose, and only 15% of patients have regular dose assessments. In a preliminary data review at the University of Colorado Hospital (UCH), the average daily delivered dose of CRRT after accounting for machine downtime was not routinely documented; the prescription patterns also differed widely among nephrology faculty.

Dr. Griffin et al. designed a quality improvement initiative aimed at standardizing CRRT treatments at UCH. The researchers sought to increase the percentage of daily CRRT sessions within the target range of 20 to 25 mL/kg/hour to at least 65% within 1 year. The initiative and results were reported in the *American Journal of Kidney Diseases* [2019;74(6):727-735].

Participants in the initiative were adult patients treated with CRRT at the UCH between January 2016 and October 2017. The primary objective outcome measure was the percentage of treatments per week in which the average daily dose of CRRT was 20 to 25 mL/kg/hour. Secondary measures included mortality, number of CRRT treatments, length of stay in the ICU, and length of stay in the hospital. The average CRRT dose and compliance rates specifically on the first day of treatment were also recorded.

An assessment of the magnitude of the variability in CRRT dosing and four specific interventions were implemented during the course of 1 year: (1) modification of the electronic medical record (EMR) to include calculated average 24-hour dose in real time; (2) modification of the CRRT procedure note to include comments on dosing; (3) modification of the CRRT order set to display calculations; and (4) yearly educational sessions for renal fellows outlining CRRT specific dosing targets.

Prior to implementation of the interventions, dosing data from January to October 2016 were collected. During that time period, 915 treatment sessions were identified. Of those, 78 treatment sessions were excluded due to missing data, resulting in 837 sessions to analyze.

The average dose was 26.1 mL/kg/hour (standard deviation, 7.4). Of the 837 sessions, 33% (n=279) were between 20 and 25 mL/kg/hour; 21% (n=173) were <20 mL/kg/hour; and 46% (n=385) were >25 mL/kg/hour. In the group with an above-goal dose, 22% (n=187) were >30 mL/kg/hour and 2% (n=21) were >50 mL/kg/hour.

In terms of age, sex, and race, the populations of patients undergoing CRRT at UCH before and after implementation of the interventions were similar. The cause of AKI was also similar; sepsis was the leading cause of AKI in both populations. Also comparable were the ICU locations of treatment; the medical ICU accounted for the largest percentage of treatments in both populations.

In the post-intervention group, the indications for CRRT were collected; patients nearly universally had stage 2 or 3 AKI by the KDIGO definition, and oliguria/anuria and volume overload were the most common reasons for CRRT.

> Following the interventions, 66% (n=631) of treatments achieved the goal dose.

Between February and October 2017, data on 952 treatments were collected. Following the interventions, 66% (n=631) of treatments achieved the goal dose. There was a substantial decline in the number of underdose treatments: 12% (n=113) received doses <20 mL/kg/hour. There was also a decline in the number of overdoses treatments: 22% (n=209) of patients received doses >25 mL/kg/hour. Only 4% (n=37) had doses >30 mL/kg/hour, and there were no treatments with an extremely above-goal dose (>50 mL/kg/hour). There was a notable decrease in week-to-week variance in dosing.

In terms of secondary outcomes, there was a statistically significant decrease in mortality: 60% preintervention versus 45% postintervention. There were no differences in days of CRRT treatment, length of stay in the ICU, or length of stay in the hospital.

Limitations to the study included the single-center design, potentially limiting the generalizability of the findings to institutions with different CRRT nursing models or different EMR systems.

In conclusion, the authors said, "An important component of CRRT delivery is ensuring that patients on CRRT receive an average effluent dose of 20 to 25 mL/kg/hour. Using a series of interventions including changes to the EMR, changes in documentation templates, and specific education of renal fellows, we were able to double our institution's rate of dosing compliance." ■

TAKEAWAY POINTS

- There is wide variation in practice patterns of dosing of continuous renal replacement therapy (CRRT) in patients in the intensive care unit with acute kidney injury. A quality improvement initiation was implemented at the University of Colorado Hospital.
- The initiative sought to standardize CRRT practice patterns and reduce dosing variability; the primary outcome measure was the weekly percentage of CRRT treatments with an average delivered daily dose of 20 to 25 mL/kg/hour.
- Following implementation of the interventions, the rate of appropriate CRRT dosing was doubled and dosing variability was reduced.

Anticoagulation Therapy in Patients with Primary MN

Primary membranous nephropathy (MN) is a leading cause of nephrotic syndrome in adults. Therapy for primary MN focuses on the prevention of end-stage renal disease (ESRD). ESRD commonly occurs several years following presentation with primary MN; however, other complications may occur much earlier in the course of the disease.

Researchers in one study developed a Markov-based decision analysis model to estimate the possibility of benefit based on an individual's bleeding risk profile, serum albumin level, and acceptable benefit-to-risk ratio.

TAKEAWAY POINTS

- Patients with primary membranous nephropathy (MN) are at increased risk for thromboembolic complications, including venous thromboembolic events (VTEs).
- Researchers conducted a literature review to provide suggestions on decision making regarding anticoagulant management in patients with primary MN at high risk of thrombosis or with thromboembolic complications.
- The use of prophylactic aspirin or warfarin may have clinical benefits for the primary prevention of thromboembolic events in patients with primary MN with hypoalbuminemia.

Early complications of primary MN include venous thromboembolic events (VTEs) such as deep venous thrombosis (DVT), renal vein thrombosis (RVT), and pulmonary embolism (PE). These complications are associated with significant morbidity and mortality. Hypoalbumineia is the most significant indicator of risk of VTE. Patients with primary MN also experience increased high absolute risk of arterial thromboembolic events (ATEs) within 6 months of presentation. Predictors of ATEs include severe proteinuria, estimated glomerular filtration rate, and smoking. Primary cardiovascular events include acute coronary syndrome (ACS) and ischemic stroke (IS).

Given the need to carefully manage anticoagulants and antiplatelet agents and to tailor therapeutic regimens to an individual's risk of thromboembolic events, the 2012 Kidney Diseases Improving Global Outcomes (KDIGO) evidence supporting prophylactic and therapeutic anticoagulation is, according to researchers, too weak to meet the needs of primary MN patients with hypoalbuminemia. **Honghong Zou** and **Yebei Li, PhD,** conducted a review to provide suggestions to help guide decision making on the management of anticoagulation in patients with primary MN at high risk of thrombosis or with thromboembolic complications. Results of the review were reported online in *BMC Nephrology* [doi.org/10.1186/s12882-019-1637-y].

The researchers extracted relevant studies by searching the Cochrane Library, Medline, PubMed, and Web of Science from March 1968 to March 2018. Eligible publications included guidelines, reviews, case reports, and clinical trial studies regarding the rational management of anticoagulation therapy in the primary MN population.

The review demonstrated that the risk of thromboembolic events is particularly high in primary MN when compared with other pathological types of nephrotic syndrome and that most patients remain asymptomatic. This finding suggests considering the prophylactic use of anticoagulants or antiplatelet agents to prevent VTEs and ATEs in this patient population. The findings also suggest that the rational management of therapeutic anticoagulation and antiplatelet agents in patients with primary MN and thromboembolic complications may result in the reduction in the risk of recurrent cardiovascular events.

Low serum albumin is a strong independent risk factor for VTEs in patients with primary MN. The increasing risk was proportionally associated with declining albumin levels in a retrospective study accessed by the review. There was an association between each 1.0-g/dL increase in albumin level and a 2.13-fold increase risk of VTE. The study identified the threshold albumin level for the overall risk of VTEs as 2.8 g/dL (i.e., a serum albumin level <2.8 g/dL indicated a high risk of a VTE). In another study, anticoagulation was indicated in patients with primary MN who initially presented with thrombotic events due to the high risk of thromboembolic complications. However, the use of prophylactic anticoagulation therapy remains controversial in primary MN.

The 2012 KDIGO guidelines indicate that prophylactic oral warfarin can be considered in primary MN patients when serum albumin is <2.5 g/dL in the presence of additional risks for thrombosis; some physicians believe prophylactic anticoagulation should be initiated earlier. Studies have shown that aspirin has a therapeutic benefit for the prevention and recurrence of VTEs and significantly reduces the rate of major vascular events with no apparent increase in the risk of major bleeding. Some of the researchers in the reviewed studies felt that patients with primary MN could receive antiplatelet agents such as aspirin for the primary prevention of thrombotic events at an early stage of the disease.

The studies also indicated that the benefits of anticoagulation in the prevention of VTEs should be weighed against the risk of hemorrhage complications in individual patients. Researchers in one study developed a Markov-based decision analysis model to estimate the possibility of benefit based on an individual's bleeding risk profile, serum albumin level, and acceptable benefit-to-risk ratio.

The treatment regimen for thromboembolic complications in patients with primary MN was similar to that in patients in the general population with thromboembolic events. D-dimer level may be affected by proteinuria and may not be an independent predictor of stopping anticoagulant therapy in patients with primary MN and VTEs. Further, the reduction of proteinuria and the increase of serum albumin are important goals for the treatment of primary MN with VTEs. Clinicians should continue the previous steroid therapy or combine it with immunosuppressive agents over the entire treatment period until the primary MN treatment protocol is completed. There are no clinical trial data regarding the optimal length of anticoagulation therapy in this patient population; one potential approach is to treat patients with anticoagulation therapy at least 3 to 6 months (if there are no contraindications) until serum albumin levels normalize and patients achieve remission.

The researchers cited some limitations to the review, including the majority of the evidence for prophylactic anticoagulation recommendations being derived from retrospective studies.

"The utility of prophylactic aspirin or warfarin may have clinical benefits for the primary prevention of thromboembolic events in primary MN patients with hypoalbuminemia," the researchers said. "It is necessary to perform large randomized controlled trials and to formulate relevant guidelines to support the present review," they added. ■

VITAL-DKD Results: Vitamin D and Omega-3 Fatty Acids in Diabetic Kidney Disease

Chronic kidney disease (CKD) is a common complication of type 2 diabetes and is associated with poor health outcomes. Despite advances in diabetes care, the prevalence of CKD in that patient population remains more than 25% and increases with the duration of diabetes. In the United States, type 2 diabetes is the leading cause of end-stage renal disease requiring dialysis or kidney transplantation, and CKD is associated with increased risks of cardiovascular events and mortality in patients with diabetes.

The development and progression of CKD (defined as persistently reduced glomerular filtration rate [GFR] or elevated urinary albumin excretion) may be prevented with interventions such as vitamin D and omega-3 fatty acid supplements. Previous clinical trials designed to evaluate the renal effects of vitamin D and omega-3 fatty acid supplements have been of short duration, only evaluated urine albumin excretion as an outcome, or examined kidney outcomes as secondary post hoc analyses.

Ian H. de Boer, MD, and colleagues conducted VITAL-DKD (Vitamin D and Omega-3 Trial to Prevent and Treat Diabetic Kidney Disease) to examine the efficacy and safety of vitamin D and omega-3 fatty acids for the prevention and treatment of CKD in patients with type 2 diabetes. Results were reported online in *JAMA* [doi:10.1001/jama.2019.17380].

VITAL-DKD was conducted among 1312 adults with type 2 diabetes who were recruited between November 2011 and March 2014 from all 50 US states as an ancillary study to the VITAL (Vitamin D and Omega-3 Trial) coordinated by a single center in Massachusetts. Follow-up was completed in December 2017.

Participants were randomized to receive Vitamin D_3 (23000 IU/d) and omega-3 fatty acids (eicosapentaenoic acid and docosahexaenoic acid; 1 g/d) (n=370), vitamin D_3 and placebo (n=333), placebo and omega-3 fatty acids (n=289), or two placebos (n=320) for 5 years. The primary outcome of interest was change in GFR estimated from serum creatine and cystatin C (eGFR) from baseline to year 5. Secondary outcomes included time to the composite outcome of at least a 40% decrease in eGFR from baseline, kidney failure, or death; time to at least a 40% decrease in eGFR from baseline; and change in urine albumin-creatinine ratio (ACR) from baseline to study year 5.

At baseline, mean age of study participants was 67.6 years and median duration of diagnosed diabetes was 6 to 10 years; 46% were women, and 31% were of racial or ethnic minority. The most commonly used glucose-lowering medications were biguanides, followed by sulfonylureas. Twenty percent of the cohort reported insulin use. Less than 10% reported using a dipeptidyl peptidase 4 inhibitor or glucagon-like peptide 1 receptor agonist; sodium-glucose cotransporter 2 inhibitors were not yet commercially available.

Eighty percent of the participants used antihypertensive medications, including 61% who used a renin-angiotensin system inhibitor. Mean eGFR at baseline was 85.8 mL/min/1.73 m^2; 13% of participants (n=165) had eGFR <60 mL/min/1.73 m^2. Nine percent of participants (n=117) had urine ACR of at least 30 mg/g, including 2% (n=24) with an ACR of at least 300 mg/g. A total of 1090 of the 1312 randomized participants (83%) provided at least one follow-up blood sample, including 934 at year 5. At least one follow-up urine sample was provided by 1091 participants, including 945 at year 5 after randomization.

At 2 years following randomization for vitamin D or placebo, adherence to at least two-thirds of study medications was reported by 92% of participants; at 5 years, the percentage was 88%; medication adherence was reported by 91% and 89%, respectively, at 2 and 5 years for omega-3 fatty acids (or matching placebo).

At year 2, mean serum 25(OH)D concentrations were 41.4 ng/mL for those in the Vitamin D group and 29.8 mg/mL for those in the vitamin D placebo group (P<.001). For participants in the omega-3 fatty acid group, mean omega-3 indexes at year 2 were 3.6% compared with 2.3% for those in the omega-3 fatty acid placebo group (P<.001).

Mean eGFR was 85.8 mL/min/1.73 m^2 at baseline, 80.0 mL/min/1.73 m^2 at year 2, and 73.5 mL/min/1.73 m^2 at year 5. In the full analytic population, mean change in eGFR from baseline to year 5 was –12.7 mL/min/1.73 m^2; among the 932 participants with eGFR data at both baseline and year 5, the mean change from baseline to year 5 was –12.4 mL/min/1.73 m^2.

Mean change in eGFR from baseline to year 5 in the vitamin D3 group was –12.3 mL/min/1.73 m^2 versus –13.1 mL/min/1.73 m^2 with placebo. Mean change in eGFR was –12.2 mL/min/1.73 m^2 in the omega-3 fatty acids group compared with –13.1 mL/min/1.73 m^2 in the placebo group. At year 5, there was no significant difference in change in eGFR according to treatment and no significant interaction between treatment assignments.

Of the three prespecified secondary outcomes, there were no significant differences by treatment assignment for either intervention.

In comparisons of both vitamin D and omega-3 fatty acid supplementation with respective placebos, adverse events were similar. Kidney stones occurred in 58 patients (32 receiving vitamin D3 and 26 receiving placebo) and gastrointestinal bleeding occurred in 45 participants in the omega-3 fatty acid group and 17 in the placebo group.

Limitations cited by the authors included the modest numbers of eGFR and urine ACR measurements collected per participant, the insufficient numbers of events for surrogate kidney end points, and not receiving a serum sample from all participants to calculate year 5 eGFR.

In summary, the researchers said, "Among adults with type 2 diabetes, supplementation with vitamin D_3 or omega-3 fatty acids, compared with placebo, resulted in no significant difference in change in eGFR at 5 years. The findings to not support the use of vitamin D or omega-3 fatty acid supplementation for preserving kidney function in patients with type 2 diabetes." ■

TAKEAWAY POINTS

- The VITAL-DKD study was conducted to examine the efficacy and safety of vitamin D and omega-3 fatty acid supplementation to prevent and treat chronic kidney disease (CKD) in patients with type 2 diabetes.
- There were no significant differences in change in estimated glomerular filtration rate at 5 years between the groups receiving vitamin D or omega-3 fatty acid supplementation and those receiving the respective placebos.
- The use of vitamin D or omega-3 fatty acid supplementation to preserve kidney function in patients with type 2 diabetes is not supported by the findings of this study.

Weight Gain Following Living Donor Kidney Transplantation

TAKEAWAY POINTS

- Kidney transplant recipients commonly experience weight gain in the 12 months post-transplant. Researchers conducted a prospective observational study to examine the factors associated with weight gain after kidney transplant.
- The study population included recipients of living donor kidney transplants; among the participants, there was significant weight gain at 3 and 12 months post-transplant.
- The weight gain was due primarily to accumulation of adipose tissue in the truncal region; there were no increases in muscle mass or fluid accumulation.

Patients who undergo successful kidney transplantation often experience weight gain; however, there are few data available on the specific changes in body composition that underlie the weight gain in low–immunity-risk patients. Further, the metabolic mechanisms that cause changes in body composition are not clearly identified.

Weight gain after kidney transplantation may be associated with the development of cardiovascular diseases and increased risk of mortality, and the amount of weight gained is an independent predictor of the development of insulin resistance and the risk of developing cardiovascular diseases. **Biruh Workeneh, MD,** and colleagues conducted a study to evaluate the weight gain and its composition and location in patients who underwent living donor kidney transplantation. The single-site, prospective, observational study examined metabolic determinants that could contribute to weight gain in that patient population. Results of the study were reported in the *Journal of Renal Nutrition* [2019;29(6):548-555].

A total of 187 living donor transplant candidates were screened for study participation between September 2014 and October 2016. Of those, 113 met inclusion criteria. Thirty-eight consented to participation and 33 were enrolled; five could not commit to the scheduled visits due to time constraints or transportation. Of the 33 enrolled, two withdrew following completion of the baseline studies due to transportation issues, resulting in a final study cohort of 31 subjects.

Among the 31 participants, mean age was 47.9 years, 87% (n=27) were men, mean weight at baseline was 83.3 kg, mean body mass index was 28.0 kg/m^2, mean ideal body weight was 73.8 kg, 18 were white, five were black, one was Asian, and seven were Hispanic. The etiology of kidney failure was hypertension in seven participants, diabetes in five, glomerulopathy in nine, failed transplant in three, polycystic kidney disease in three, and unknown in four. Two of the patients received preemptive kidney transplantation and none required dialysis following transplantation. Three participants experienced acute rejection during the 12-month observation period; all three were successfully treated with a steroid taper.

At three months post-transplantation, there was a statistically significant increase in body weight (2.2 kg, $P<.032$); body weight increased further at 12 months post-transplantation (6.6 kg; $P<.001$). Measurements of body composition further contributed to the distribution of weight increase; the increase was largely due to an expansion of adiposity. In a four-component model that divides the body into fat, water, protein, and mineral used to measure body composition, the fat component was the only component found to have increased. At 12 months post-transplantation, the fat component increased by 5.4 kg; $P=.002$.

Dual-energy x-ray absorptiometry (DXA) analysis provided further insight into the distribution of fat. At both post-transplantation time points, there were increases in body fat (2.1 kg at 3 months and 5.1 kg at 12 months; $P=.002$ and $P<.001$, respectively). The DXA analysis showed that 71% of fat accumulation was in the truncal region. Additionally, the mean android-to-gynoid fat mass ratio significantly increased after kidney transplantation, indicating a redistribution or dysregulation of fat deposition. There were also significant increases in visceral and subcutaneous fat volumes at both time points.

Despite significant increases in fat mass, there were no significant changes in lean or skeletal muscle masses from baseline to either time point. The analyses of the 4-component model revealed that in contrast to changes in adipose tissue, there were no significant changes in the sizes of the remaining components.

The study also examined clinical factors that could contribute to the increase in adipose tissue. Differences in dietary factors were assessed prior to and after transplantation. With the exception of dietary fat, there were no significant differences in macronutrient and kilocalorie intake between visits. In measurements of resting energy expenditure, there were no significant changes in the resting metabolic rate between baseline and 3 months or 12 months. However, when standardized for body weight, there was a statistically significant decrease in basal metabolic rate per kg, indicating adipose tissue gain.

In analyses of the effects of physical activity on weight gain, transplant recipients were significantly more ambulatory post-transplant. The number of minutes of moderate and vigorous physical activity increased post-transplant; the difference between baseline and values at 12 months reached statistical significance.

Following exclusion of participants receiving insulin for diabetes control, results of analyses of changes in insulin sensitivity indicated worsening of insulin resistance. In measurements of the presence of total, subcutaneous, truncal, and visceral adipose stores at baseline and at 3 and 12 months, each of the adipose stores was associated with insulin resistance to varying degrees. Visceral adipose tissue had the strongest correlation with insulin resistance when correlated with the homeostatic model assessment of insulin resistance (r=0.67; $P<.001$).

The researchers did cite some limitations to the study, including the significant commitment required of the participants and the high proportion of men in the study population.

In conclusion, the researchers said, "Successful transplantation was associated with increased insulin resistance and weight gain without increases in muscle or fluid. This metabolic pattern suggests potential interventions that could prevent or mitigate the consequences of adipose tissue accumulation in transplant recipients." ■

Education Delivered Directly to Patients Increased Transplantation Knowledge

There are more than 678,000 individuals in the United States with kidney failure, and nearly 100,000 are diagnosed each year. Compared with ongoing dialysis as treatment for kidney failure, kidney transplantation is associated with longer survival and improved quality of life. Per regulations from the Centers for Medicare & Medicaid Services, patients with kidney failure must be informed of their options regarding kidney transplantation, including the choice to continue receiving maintenance dialysis or to pursue a deceased or living donor kidney transplant. However, despite availability of information about kidney transplantation, more than 70% of patients with kidney failure remain on dialysis therapy.

Lack of access to kidney transplantation affects patients disproportionately in the United States. Black patients are 3.1 times more likely than white patients to develop kidney failure, yet are less likely to receive transplants, particularly living donor kidney transplants. Further, independent of race, patients with low socioeconomic status are up to 75% less likely to receive a living donor transplant.

The American Society of Transplantation recommends providing culturally tailored community-based living donor kidney transplant education to patients earlier in the transplantation referral process. Supplementary education directly available to dialysis patients over a longer time frame may enhance kidney education programs in dialysis centers. **Amy D. Waterman, PhD,** and colleagues, conducted a prospective, three-arm parallel-group, randomized, controlled trial to examine the efficacy of two supplementary kidney transplant education approaches delivered directly to patients. Results were reported in the *American Journal of Kidney Diseases* [2019;74(5):640-649].

The study included adult, black, and low-income participants receiving dialysis in Missouri. Patients were randomly assigned to receive one of three educational conditions over an 8-month period: (1) standard transplantation education provided in dialysis centers only (standard of care); (2) the patient-guided Explore Transplant @ Home program with no access to an educator; or (3) the educator-guided Explore Transplant @ Home program facilitated by an educator via telephone. The primary outcome of interest was patient knowledge of living and deceased donor kidney transplantation. Secondary outcomes included informed decision making, change in attitudes in favor of living and deceased donor transplantation, and change in the number of steps taken toward kidney transplantation.

Of the 836 patients who responded to advertisements to participate in the study, 673 met eligibility criteria. Of those, 561 (83%) completed a baseline survey and were randomly assigned to either the educator-guided Explore Transplant @ Home program (n=189), the patient-guided Explore Transplant @ Home program (n=185), or to the standard-of-care control group (n=187). Of those patients, 105 withdrew, died, or were lost to follow-up, resulting in the modified intent-to-treat sample of 144 in the educator-guided group, 152 in the patient-guided group, and 160 in the control group. At baseline, the three groups were similar in demographic characteristics and health insurance status.

Mean transplantation knowledge score at baseline was 7.2 (range, 0-14), indicating that patients responded correctly to <50% of the 15 questions. Compared with the control group, patients in the educator- and patient-guided groups had significant increases in transplantation knowledge following the intervention: patients in the intervention groups had a 1.4 point increase compared with a 0.8 point increase in the control group (P=.02 and P=.01, respectively).

At baseline, patients reported having completed a median of two of 11 steps toward transplantation. The most common steps included calling the transplantation center to begin the transplant evaluation process (40%) and talking to transplant recipients about their experiences (34%). For all of the study participants, following the intervention, the most common new steps were: (1) sharing interest in living donor kidney transplant with family and friends (25%); (2) talking to transplant recipients about their experiences (23%); (3) calling the center to begin the evaluation process (17%); (4) making a list of potential living donors (17%); (5) talking to living donors about their experiences (16%); and (6) telling a transplantation coordinator about their interest in living donor transplant (15%).

More patients in the intervention groups were able to make informed decisions regarding initiating the kidney transplant evaluation process than in the control group: 91% and 95% versus 82% (P=.003); regarding pursuing deceased donor kidney transplant (84% and 84% versus 70% (P=.003); and regarding pursuing living donor kidney transplant (91% and 92% versus 73% [P<.001]).

There were some limitations to the findings cited by the authors, including the lack of dialysis center-level randomization that could have created contamination due to communication among patients across the three study arms, and the lack of hard clinical end points such as completion of the transplantation evaluation or receipt of a living or deceased donor kidney transplant.

In conclusion, the researchers said, "This study established the efficacy of the Explore Transplant @ Home program in two forms to increase learning and informed decision making for black and low socioeconomic patients. A broader implication is that delivering educational content to patients directly, with the option of short telephone conversations with educators, may help increase knowledge and informed transplantation decision making for large numbers of patients receiving dialysis without placing additional burdens on dialysis providers." ■

TAKEAWAY POINTS

- Black and low-income patients on maintenance dialysis are less likely to receive education on kidney transplantation at dialysis centers.
- Researchers conducted a study to examine the efficacy of two supplementary kidney transplantation education approaches delivered directly to patients.
- With or without coaching, direct delivery of kidney transplant education to patients increased patient kidney transplantation knowledge and informed decision making, with no additional burden on dialysis providers.

Hearst Foundation Funds American Kidney Fund Fellowship

In a recent press release, the American Kidney Fund (AKF) announced the receipt of a $100,000 grant from the Hearst Foundation. The grant will support a postdoctoral fellowship in the AKF Clinical Scientist in Nephrology Program. The program helps fund promising young researchers who are working to improve the diagnosis, treatment, and outcomes for patients with chronic kidney disease.

The program is designed to drive innovation in postdoctoral nephrology education and attract young scholars to the field of clinical research. The students receive a two-year fellowship that allows them to conduct patient-centric research in prevention and outcomes of kidney disease. Research that focuses on prevention seeks to develop strategies to prevent disease onset or delay disease progression. Outcomes research examines the effectiveness of therapies and interventions.

"The Hearst Foundation is honored to support the American Kidney Fund's efforts to drive quality and innovation in kidney patient care," **George Irish,** eastern director, the Hearst Foundation, said. "AKF's Clinical Scientist in Nephrology Program has a decades-long track record of important contributions to clinical research in nephrology and we are pleased to fund work that improves the lives of kidney patients and paves the way for better outcomes."

LaVarne A. Burton, AKF president and CEO, said. "Tomorrow's innovations in kidney care will come from today's young researchers, and we have been filling that pipeline for more than 30 years. The Hearst Foundation's generous gift will enable AKF to continue advancing quality in kidney care, while inspiring a new generation of nephrologists to innovate how we prevent and treat kidney disease."

Israeli Researchers Develop Technology to Rejuvenate Kidney Cells

A study published in *Cell Reports* has reported that it is possible to rejuvenate kidneys and improve their function by using the patient's stem cells. The study was conducted by **Benjamin Dekel, MD, PhD,** head of pediatric nephrology and the Pediatric Stem Cell Research Institute in the Edmond and Lily Safra Children's Hospital at Sheba Medical Center, Tel HaShomer in Israel.

"This treatment is aimed at the millions of patients who have yet to require dialysis treatment, and focuses on improving stabilizing their renal function in order to avoid the need for dialysis," Professor Dekel said.

Previous studies have found that the adult kidney can renew itself over time through the activity of colonies of cells that function to replace lose and degenerated cells in the kidney. Professor Dekel and colleagues have developed a technology that allows for extraction of such healthy kidney cells from diseased kidneys. The extracted cells are expanded into large numbers in a laboratory setting and subsequently administered back into the kidney.

To date, the method has been tested on mice, where the cells have shown an ability to generate new renal structures, resulting in improved renal function in treated mice.

Professor Denkel said, "The breakthrough in this technology, which was developed at Sheba Medical Center, is not only in the ability to maintain the kidney renewing cells outside the body, but also in the fact that we are able to multiply them to generate large numbers of cells and make them work properly using the 3D culture. This is important news for patients with chronic kidney disease, which hopefully could benefit from these discoveries in following years. The ability to generate new kidney tissue that could replace the damaged tissue might help millions of patients worldwide who suffer from kidney disease."

Bipartisan Legislation to Extend Immunosuppression Coverage

Reps. Ron Kind (D-WI) and **Michael C. Burgess, MD (R-TX)** recently introduced H.R. 5534, the Comprehensive Immunosuppressive Drug Coverage for Kidney Patients Act of 2019. According to a press release from Rep. Kind's office, the bipartisan legislation would improve coverage under Medicare for immunosuppressive drugs for kidney transplant recipients. The bill was on the agenda of a January meeting of the House Energy and Commerce Subcommittee on Health. The subcommittee meeting included testimony from experts such as **Matthew Cooper, MD,** director of kidney and pancreas transplantation at the MedStar Georgetown Transplant Institute and a professor of surgery at Georgetown University School of Medicine.

The bill would allow kidney transplant recipients to maintain Medicare Part B coverage for immunosuppressive medications for the lifetime of the transplanted kidney, and save Medicare an estimated $300 million over 10 years, according to the US Department of Health and Human Services.

In a press release from Honor the Gift, a national patient-centered coalition of 26 leading kidney and transplant organizations, Dr. Cooper said, "The current Medicare reimbursement system for kidney patients' post-transplant care makes no sense morally or financially and I'm thrilled so many members of Congress are working hard to see that it's changed. Since we've also received support from the Administration, we're more hopeful now than ever that we can finally get this legislation passed and do right by kidney recipients and their donors."

Reps. Kind and Burgess were joined by **Reps. Anna Eshoo (D-CA), Jamie Herrera Beutler (R-WA), Donald McEachin (D-VA),** and **Jason Smith (R-MO)** in cosponsoring the legislation. A similar bill is expected to be introduced by the Senate later this year.

American Kidney Fund Convenes 2020 Research Summit

The American Kidney Fund (AKF) is sponsoring a 2020 summit designed to advance the science of diagnosing the underlying causes of kidney disease and kidney failure. According to a recent press release, the summit will include scientists, patients, academic and industry researchers, and other stakeholders.

Results of studies suggest that in approximately 10% of new cases of chronic kidney disease the cause is unknown. Undiagnosed or misdiagnosed causes of kidney disease have a direct impact on patient care and outcomes. Diabetes and hypertension are the most common causes of kidney disease and kidney failure; however, kidney-related rare diseases and genetic disorders may also contribute to kidney disease. The AKF summit will identify ways to drive innovation in research, diagnosis, and treatment of kidney disease. Initial funding is provided by Sanofi Genzyme.

LaVarne A, Burton, president and CEO of AKF, said, "Kidney disease has become more of a national priority than ever before with the federal government's Advancing American Kidney Health initiative, which is helping to spur innovation in research and treatment for this disease that affects so many Americans. This new AKF initiative will help to assess and address the gap in patient care that occurs when the underlying cause of kidney disease is not identified."

"In addition to benefiting from industry experts, the patient voice will be central to this project, which is an opportunity to foster greater collaboration across disciplines in nephrology research with the ultimate goal of improving patient outcomes. We are grateful to Sanofi Genzyme for signing on as a lead sponsor for this initiative and look forward to welcoming a coalition of additional partners to support this important work," she added.

Proposed DHHS Rule to Encourage Living Organ Donation

Late last year, the US Department of Health and Human Services (DHHS) announced efforts to reduce financial barriers to living organ donation for potential donors.

In a press release from Fresenius Medical Care North America, **Bill Vale,** chief executive officer, said, "We strongly believe that the best option for all patients with kidney failure is the option to receive a transplant. Reducing financial barriers by reimbursing kidney donors for lost wages, childcare, and other expenses is a positive step forward in supporting those willing to give life back to others, and therefore making living donation a more viable option for many Americans."

The Fresenius Medical Care Foundation and Donate Life America have formed a partnership to launch a National Donate Life Living Donor Registry and at-home testing kit. Mr. Valle said that the proposed DHHS rule "reinforces the partnership between the Fresenius Medical Care Foundation and Donate Life America to establish the first national, universal living donor registry, and at-home testing kit. We appreciate the efforts of the government to further encourage living donation for those in need of a kidney, providing a better and faster path to transplant for our patients." ■

Major Meetings 2020

National Kidney Foundation Spring Clinical Meetings 2020

March 25-29, 2020

New Orleans, Louisiana

www.kidney.org/spring-clinical/future-dates

American Nephrology Nurses Association 2020 National Symposium

April 19-22, 2020

Orlando, Florida

www.annanurse.org/events/national

National Kidney Foundation Spring Clinical Meetings 2020

March 25-29, 2020

New Orleans, Louisiana

www.kidney.org/spring-clinical/future-dates

American Transplant Congress 2020

May 30-June 3, 2020

Philadelphia, Pennsylvania

https://atcmeeting.org

American Society of Nephrology Kidney Week 2020

October 20-25, 2020

Denver, Colorado

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

Abstract Roundup

ACUTE KIDNEY INJURY

Use of Renin-Angiotensin System Blocker and Recurrent AKI

Clinical Journal of the American Society of Nephrology. 2020;15(1):26-34

The treatment of choice for management of patients who survived hospitalized acute kidney injury (AKI) is unclear; the use of renin-angiotensin system blockers in that patient population may increase the risk of recurrent AKI. **Chi-yuan Hsu, MD, MS,** and colleagues conducted a cohort study to examine outcomes in patients who experienced AKI and survived a hospitalization between January 1, 2006, and December 31, 2103.

The cohort included 10,242 members of an integrated healthcare delivery system in Northern California. Eligible patients did not have prior heart failure or use of angiotensin-converting enzyme inhibitors (ACE-Is) or angiotensin receptor blockers (ARBs) up to 5 years prior to the index hospitalization. Outpatient health plan pharmacy databases were used to identify new receipt and time-updated exposure of ACE-Is/ARBs.

The primary outcome of interest was a subsequent episode of hospitalized AKI after discharge from an initial index hospitalization complicated by AKI. Acute changes in serum creatinine concentrations were used to define recurrent AKI. Marginal structural models adjusted for baseline and potential time-dependent confounders.

Of the 10,242 patients, 47% had a documented estimated glomerular filtration rate <60 mL/min/1.73 m^2 or documented proteinuria prior to hospitalization. During a median 3 years of follow-up (interquartile range, 1-5 years), 18% of patients (n=1853) initiated use of ACE-Is/ARBs and 21% (n=2124) experienced recurrent AKI. The crude rate of recurrent AKI was 6.1 per 100 person-years off ACE-I/ARBs and 5.7 per 100 person-years on ACE-Is/ARBs.

Following adjustment for baseline and potential time-dependent confounders, marginal structural causal inference models found no association between exposure to ACE-Is/ARBs use and higher incidence of recurrent AKI (adjusted odds ratio, 0.71; 95% confidence interval, 0.45-1.12).

In conclusion, the researchers said, "In this study of AKI survivors without heart failure, new use of ACE-Is/ARB therapy was not independently associated with risk of recurrent hospitalized AKI."

ADPKD

Changes in Proximal Tubular Secretion in Patients with ADPKD

Clinical Journal of the American Society of Nephrology. 2020;15(1):80-88

In patients with autosomal dominant polycystic kidney disease (ADPKD), glomerular filtration rate (GFR) commonly remains normal despite significant nephron loss; proximal tubular secretory clearance may be reduced in that patient population prior to detectable changes in GFR.

Researchers, led by **Ke Wang, MD,** used targeted mass spectrometry to quantify secretory solutes from blood and urine samples from 31 patients with ADPKD and preserved GFR (mean estimated GFR [eGFR], 111 mL/min/1.73 m^2) and 25 healthy controls as well as from 95 patients with ADPKD and reduced GFR (mean eGFR, 53 mL/min/1.73 m^2) and 92 individuals with non-ADPKD chronic kidney disease (CKD). Among 112 patients with ADPKD, associations between solute fractional excretion and height-adjusted total kidney volume were determined using linear regression.

Following adjustment for demographics, clinical characteristics, and

measures of kidney function, the fractional excretions of three secretory solutes were lower in patients with ADPKD and preserved GFR compared with healthy individuals: cinnamoylglycine excretion, 52% lower (95% confidence interval [CI], 24%-70%); tiglylglycine excretion, 53% lower (95% CI, 23%-71%); and xanthosine excretion, 91% lower (95% CI, 83%-95%).

Patients with ADPKD and reduced GFR also demonstrated 37% lower dimethyluric acid excretion (95% CI, 21%-50%), 58% lower hippurate excretion (95% CI, 48%-66%), 48% lower isovalerylglycine excretion (95% CI, 37%-56%) and 31% lower pyridoxic acid excretion (95% CI, 16%-42%) compared with patients with non-ADPKD CKD and comparable GFR.

There were no associations between solute fractional excretions and differences in kidney volume in patients with ADPKD.

"Patients with APDKD and preserved and reduced GFR demonstrate lower tubular secretory solute excretion compared with healthy controls and patients with non-ADPKD CKD," the researchers said. "Our results suggest that tubular secretion is impaired in ADPKD independent of GFR."

Print-only Content

CHRONIC KIDNEY DISEASE

FGF23 and Fractional Excretion of Sodium

Nephrology Dialysis Transplantation. 2019;34(12):2015–2057

Results of recent studies suggest that the phosphaturic hormone fibroblast growth factor 23 (FGF23) is involved in regulation of renal sodium excretion and blood pressure. There are data demonstrating direct effects via regulation of the sodium-chloride symporter in the distal tubule, and indirect effects through interactions with the renin-angiotensin-aldosterone system. However, according to **Hong Xu, MD,** and colleagues, there are few clinical data regarding the association between FGF23 and renal sodium regulation. The researchers conducted a cross-sectional study to examine the associations of FGF23 and renal sodium handling and blood pressure in patients with non-dialysis dependent chronic kidney disease (CKD).

The study included 180 patients with stages one to five CKD who underwent renal biopsy. Baseline measurements included plasma intact FGF23, 24-hour urinary sodium excretion, fractional excretion of sodium (FENa), and blood pressure. Multivariate regression analysis was used to examine the association between FGF23 and renal sodium handling.

Median age of the cohort was 52.8 years, 60.6% were men, and median estimated glomerular filtration rate (eGFR) was 50.6 mL/min/1.73 m^2. In univariate analysis, there was a positive association between FENa (Spearman's rho=0.47; $P<.001$) and systolic blood pressure (rho=0.17; $P<.05$). There was no association with plasma sodium, 24-hour urinary sodium excretion, or mean arterial blood pressure.

Following adjustment for potential confounders, the association between FGF23 and FENa remained significant. The association was stronger among the 107 individuals with eGFR <60 mL/min/1.73 m^2 and in the 73 individuals on any diuretics. There was no change in the relationships following adjustment for measured GFR.

In conclusion, the researchers said, "FGF23 is independently associated with increased FENa in non-dialysis CKD patients. These data do not support the notion that FGF23 causes clinically significant sodium retention. Further studies are warranted to explore the mechanism underlying this association."

continued on page 22

continued from page 21

DIALYSIS

Racial and Ethnic Differences in Dialysis Discontinuation Rates

Journal of the American Society of Nephrology. 2020;31(1):149-160

Previous studies have shown that racial and ethnic minorities on dialysis survive longer than whites, and are less likely to discontinue dialysis therapy. **Abdulkareem Agunbiade, MD,** and colleagues conducted a retrospective cohort study to determine whether racial and ethnic differences in dialysis discontinuation reflect better health among those patient populations. The cohort included patients on maintenance dialysis in the US Renal Data System following hospitalization for stroke (n=60,734), lung cancer (n=4100), dementia (n=40,084), or failure to thrive (n=42,950) between 2003 and 2014.

The researchers assessed the frequency of dialysis discontinuation and used simulations to estimate survival in minorities relative to whites if minorities had the same pattern of dialysis discontinuation as whites.

In each hospital cohort, the frequency of dialysis discontinuation was substantially lower in blacks, Hispanics, and Asians than in whites. Blacks, Hispanics, and Asians also had lower observed risks for mortality. In simulation models that assigned discontinuation patterns similar to those found among whites to racial and ethnic groups, the differences in survival were attenuated and hazard ratios approached 1.0. American Indians and Alaska Natives had survival and dialysis discontinuation frequencies similar to those of whites.

In conclusion, the researchers said, "Racial and ethnic differences in dialysis discontinuation were present among patients hospitalized with similar health events. Among these patients, survival differences between racial and ethnic minorities and whites were largely attributable to differences in the frequency of discontinuation of dialysis."

HYPERKALEMIA

Hyperkalemia and Risk of RAAS Inhibitor Treatment Cessation

Nephrology Dialysis Transplantation. doi.org/10.1093/ndt/gfz263

There are few data available regarding the rates of hyperkalemia in users of renin angiotensin aldosterone system (RAAS) inhibitors and factors associated with treatment interruptions and cessation.

Researchers, led by **James B. Wetmore, MD, MS,** identified RAAS inhibitor users in the linked UK Clinical Practice Research Datalink-Hospital Episodes Statistics data set, from 2009 to 2015. Treatment interruptions were defined as no active prescription followed by reappearance. Interruptions and cessations were examined. Hyperkalemia was defined as serum potassium >5.5 mmol/L.

Time-varying Cox regression models were used to calculate rates of hyperkalemia and the factors associated with interruptions and cessations; hyperkalemia was included as a time-dependent variable.

The data set revealed 434,027 users of RAAS inhibitors. Among those, the rate of hyperkalemia was 1.30 (95% confidence interval [CI], 1.28-1.32) per 100 patient-years. A total of 73.7% of patients experienced periods of off treatment. Of those, 57.6% experienced interruption, 7.5% experienced cessation, and 8.6% experienced both interruption and cessation. Approximately one-third of patients experienced interruption or cessation within 1 year of initiation of RAAS inhibitor treatment.

The hazard ratios for patients with severe hyperkalemia were 1.10 (95% CI, 1.05-1.16) for treatment interruptions and 3.37 (95% CI, 3.25-3.50) for treatment cessation. In comparison with individuals with no chronic kidney disease (CKD), the risks of interruption for stages 4 and 5 were 1.20 (95% CI, 1.16-1.25) and 1.57 (95% CI, 1.44-1.72), respectively. The risks of cessation were 2.20 (95% CI, 2.07-2.33) and 2.87 (95% CI, 2.56-3.22), respectively.

For patients with heart failure and diabetes, the risks of interruption increased: 1.04 (95% CI, 1.02-1.05) and 1.13 (95% CI, 1.12-1.14), respectively. However, the risk of cessation decreased in patients with heart failure and diabetes: 0.85 (95% CI, 0.82-0.87) and 0.92 (95% CI, (0.90-0.94), respectively.

The researchers said, "Risk of RAAS inhibitor interruption and cessation increased as CKD stage progressed. Efforts targeting reasons for interruptions and, especially, cessations, such as hyperkalemia prevention, could decrease off-treatment periods for patients who would otherwise benefit, such as those with CKD, heart failure, or diabetes."

PEDIATRIC NEPHROLOGY

Potentially Nephrotoxic Medication Prescriptions to Children with CKD

Clinical Journal of the American Society of Nephrology. 2020;15(1):61-68

Management of pediatric chronic kidney disease (CKD) focuses on limiting kidney injury, including avoidance of nephrotoxic medications. There are few data available on nephrotoxic medication prescription practices for children with CKD. **Claire E. Lefebvre, MD,** and colleagues conducted a retrospective, matched population-based cohort study to examine the prevalence and rates of primary care prescriptions for potentially nephrotoxic medications in children with CKD versus without CKD.

The cohort included patients <18 years of age registered at a general practice that participated in the UK Clinical Practice Research Datalink (CPRD) from 1997 to 2017. Children with an incident diagnosis of CKD were matched 1:4 to patients without CKD on CKD diagnosis date, sex, age, CPRD practice, and number of general practitioner visits in the year prior to cohort entry.

The researchers calculated the prevalence and rate of prescriptions for potentially nephrotoxic medications during the follow-up period in patients with versus without CKD. Primary analyses included aminoglycosides, antivirals, nonsteroidal anti-inflammatory drugs, salicylates, proton pump inhibitors, and immunomodulators. In secondary analyses, the researchers used an expanded definition of nephrotoxicity that included, among others, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers. Multivariable binomial regression models were used to calculate adjusted prescription rates.

From a total of 1,535,816 eligible individuals, the final study cohort included 1018 patients with incident CKD and 4072 non-CKD matches. Mean age was 9.8 years, 52% were male, and median follow-up time was 3.3 years. During follow-up, 26% of patients with CKD and 15% of those without CKD were prescribed one or more potentially nephrotoxic medications. The overall rate of nephrotoxic medication prescriptions in patients with CKD was 71 prescriptions per 100 person-years versus eight prescriptions per 100 person-years in those without CKD (adjusted rate ratio, 4.1; 95% confidence interval, 2.7-6.1).

"Potentially nephrotoxic medications are prescribed at high rates to children with CKD," the researchers said. ■

Sarah Tolson

Updates to TCM Services Coverage for 2020

In the last edition of From the Field, we discussed the basics of Transitional Care Management (TCM). This edition will take a close look at this year's new changes to TCM service coverage as well as a couple of TCM service frequently asked questions. In the 2020 CMS Physician Fee Schedule Final Rule published to the Federal Register, the Centers for Medicare & Medicaid Services (CMS), and US Department of Health and Human Services sites, a recent study of 2018 TCM claims data demonstrated that beneficiaries who received TCM services had reduced readmission rates and lowered mortality in addition to decreased healthcare costs. Additionally, the study showed that recent utilization of TCM services was low compared with the number of patients who would have qualified to receive TCM services. Based on this information, a move was made by CMS to increase utilization of TCM services.

During the first six years that TCM services were a billable, covered service, Medicare would not allow providers to bill for TCM services in conjunction with the services listed below during the TCM service period.

- Care plan oversight services
- Home health or hospice supervision
- End-stage renal disease (ESRD) services
- Chronic care management services
- Prolonged evaluation and management services without direct patient contact
- Other services excluded by Current Procedural Terminology Codes reporting rules

In their efforts to increase utilization of TCM services, CMS has loosened the restrictions on the codes that can be billed concurrently with TCM services by the same provider by allowing providers to bill concurrently for the services listed below, effective January 1, 2020.

- ESRD services (for patients ≥20 years of age)
- Complex chronic care services
- Care plan oversight services
- Prolonged services without direct patient contact
- Home and outpatient international normalized ratio monitoring services
- Analysis of Data

CMS has also increased the allowed reimbursement for TCM services. These changes are great news for nephrologists, as Medicare now allows an ESRD patient's nephrologist to be reimbursed for both the Medicare Capitation Payment and TCM services during the same month.

While it is fantastic that CMS has made these changes, there has been little communication with the provider community regarding these specific changes. One significant factor that has caused confusion for providers and billing staff is the CMS TCM fact sheet. During my research for this article, I found that the most recently available CMS TCM fact sheet had a release date of January 2019.

TCM SERVICES FAQs

In recent months, I've received many questions about the specifics of TCM services regarding two basic questions below.

Q: TCM services are only reimbursable by Medicare to one provider, per patient, per 30-day period following a discharge. How does Medicare determine who to pay if more than one provider submits a claim for TCM services for the same beneficiary?
A: The first eligible claim received by Medicare for TCM services will be reimbursed. As only the first claim is reimbursed, it is critical that TCM claims are submitted in a timely manner.

Q: In the event the patient passes away before the 30th day following discharge, can the provider still report TCM Services?
A: As the TCM services codes include 30 days of care, providers would not report TCM services in the event the patient passes away less than 30 days after discharge. However, providers may report any face to face visits that occurred under the appropriate evaluation and management code.

Despite my best internet sleuthing efforts, I have come up empty handed on any details regarding billing specifics from CMS or the Medicare Administrative Contractors for providers billing concurrently for TCM services and the six services that are no longer excluded. As there is little documentation available regarding the billing and reimbursement specifics when providers bill concurrently for TCM services and ESRD services, providers may receive Medicare denials in error. Billing staff may find it helpful to familiarize themselves with the pertinent pages of the CMS 2020 PFS Final Rule. Being well versed in the 2020 updates may come in handy in the event erroneous denials are received for TCM services billed during the same month as ESRD services for the same Medicare beneficiary. ■

SOURCES:
CMS TCM FAQs: www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeeSched/Downloads/FAQ-TCMS.pdf

CMS TCM Fact Sheet: www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNProducts/Downloads/Transitional-Care-Management-Services-Fact-Sheet-ICN908628.pdf

CMS 2020 Final Rule: s3.amazonaws.com/public-inspection.federalregister.gov/2019-24086.pdf

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