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Gram-Negative Bloodstream Infections in Hemodialysis Outpatient Centers

In the United States, more than 450,000 patients receive hemodialysis in approximately 6500 outpatient centers. Patients receiving maintenance dialysis are at high risk for morbidity and mortality. In 2014, the Centers for Disease Control and Prevention (CDC) received 29,516 reports of bloodstream infections among hemodialysis outpatients.

The most common cause of bloodstream infections in hemodialysis patients is Gram-positive organisms; bloodstream infections due to Gram-negative organisms are less common. However, there have been reports of outbreaks associated with Gram-negative organisms in outpatient hemodialysis facilities attributed to water sources, such as contaminated reprocessed dialyzers, improper handling of medications, hemodialysis equipment, and dialysate. Infections associated with water reservoirs have also been reported.

Shannon A. Novosad, MD, MPH, and colleagues conducted matched case-control investigations at three outpatient hemodialysis facilities to examine an outbreak of Gram-negative bloodstream infections. Results of the investigations were reported in the *American Journal of Kidney Diseases* [2019;74(5):610-619].

Through an August 2016 review of routine surveillance data reported to the National Healthcare Safety Network, the CDC detected a cluster of five bloodstream infections caused by *Serratia marcescens* in an outpatient hemodialysis

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AKI with VAD Placement Increased from 2006 to 2015

An estimated 6.5 million adults in the United States are affected by heart failure and the prevalence is expected to increase by nearly 50% from 2012 to 2030. The lifetime risk for heart failure is estimated at 20% to 45%. Increasingly, ventricular assist devices (VADs) are used for treatment of patients with advanced heart failure that is not managed with more conservative therapies. Outcomes in patients with VADs and reduced kidney function are poor both pre- and postoperatively. Estimates of the incidence and outcomes of acute kidney injury (AKI) in the setting of VAD placement are hampered by the wide variation in the definition of AKI.

In conjunction with an increase in the use of VADs, containment of healthcare costs becomes an issue. Among patients covered by Medicare who received VADs from 2006 to 2011, the mean Medicare payment for the VAD implantation hospitalization was $210,000; the costs remained stable during that 5-year period.

Carl P. Walther, MD, MS, and colleagues conducted a cohort study to compare

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Web-based Decision Aid Facilitates Patient Decision Making Regarding Dialysis Modality

In 2015, more than 120,000 patients in the United States initiated dialysis for treatment of end-stage renal disease. Among US patients on dialysis, approximately 90% receive hemodialysis at a dialysis center, 10% receive peritoneal dialysis, and 0.4% use home hemodialysis as their initial modality. Rates of quality of life and mortality are similar among patients treated with hemodialysis and peritoneal dialysis; however, use of peritoneal dialysis in the United States is much lower than in other countries.

According to **Lalita Subramanian, PhD,** and colleagues, "Most patients are eligible for both treatment options and the treatment choice should reflect patient preferences." However, previous studies have demonstrated that patients feel ill-

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Should eGFR Thresholds Be Adjusted for Age?

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In a point-counterpoint-editorial contribution in the January 1 issue of *Kidney International*, Richard Glassock and colleagues[1] debate with Andrew Levey and colleagues[2] about whether decline in kidney function in the elderly is a normal phenomenon or a manifestation of disease; Brad Rovin[3] provides an accompanying editor's overview.

The debate centers on whether estimated (or measured) glomerular filtration rate (GFR) should be adjusted for age. Is kidney senescence a real thing? Glassock and colleagues argue that it is and that there should be age-adjusted GFR thresholds in place, whereas Levey and colleagues argue that this is not necessary and that it makes diagnosis and classification of CKD more complicated; rather, Levey et al argue that the focus should shift to defining and managing kidney risk. In his editorial, Brad Rovin leans toward incorporating age thresholds.

No one disputes that there is an age-related decline in GFR. This has been known for decades. A study by Lindeman et al.[4] reported longitudinal creatinine clearance measurements in a subset of healthy subjects that had enrolled between 1958 and 1981 in the Baltimore Longitudinal Study of Aging. The mean decrease in creatinine clearance over time was 0.75 mL/min/year. Drawing from more recent studies of healthy kidney donors, Hommos et al also report a similar age-related decline in GFR of ~6 to 7 mL/min/1.73 m^2 for every decade beginning after about age 35 to 40 years[5]. A 20-year-old with an average GFR of ~107 mL/min/1.73 m^2 undergoes a decline GFR over time, and by age 65 years, the GFR is down to an average of about 83 mL/min/1.73m^2. By about 75 years of age, the GFR is down to ~76 mL/min/1.73m^2. Denic and colleagues[6] have reported previously that the decline in GFR of aging has a different histology to that of CKD—aging results in glomerulosclerosis in the superficial cortical region, whereas glomerulosclerosis associated with diabetes and proteinuria is located in the deep and middle regions of the cortex. In addition, in an elegant study, Denic et al. calculate single nephron GFR in healthy adults and suggest that glomerular hyperfiltration is not a feature of the aging kidney[7].

Yet, Levey and colleagues make valid points in that classifying an individual to a particular CKD group is not the the end of a patient's work-up, and other clinical and laboratory tools are frequently used to prevent misclassification of kidney disease. While this is obviously true, the reality is that for elderly patients who are told that they have a GFR <90 mL/min/1.73m^2 and have a diagnosis of CKD, there is a risk of eliciting alarm and anxiety. For these patients, knowing that reduced GFR is not a disease but likely reflects aging could be reassuring. Likewise, for primary care physicians, it might be reassuring to them that a referral to a nephrologist is not necessary because their patient does not have a disease. Overall, avoiding labeling a reduced GFR as CKD might reduce healthcare costs through less frequent testing and fewer doctor visits. Glassock and colleagues point out epidemiological studies suggest that the reduced GFR of aging does not appear to have deleterious adverse consequences. Besides, they argue, the public policy implications of overestimating the burden of kidney disease are not trivial. With an aging population, teasing out a portion of the population that might have reduced GFR but does not have a disease could allow better allocation of healthcare resources. These elderly people do just fine, at least with respect to kidney issues.

The other point that Levey and colleagues make is that age thresholds don't really inform treatment decisions. They argue that what patients really want to know about is prognosis, and that this can be provided by kidney risk equations that they and others have developed. They recommend that the focus should shift to determining the cause of kidney disease rather than continuing to dwell on classification. To be sure, patients probably want to know what the cause of their reduced GFR is and they would probably benefit in understanding the prognosis related to their CKD in order to make informed decisions about treatment. However, properly classifying someone (CKD or no CKD) and then, among those with CKD, predicting risk seems the best of both worlds.

Brad Rovin in his accompanying editorial suggests that we use age adjustment for classifying patients with reduced GFR. I ended up agreeing with him. While the case that Levey and colleagues make for staying the course is forcefully argued and well reasoned, is not sufficiently convincing. Overall, the take homes for me were as follows: (1) both measured and estimated GFR decline with age beginning in the thirties and this decline is senescence and physiological; (2) the histology of this kidney function decline is different from that of the typical pathology one might see with common causes of CKD, and reinforces the point that, at least in the elderly, it is not a disease process per se; and (3) clarifying the distinction between kidney senescence and kidney disease could be important in caring for patients. ■

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Gram-negative Bloodstream Infections

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facility (Facility A). In subsequent consultations with state health departments, two additional outbreaks caused by similar Gram-negative organisms were identified at facilities owned by the same company (Facility B and Facility C). The most commonly involved Gram-negative organisms were *S marcescens, Pseudomonas aeruginosa,* and *Enterobacter cloacae.*

The investigation defined a case as a blood culture from which any Gram-negative bacteria was identified from a patient who received hemodialysis at Facility A, B, or C from July 1, 2105, to November 30, 2016. For more than one case in a single patient, there had to have been 21 days between positive cultures.

To examine risk factors for becoming a case, two 1:1-matched case-control investigations were performed at Facilities A and B. The focus of the first investigation was patient-specific risk factors such as age and comorbid conditions. Case-patients were matched with randomly selected control patients who received hemodialysis at the same facility and did not develop a Gram-negative bloodstream infection during the study period.

The exposures of interest were infection control practices, sources of water, dialyzer reuse, handling of medication, dialysis circuit priming, findings of water and dialysate testing, environmental reservoirs such as wall boxes, vascular access care practices, pulsed-field gel electrophoresis, and whole-genome sequencing of bacterial isolates. Outcomes of interest were cases defined by a positive blood culture for any Gram-negative bacteria drawn from July 1, 2015, to November 30, 2016, from patients who had received hemodialysis at Facility A, B, or C.

The three facilities were less than 20 miles apart and had between 12 and 36 dialysis stations. All three shared corporate ownership and some products (medication, dialyzers, acid, and bicarbonate) came from the same distributors. The same municipal water supply was used by Facilities A and B; Facility C had a different supply. The three facilities did not commonly share staff.

During the study period, there were 58 cases of bloodstream infections associated with Gram-negative organisms; the infections occurred in 51 patients. Facilities A and B had the majority of cases (n=52; 90%). In comparison, during the previous year, the three facilities identified 12 Gram-negative bloodstream infections. The most commonly identified Gram-negative organisms were *S marcescens* (n=21; 36%), *P aeruginosa* (n=12; 21%), and *E cloacae* (n=11; 19%).

Multiple Gram-negative organisms were isolated in 16 cases (28%). Hospital admission was required in 48 cases (83%), with median length of stay of 8 days. Fifty of the cases (86%) had central venous catheter for dialysis access. There were no associations between infections and individual staff members across or within facilities and no association between a single dialysis machine and a majority of the infections.

Case patients and the matched control-patients were similar in age, sex, and comorbid conditions. The examination of patient-specific risk factors found a significant association between longer dialysis vintage and lower odds of infection (matched odds ratio [mOR], 0.19; 95% confidence interval [CI], 0.05-0.57). In session-specific analyses, there was a significant association between using a CVC for dialysis access and increased odds of bloodstream infection (mOR, 54.32; lower bound of the 95% CI, 12.19). Receiving dialysis after the first shift and having more than three staff members involved in care were more common among case-patients than control-patients (mOR, 2.83; 95% CI, 1.07-8.78 and mOR, 3.75; 95% CI, 1.20-15.52, respectively).

The investigation identified deficiencies in infection control at all three facilities, including inadequate aseptic technique during CVC care and multiple missed hand hygiene opportunities such as not changing gloves or not performing hand hygiene when changing gloves. There were multiple lapses in the more than 20 separate machine and station cleaning and disinfection processes, including not applying disinfectant to all surfaces or applying inadequate amount of disinfectant.

At Facility A, staff reported problems with wall boxes that emerged in early 2016 and peaked in summer 2016, including clogging and regurgitation of fluid from the drain, odors, and insect infestation. Staff were observed touching wall boxes and then going directly to CVC or other patient care without performing hand hygiene. At all three facilities, wall box basins were damp and often had visible pools of fluid, foaming, and waste fluid backing out of the drain.

Forty-three environmental samples from the three facilities underwent testing. Multiple environmental sources were found to have Gram-negative bacteria, including tap water, sinks, and surfaces. All wall boxes contained at least one of the three most common pathogens. *S marcescens* isolated from wall boxes were closely related to pulsed-field gel electrophoresis and whole-genome sequencing.

The investigators recommended addressing the observed lapses in infection control, including improving aseptic technique during AVC access, care, and maintenance; machine and station cleaning and disinfection, and hand hygiene.

There were some limitations to the investigation cited by the authors, including the limited number of patient isolates available for testing, the inability to sample every wall box or water source, and conducting the on-site testing after the peak of the infections.

"Providers should be aware that wall boxes are a potential source of Gram-negative bloodstream infections in dialysis settings," the researchers said.

"Infections with Gram-negative organisms commonly found in water-related biofilms should prompt investigation into water and sources of waste fluid serving as potential reservoirs in the healthcare environment. Infection prevention and control practices should be regularly assessed and incorporated into routine quality improvement activities in all healthcare settings to decrease the likelihood of pathogen transmission from the environment to patients." ■

TAKEAWAY POINTS

- Reports to the CKC in 2016 resulted in an investigation of an outbreak of Gram-negative bloodstream infections at three outpatient dialysis facilities; the investigations focused on patients who received dialysis at one of the three facilities from July 2015 to November 2016.
- During the study period, 58 cases of Gram-negative bloodstream infections occurred in 51 patients; of those, 48 patients required hospitalization.
- The outbreak was attributed to wall boxes, a previously unidentified source of contaminated fluid and biofilms in the area providing immediate patient care.

AKI with VAD Placement

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outcomes by the absence versus presence of diagnosed AKI and AKI requiring dialysis (AKI-D) during hospitalizations with implantable VAS placement in the United States. The researchers sought to examine whether recent trends in relevant outcomes differed in the two AKI categories. Results of the study were reported in the *American Journal of Kidney Diseases* [2019;74(5):650-658].

The study extracted data from the National Inpatient Sample (NIS) database from January 1, 2006, to December 31, 2015. The NIS, a 20% stratified sample of discharges from US community hospitals, includes data on all payers of inpatient healthcare in the United States from more than 7 million hospital stays annually.

Patients ≥18 years of age who received an implanted VAD and had a diagnosis code indicating heart failure and/or shock or had a separately coded cardiac surgery during the hospitalization were included in the study. In 2005, the *International Classification of Diseases, Ninth Revision, Clinical Modification,* refined procedure codes to distinguish implantable VADs from nonimplantable VADs. Exclusion criteria were codes for end-stage renal disease (ESRD) but none for AKI, and receiving dialysis but not having codes for either AKI or ESRD. Individuals with codes for AKI and ESRD were included.

The primary outcome of interest was in-hospital mortality; length of stay was also evaluated.

Hospital costs were estimated using total hospital charges, reported for each discharge in the NIS, multiplied by the applicable cost-to-charge ratios. The Consumer Price Index for Hospital and Related Services was used to adjust costs to reflect changes in hospital-related costs, indexed to 2015.

During the study period, there were an estimated 24,140 hospitalizations with VAD implantation. The number increased from 853 in 2006 to 3945 in 2015.

Of the 24,140 hospitalizations with VAD implantation, AKI was among the first 15 discharge codes in 56.1%: 49.6% had a code for AKI but no dialysis procedure and 6.5% had AKI and dialysis procedure coded. There was an increase from 2006 to 2015 in the proportion of hospitalizations with coded AKI, both with and without dialysis, from 44.0% in 2006 to 2007 to 61.7% in 2014 to 2015. During the same period, the proportions of hospitalizations with AKI-D declined from 9.3% to 5.2%. The proportion of AKI would increase from 56.1% to 57.8% if AKI diagnosis ascertainment were extended to all codes in each record.

Overall, in-hospital mortality was 14.5% (95% confidence interval [CI], 13.3%-15.8%). During the study period, mortality declined from 36.7% (95% CI, 29.7%-43.7%) in 2006 to 2007 to 10.2% (95% CI, 8.7%-11.7%) in 2014 to 2015. In patients without a diagnosis of AKI and among those with an AKI diagnosis without dialysis, there was a marked decline in unadjusted in-hospital mortality during the study period; the decline was more prominent in the earlier years. Among those with AKI-D, the decline in mortality was much less pronounced.

The median length of stay was 29 days. Among the patients who survived the index hospitalization, patients with AKI-D had the longest length of stay (48 days) compared with those without AKI (25 days) or those with AKI not requiring dialysis (33 days).

In 2006 to 2007, mean hospitalization cost (in 2015 terms) was $319,096 (95% CI, $288,145-$350,047); costs decreased to $245,943 (95% CI, $234,697-$257,191) in 2014 to 2015. Among patients without AKI, mean hospitalization costs were $232,492 (95% CI, $223,905-$241,078), compared with $288,448 (95% CI, $278,321-$298,575) among patients with AKI not requiring dialysis and $365,080 (95% CI, $337,662-$392,497) among patients with AKI-D.

Compared with hospitalizations without AKI, costs were 19.1% (95% CI, 15.4%-22.9%) higher in patients with AKI without dialysis and 39.6% (95% CI, 30.6%-49.3%) higher in patients with AKI-D, following adjustment for demographics, comorbid conditions, and hospitalization circumstance.

At discharge, 19.6% of patients without AKI were transferred to another facility (another acute-care hospital, skilled nursing facility, or rehabilitation facility). Among patients with AKI not requiring dialysis, the proportion was 31.5%; among those with AKI-D, the proportion was 47.7%.

The inability to determine the timing of AKI with respect to VAD implantation was cited by the authors as a limitation to the study. Also cited were limitations in determining the prevalence of pre-existing chronic kidney disease and not determining discharge weights for a subpopulation of interest.

"In conclusion, as VADs are increasingly used in the management of end-stage heart failure refractory to medical management, understanding and ameliorating pre- and postoperative decreases in kidney function is necessary. Diagnosis of AKI has increased during the study period, likely due to more appreciation of the importance of AKI and increasing sensitivity of AKI definition, but dialysis-requiring AKI has decreased. Mortality risk among VAD recipients with AKI not requiring dialysis is improving, but among persons with AKI-D, excess mortality remains high. This study highlights the need for further investigations into understanding and reducing the severity of AKI related to end-stage heart failure and VAD implantation," the researchers said. ■

TAKEAWAY POINTS

- Patients undergoing implantation of ventricular assist devices (VADs) to manage end-stage heart failure are at risk for acute kidney injury (AKI) that may or may not require dialysis.
- Of patients who underwent implantation of a VAD from 2006 to 2015, 56.1% developed AKI; of those, 6.5% required dialysis (AKI-D). AKI diagnosis increased during the study period; the prevalence of AKI-D declined. Mortality declined in all AKI categories; the smallest decline was among patients with AKI-D.
- Compared with patients with no AKI, adjusted hospitalization costs were 19.1% higher in patients with AKI and 39.6% higher among patients with AKI-D.

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Web-based Decision Aid

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informed and unprepared to make decisions regarding dialysis modality. Low health literacy can also be a barrier to understanding differences in treatment options and making decisions about dialysis modality.

The EPOCH-RRT (Empowering Patients on Choices for Renal Replacement Therapy) study was a collaborative development of a web-based decision aid; the study involved researchers and an advisory panel that included patients, care partners, and patient advocates. Dr. Subramanian et al. conducted a parallel-group randomized controlled trial designed to assess the efficacy of the decision aid on decision-making outcomes. Results were reported in the *American Journal of Kidney Diseases* [2019;74(3):351-360].

Social media outreach, nationally and in local clinics, was used to recruit study participants. Eligible patients were ≥18 years of age, had estimated glomerular filtration rate (eGFR) <25 mL/min/1.73 m^2, had internet access via a computer or tablet, and had English language fluency. The outcomes of interest were treatment preference, decisional conflict, decision self-efficacy, knowledge, and preparation for decision making.

Participants were randomly assigned to an intervention arm or to a control arm. Those in the intervention arm received information regarding chronic kidney disease, peritoneal dialysis, and hemodialysis. They also engaged in a value clarification exercise via the study website using their own electronic devices. Those in the control arm were only required to complete the control questionnaire.

Following application of exclusion and inclusion criteria, of the 556 patients in the initial screening, 140 were included in the study, 70 in each arm. Seven of the participants in the intervention arm began the study and completed the pretest, but did not complete the posttest. Fifty of the remaining 63 in the intervention arm (79%) completed the pre- and posttests within 1 week; 60% of those on the same day. In sensitivity analyses with and without the 13 participants with a gap of more than 7 days between completion of the two questionnaires, none of the mean values of measured outcomes or reported statistical differences changed.

Demographics were self-reported in the control and pretest questionnaires; characteristics were similar between the intervention and the control group. The study sample was younger that the 2014 US chronic kidney disease (CKD) stages 4 and 5 population. Mean age was 76.8 years, eGFR was <30 mL/min/1.73 m^2, 46.2% were men, and 77.6% were white. Nearly all (96%) had a high school diploma and 94% considered English their native language. At the start of the study, literacy and subjective numeracy were similar in both groups.

At baseline, the intervention group had 47% uncertainty on treatment choice and the control group had 40% treatment choice uncertainty. Following the intervention, the proportion of those responding "not sure" was 24 percentage points lower in the intervention group than the corresponding proportion in the control group. In the intervention group, following use of the decision aid, the proportion of not sure responders was 30 percentage points lower than prior to use of the decision aid. Twenty-nine of the participants in the intervention group selected not sure prior to the intervention. Following use of the decision aid, eight remained unsure, 15 selected hemodialysis, five selected peritoneal dialysis, and one selected other.

On average, the intervention group scored 13.4 points less than the control group in decisional conflict; the decision aid was effective in decreasing the average decisional conflict score by 15 points. There was no modification of the effect of the decision aid by age, sex, or race. Following use of the decision aid, there was little change in decision self-efficacy scores and no evidence of modification by subgroups.

Participants in the control arm answered 77% of the knowledge questions accurately, on average. Following use of the decision aid, participants in the intervention arm answered 90% of the knowledge questions accurately. There were no observed effect modifications by age, sex, or educational level.

More than 90% of participants in the intervention arm indicated the decision aid helped somewhat to a great deal, both for preparing for dialysis and for follow-up with care providers. Ninety-two percent found the content balanced and not slanted toward either option, 88% trusted it, 87% agreed or strongly agreed that it was relevant to them, and 89% said they would recommend it to others; 49% described the decision aid as being extremely helpful in understanding dialysis options. One person did not like the website at all and two would definitely not recommend the decision aid to others.

There were some limitations to the study cited by the authors, including limited generalizability due to the self-selected study participants who were required to have access to the internet, speak English, and be computer literate; the high postrandomization loss to follow-up; and evaluating short-term outcomes only.

In summary, the researchers said, "Our work suggests that this decision aid, developed through a stakeholder-engaged process, informs and supports patients with CKD in making the difficult choice of dialysis modality. The broader implementation of this decision aid could complement current CKD education in clinical practice and could support both care providers and patients in shared decision making by facilitating communication about treatment options. Additionally, the decision aid could also become a resource for disseminating end-stage kidney disease knowledge with the potential for improving health outcomes through more active engagement in care." ■

TAKEAWAY POINTS

- Researchers conducted a parallel-group randomized trial to test the efficacy of a web-based decision aid designed to help patients with end-stage renal disease in the choice of dialysis modality.
- The study demonstrated that the decision aid improved decision-making immediately following use; more than 90% of users reported that it helped in their decision making regarding dialysis modality.
- The researchers incorporated feedback from the participants to further refine the decision aid; the final version is available at http://choosingdialysis.org/.

Kidney Week

Identifying Urine Biomarkers for Kidney Injury in Patients with IgAN

Washington, DC–Renal pathology is critical in clinical management and prognosis in patients with immunoglobulin A nephropathy (IgAN), a primary glomerular disease commonly leading to chronic kidney disease, creating a need for reliable biomarkers for noninvasive evaluation of the kidney. Researchers at Ohio State University, Columbus, led by **Li Zhang, MD,** conducted a study designed to identify potential biomarkers of severity of kidney injury in patients with IgAN.

The study included 45 patients with IgAN and 29 healthy volunteers (control group). Spot urine samples were collected at the time of diagnostic kidney biopsy from the IgAN patients. Results of the spot urine tests were classified by the Oxford system and the renal pathologist recorded the degree of activity and chronic damage blindly as none, mild, moderate, or severe. Study results were reported during a poster session at Kidney Wek 2019 in a poster titled *Urine Biomarkers for Kidney Injury in IgA Nephropathy*.

The potential biomarkers of kidney injury assessed were adiponectin, CD163, epidermal growth factor (EGF), neutrophil gelatinase-associated lipocalin (NGAL), ICAM-1, VCAM-1, and complement component C5a.

There were significant differences in urine adiponectin, CD163, C5a, and VCAM-1 in patients with IgAN compared with the controls, with fold-increases of 7, 399, 28, and 7, respectively (all $P<.0001$). EGF decreased -1.4-fold compared with controls ($P=.0015$). There was an inverse correlation between EGF and interstitial fibrosis and tubular atrophy (IFTA) and overall chronicity. There was a positive correlation between C5a and IFTA. There were positive correlations between adiponectin and C5a and overall activity. Using receiver operating characteristic analysis, the area under the curve for EGF to differentiate between mild and moderate-severe chronic injury is 0.91 ($P<.0001$). The area under the curve for adiponectin to detect the presence of active lesions is 0.96 ($P=.0011$).

In summary, the researchers said, "Urine EGF could serve as a biomarker for chronic kidney lesions in IgAN while adiponectin and complement C5a may be biomarkers for active kidney lesions. These biomarkers could be helpful in noninvasively evaluating the efficacy of therapies for IgAN."

Source: Zhang L, Zhang X, Birmingham DJ, Satoskar AA, Rovin BH. Urine biomarkers for kidney injury in IgA nephropathy. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2019, November 8, 2019 (Abstract FR-P0837), Washington, DC.

Outcomes of Importance to Young People with CKD and Their Caregivers

For young people living with chronic kidney disease (CKD) and their families, the consequences of the disease are devasting, long-term, and wide-ranging. Compared with age-matched peers, the mortality rate among children with CKD is 30 times higher and quality of life is marked by debilitating symptoms, comorbid conditions, burdens of treatment, side effects, and complications. Impaired cognitive and psychosocial development and growth are associated with poor outcomes that last through adulthood, including lower educational level and vocational and social difficulties. Caregivers and family members of a child with CKD experience psychological distress and financial burdens.

Previous studies have identified outcomes that are important to adults with CKD, but there are few data available regarding outcomes that are important to young people with CKD and their caregivers. **Camilla S. Hanson, PhD,** and colleagues recently conducted a study designed to identify outcomes that are important to young people across all stages of CKD as well as to caregivers to help inform patient-centered decision making in CKD care. Results of the study were reported in the *American Journal of Kidney Diseases* [2019;74(1):82-94].

Patients were recruited from three centers in Australia (Sydney, Brisbane, and Melbourne), two centers in Canada (Vancouver and Calgary), and one center in the United States (Houston, Texas). Inclusion criteria were patients 8 to 21 years of age with CKD stages 1-5 and non–dialysis-dependent, receiving dialysis, or transplant recipient with functioning transplant; caregivers of patients 0 to 21 years of age with CKD were also eligible to participate.

The researchers conducted face-to-face focus groups using the nominal group technique, including brainstorming to develop a list of outcomes important for research in young people with CKD. Individual participants then prioritized the outcomes and discussed their preferences as a group. Separate groups for patients and caregivers were conducted.

The study included 62 caregivers (in eight groups) and 34 patients (in eight groups). At least one parent of 29 patients participated in the study. Caregivers consisted of 10 pairs of participants who were related or spouses. Patient age ranged from 8 to 21 years, 56% (n=19) were male, 50% (n=17) had non–dialysis-dependent CKD, 15% (n=5) were on dialysis therapy (one hemodialysis and four peritoneal dialysis), and 35% (n=12) had received a transplant. Caregivers were 25 to 60 years of age (with children 1-22 years of age), and 76% were mothers. Forty percent (n=25) of the caregivers had children who had non–dialysis-dependent CKD, 23% (n=14) had children on dialysis therapy, and 35% (n=22) had children with a transplant. One parent did not report the child's CKD stage.

The patients ranked 34 outcomes and the caregivers ranked 33 outcomes; in combination, there were 48 unique outcomes included in the study. The patients ranked the following five outcomes highest: (1) survival, importance score 0.25; (2) physical activity/sport, importance score 0.24; (3) fatigue, importance score 0.20; (4) lifestyle restrictions, importance score 0.20; and (5) growth, importance score (0.20). The five highest outcomes for caregivers were: (1) kidney function, importance score 0.53; (2) survival, importance score 0.28; (3) infection, importance score 0.22; (4) anemia, importance score 0.20; and (5) growth, importance score 0.17. In both patients and caregivers, survival, growth, kidney function, and infection were in the top ten outcomes.

For patients, physical activity/sports participant was important across all treatment types. Patients on dialysis therapy ranked lifestyle restriction higher compared with patients with CKD stages 1 to 5 and transplant recipients. Patients in all age groups included survival, fatigue, and lifestyle restrictions among the top ten outcomes.

Growth, kidney function, and survival were important for caregivers across all treatment types. Growth was ranked as more important among caregivers of younger patients; school was more important to caregivers of young adults. There were differences in importance scores by country; however, growth, fatigue, and survival were in the top ten for all patients, and kidney function and growth were in the top ten for all caregivers.

The researchers identified themes that reflected patient and caregiver immediate and current priorities: wanting to feel normal, strengthening resilience for daily challenges, imminent threats to life, devastating family burden, and seeking control over current health. Themes that reflected future and long-term focus were: parental responsibility to protect health and development, remaining hopeful, concern for limited opportunities, prognostic uncertainty, dreading painful and invasive interventions, and managing expectations.

Limitations to the study cited by the authors included recruiting only English-speaking participants, participation from only one child on in-center hemodialysis therapy, and limited data on comorbid conditions of the participants.

In conclusion, the researchers said, "Kidney function, infection, survival, and growth are shared priorities for young people and their caregivers across all stages of CKD. Young people focus on current impacts of CKD, including physical activity, fatigue, lifestyle restrictions, hospitalization, social functioning, and medication burdens, because these impair their ability to feel normal. Caregivers were focused on gaining control over their child's current health, believed the family and the financial impact to be important considerations, and placed emphasis on their child's long-term health, development, and survival. Research that reports outcomes that are important to young people with CKD and their caregivers can better inform shared decision making, The outcomes identified in this study will inform the development of a core outcome set through the SONG-Kids initiative." ■

TAKEAWAY POINTS

- Using the nominal group technique, researchers conducted a study to identify outcomes associated with chronic kidney disease (CKD) important to young people with CKD and their caregivers.
- Patients and caregivers from six centers in Australia, Canada, and the United States participated; kidney function, infection, survival, and growth were the highest priorities for patients and caregivers.
- Young people with CKD ranked outcomes that directly affected their lifestyle and sense of normality highly; caregivers highest priorities were the long-term health of their child, current health problems, and the financial and family burdens of caring for a child with CKD.

Chronic Kidney Disease and Incident Dementia: The HUNT Study

Previous studies have reported associations between chronic kidney disease (CKD) and an increase in risk for cardiovascular disease and worse cognitive performance. The risk factors for CKD and dementia share similar factors including hypertension, diabetes mellitus, stroke, myocardial infarction, and hyperlipidemia. However, according to **Jessica Mira Gabin, MD,** and colleagues, there are few data on the association between CKD and dementia. Epidemiological studies have found an association between albuminuria and low glomerular filtration rate (GFR) and Alzheimer's disease (AD) and vascular dementia (VaD), but the findings have been mixed and no associations have been published.

Moderately increased albuminuria (formerly called microalbuminuria [MA]), is an early risk marker of renal endothelial dysfunction. The importance of MA in cardiovascular disease is well documented. The current population-based cohort study was designed to use baseline albumin creatinine ratio (ACR) to examine the association between MA and the risk for incident AD, VaD, and mixed AD/VaD. The researchers also examined estimated GFR (eGFR) to determine if the association differed across samples in varying stages of CKD. Results were reported online in *BMC Nephrology* [doi.org/10.1186/s12882-019-1425-8].

> Hazard regression models did not reveal any statistically significant association between eGFR and dementia or its subgroups. There were interactions between age and eGFR in dementia and its subgroups.

The HUNT 2 survey (1995-1997) conducted in Nord-Trøndelag County, Norway, included 64,978 participants. Following application of exclusion criteria, the current study included 48,508 participants. Of those, 668 were diagnosed with dementia and 47,840 were not diagnosed with dementia. A total of 7606 died during the study period.

Mean age of the study sample was 49.5 years and mean eGFR was 78.8 mL/min/1.73 m^2. Individuals diagnosed with dementia were older, had reduced eGFR, higher systolic and diastolic blood pressure, and higher prevalence of self-reported cardiovascular disease. Hazard regression models did not reveal any statistically significant association between eGFR and dementia or its subgroups. There were interactions between age and eGFR in dementia and its subgroups.

MA SUBSTUDY

The MA substudy included HUNT 2 participants who self-reported diabetes mellitus and/or treated hypertension, and a randomly selected non-diabetic/non-treated hypertensive sample. Those participants were asked to deliver three urine samples from three consecutive days.

Subgroups were created to examine those diagnosed with dementia and diabetes or treated for hypertension (n=184) and those diagnosed with dementia and without diabetes or treatment for hypertension (n=30). In addition, 5135 participants without dementia and with diabetes or treatment for hypertension, and 1675 controls who were without diabetes and were not treated for dementia were included in the analyses (total number included in the analyses: 7024).

There were no differences across quartiles of the total sample. Those diagnosed with dementia were older, had higher systolic and diastolic blood pressure, lower renal function, and higher cholesterol.

In analyses adjusted by age and other variables at different albumin creatinine ratio (ACR) levels expressed in quartiles, there was a positive association between increasing ACR and combined AD/VaD. ACR in the fourth quartile (≥1.78 mg/mmol) was associated with increased hazard ratio of VaD (3.97; 95% confidence interval, 1.12-14.07) compared with ACR in the first quartile (<.53 mg/mmol). There were no sex interactions or age interactions between ACR and total dementia, combined AD/VaD, mixed Ad/VaD, or VaD in crude analyses.

The researchers cited some limitations to the study, including competing risk from death and other causes in a population of older adults; lack of access to a national prescription registry that would have provided details regarding types of medications taken by the participants; and the small number of participants with CKD.

In conclusion, the researchers said, "Our results strengthen the hypothesis that vascular mechanisms may affect both kidney and brain as an association between moderately increased albuminuria, VaD, and combined AD/VaD was found. However, eGFR was not significantly associated with dementia independent of diabetes mellitus or hypertension." ■

TAKEAWAY POINTS

- A study in Norway was designed to examine the association between estimated glomerular filtration rate (eGFR) and moderately increased albuminuria (MA) and dementia and subtypes of dementia (Alzheimer's disease (AD), vascular dementia (VaD), and combined AD/VaD.
- There was an association between MA and VaD and combined AD/VaD.
- There was no significant association between eGFR and dementia independent of diabetes mellitus or hypertension.

Prevalence of Psychiatric Diagnosis in Hospitalized Patients on Dialysis

Patients with end-stage renal disease (ESRD) may experience depression, anxiety, organic psychiatric disorders, dementia, disorders related to alcohol or drugs, or schizophrenic disorders, among others. Patients on maintenance dialysis commonly experience psychiatric illness, however, it is difficult to determine the true prevalence in that patient population, creating the possibility that psychiatric disorders in patients with ESRD may be under-recognized in research and in clinical care.

Data on the prevalence vary; a systemic review and meta-analysis found prevalence estimates for depression in patients on dialysis ranged from 1.4% to 94.9%, with a summary prevalence estimate of 39.3% when depression was assessed by questionnaire and 22.8% when assessed by interview. Data on psychiatric illnesses in pediatric patients with ESRD are limited by small study sizes, but, as with adult patients, pediatric patients with ESRD appear to have higher rates of depression compared with healthy controls.

There is an association between the presence of depression or anxiety and lower quality of life in adults and pediatric patients with kidney disease. There is also an association between depression in adults with ESRD and lower treatment adherence, more frequent hospitalizations, and increased mortality. Among pediatric patients on dialysis, there is an association between increased disease duration and hospitalizations.

It is unknown how common psychiatric illnesses are among hospitalized patients with ESRD on dialysis; there are few data on the associations of those illnesses on outcomes in that patient population. Researchers, led by **Paul L. Kimmel, MD,** conducted a study designed to determine the prevalence of hospitalizations with psychiatric diagnoses within a year of initiation of treatment for ESRD in adults and pediatric patients who started treatment from 1996 to 2013. The researchers also sought to examine the associations between hospitalizations with psychiatric diagnoses and mortality in adult patients treated with dialysis. Results were reported in the *Clinical Journal of the American Society of Nephrology* [2019;14(9):1363-1371].

The study cohort included 9196 pediatric patients (0-21 years of age), 398,418 adult patients (22-64 years of age), and 626,344 elderly adult patients (≥65 years of age). Among the pediatric patients, 64% had a first-year hospitalization; of those, 48% had no psychiatric diagnoses, 1% had a primary psychiatric diagnosis, and 15% had a secondary psychiatric diagnosis. Among the adult patients, 66% had a first-year hospitalization; the percentages of no, primary, and secondary psychiatric diagnoses were 39%, 2%, and 25%, respectively. Among the elderly adult patients, 72% had a first-year hospitalization; the percentages for no, primary, and secondary psychiatric diagnoses were 51%, 2%, and 19%, respectively.

In the pediatric population hospitalized with a psychiatric diagnosis, the most common diagnosis was depression/affective disorders (n=67 patients; 4%). The most common psychiatric diagnoses among adults was depression/affective disorders (n=2907 patients; 3%), alcohol-related disorders (n=1142; 1%), and drug disorders (n=1041; 1%). The top primary psychiatric diagnoses among the elderly adults hospitalized were organic disorders/dementias (n=3680 patients; 3%), depression/affective disorders (n=1825 patients; 1%), and drug disorders (n=1205; 1%).

Over time, the percentage of patients hospitalized with psychiatric diagnoses increased, from 9% in 1996-1998 to 26% in 2011-2013 for pediatric patients, from 19% to 40% for adults, and from 17% to 39% for elderly adults. Women were more likely than men to have hospitalizations with psychiatric diagnoses: 17% versus 16% in pediatric patients; 29% versus 26% in adults; and 25% versus 21% in elderly adults. Patients with dual eligibility (Medicare and Medicaid) were more likely to have hospitalizations with psychiatric diagnoses compared with those without dual eligibility (17% vs 10% in pediatric patients; 30% vs 22% in adults; and 28% vs 21% in elderly adults).

Nearly the entire increase in hospitalizations with psychiatric diagnoses was due to secondary diagnoses. This may be due, in part, to the increased number of secondary codes allowed in Medicare Part A claims from nine in 2009 to 25 in 2010.

Among the pediatric patients, the percentages with anxiety/personality disorders as secondary diagnoses remained relatively stable at 13% in 1996-1998 and 16% in 2008-2010, but increased to 24% in 2011-2013. The changes in percentages were similar among adults and elderly adults: percentages of adults and elderly adults with anxiety/personality disorders as secondary diagnoses were stable at 9% to 12% and 7% to 10%, respectively, between 1996-1998 and 2008-2010, but increased to 24% and 20%, respectively, in 2011-2013.

Analyses of the association between hospitalizations with psychiatric diagnoses and death were limited to a subset of adults treated with dialysis and ever hospitalized during the first year of ESRD. The overall mortality rate was 242.4 deaths per 1000 person-years (95% confidence interval [CI], 241.6-243.2). In patients hospitalized without a psychiatric diagnosis, the mortality rate was 237.2 (95% CI, 236.2-238.2). In hospitalized patients with a secondary psychiatric diagnosis, the mortality rate was 252.1 (95% CI, 250.5-253.6). In those with primary psychiatric diagnoses, the morality rate was 275.3 (95% CI, 269.4-281.3).

Following adjustment for demographic characteristics, residential area, dual eligibility, Charlson score, and comorbid conditions at time of dialysis initiation, compared with patients hospitalized without a psychiatric diagnosis, the hazard ratios of death were 1.29 (95% CI, 1.26-1.32) in all adults hospitalized with primary psychiatric diagnoses, and 1.11 (95% CI, 1.10-1.12) in all adults hospitalized with secondary psychiatric diagnoses. Findings were similar for associations between hospitalizations with psychiatric diagnoses and first year death.

There were some limitations to the findings cited by the authors, including relying on clinical diagnosis for the primary and secondary hospitalization diagnoses that are delineated by codes that may have missed diagnoses in patients treated with dialysis.

In summary, the researchers said, "We conclude that hospitalizations with psychiatric diagnoses are common in the United States adult and pediatric patients on dialysis, and such hospitalizations are associated with higher mortality in adults. This study likely underestimates the true burden of these conditions within the dialysis population. Further research is needed to understand their prevalence in cases where the conditions may not result in (or be coded for) hospitalization. The findings suggest clinicians who care for hospitalized dialysis patients should be aware of and prepared to manage psychiatric disorders and associated negative outcomes within these populations." ■

TAKEAWAY POINTS

- Researchers conducted a study to examine the prevalence of hospitalizations with psychiatric diagnoses within a year of initiation of treatment for end-stage renal disease in adult and pediatric patients.
- The prevalence of hospitalizations with psychiatric diagnoses increased over time across groups, primarily from secondary diagnoses; hospitalizations with psychiatric diagnoses are common in both adult and pediatric patient populations in the United States.
- Hazard ratios of death from all causes were higher in all adults on dialysis hospitalized with primary or secondary psychiatric diagnoses compared with those hospitalized without psychiatric diagnoses.

Conference Coverage

Kidney Week 2019

Washington, DC | November 5-9, 2019

HIMALAYAS Study: Roxadustat versus Epoetin Alfa

Washington, DC–The HIMALYAYAS trial was a phase 3 study of the efficacy and safety of roxadustat in the treatment of anemia in incident dialysis patients. Roxadustat (FG-4592) is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor that stimulates erythropoiesis and regulates metabolism of iron. Results of the randomized, open-label, active-controlled study were reported during a presentation at Kidney Week 2019 by **Robert Provenzano, MD, FACP, FASN.** The presentation was titled *HIMALAYAS: A Phase 3, Randomized, Open-Label, Active-Controlled Study of the Efficacy and Safety of Roxadustat in the Treatment of Anemia in Incident Dialysis Patients.*

Incident dialysis patients who had not been treated with an erythropoiesis stimulating agent or had limited prior use were randomized 1:1 to roxadustat or epoetin alfa. Use of oral iron was allowed; parenteral iron was restricted. Oral roxadustat was dosed three times per week; the initial dose was weight-based. Epoetin alfa was prescribed according to the country-specific product labeling; roxadustat doses were determined using an algorithm.

The primary end point of interest for the US FDA was mean changes in hemoglobin A1c from baseline to weeks 28 to 52. For the EU EMA, the primary end point was the percentage of patients who achieved a hemoglobin response week 1 through 24. A hemoglobin response was defined at two consecutive visits during the first 24 weeks as achieving a hemoglobin level of 11 and an increase of 1 g/dL if baseline hemoglobin was >8 g/dL or 2 g/dL if baseline hemoglobin was <8 g/dL.

Adverse events, vital signs, electrocardiogram findings, and clinical laboratory values were used to assess safety and tolerability.

A total of 1043 patients ≥18 years of age in 17 countries were randomized: 522 to the roxadustat arm and 521 to the epoetin alfa arm. The majority were white; 8.4% in the roxadustat arm and 9.6% in the epoetin alfa arm were black. In the roxadustat arm, 183 patients (35.1%) had diabetes mellitus compared with 34.4% in the epoetin alfa arm. Mean baseline hemoglobin was 8.43 g/dL in the roxadustat arm and 8.46 g/dL in the epoetin alfa arm.

Mean change in hemoglobin from baseline to the average over week 28 to 53 was 2.57 in the roxadustat arm versus 2.36 in the epoetin alfa arm. The noninferiority criteria were met as the lower bound of 95% confidence interval was above the noninferiority margin of -0.785 g/dL, and the superiority over epoetin alfa was also achieved, P=.0005. Patients in the roxadustat arm had a hemoglobin response rate of 88.2% compared with 84.4% in the epoetin alfa arm, meeting EU's primary end point noninferiority criterion.

The overall safety profile was consistent with results seen in previous roxadustat trials; pooled safety findings were reported in a late breaker abstract at the meeting.

In summary, the researchers said, "Roxadustat was noninferior and subsequently demonstrated superiority over epoetin alfa in the mean change in hemoglobin from baseline in patients incident to dialysis."

Source: Provenzano R, Evgeny S, Liubov E, et al. HIMALAYAS: A phase 3, randomized, open-label, active-controlled study of the efficacy and safety of roxadustat in the treatment of anemia in incident-dialysis patients. Abstract of a presentation at the American Society of Nephrology Kidney Week 2019 (Abstract TH-OR021), November 7, 2019, Washington, DC.

Roxadustat Safe and Effective: Analyses of Pooled Results

Washington, DC–Analyses of pooled results of phase 3 studies of roxadustat for the treatment of anemia in patients with chronic kidney disease (CKD), including dialysis-dependent patients and nondialysis-dependent patients, were reported in a late breaker session at Kidney Week 2019. **Robert Provenzano, MD, FACP, FASN,** and **Steven Fishbane, MD,** reported the data during an oral presentation titled *Pooled Efficacy and Cardiovascular (CV) Analyses of Roxadustat in the Treatment of Anemia in Patients on and Not on Dialysis.* Roxadustat is an oral hypoxia-inducible factor prolyl hydroxylase inhibitor that regulates erythropoiesis and iron metabolism.

Results of phase 3 studies comparing roxadustat to placebo in patients with stage 3-5 non-dialysis-dependent CKD and to epoetin alfa in patients with dialysis-dependent CKD were pooled. Death, myocardial infarction, and stroke (MACE), and heart failure or unstable angina requiring hospitalization (MACE+) were adjudicated. Assessments of efficacy included hemoglobin and the need for rescue therapy (transfusion, intravenous iron, and erythropoiesis stimulating agents). Cardiovascular end points were MACE and MACE+.

In the nondialysis-dependent cohort, 4270 patients were randomized to roxadustat (n=2386) or placebo (n=1884). The primary end point of interest (change from baseline in mean hemoglobin in weeks 28 to 52) was +1.85 g/dL in the roxadustat arm versus 0.13 g/dL in the placebo arm (P<.0001). Patients in the roxadustat had a lower risk of rescue therapy compared with patients in the placebo arm (hazard ratio [HR], 0.19; 95% confidence interval [CI], 0.16-0.23; 81% reduction in risk; P<.0001). Using intent-to-treat long-term follow-up, the HR for time to MACE was 1.08 (95% CI, 0.94-1.24) for patients in the roxadustat arm versus placebo. Time to MACE+ was 1.04 (95% CI, 0.81-1.12) in the roxadustat arm versus the placebo arm. In a subgroup with estimated glomerular filtration rate >10 mL/min/1.73 m^2 (n=3431), the HRs were 0.99 for MACE and 0.98 for MACE+ for roxadustat versus placebo.

In the dialysis-dependent cohort, 3917 patients were randomized (n=roxadustat, 1960; epoetin alfa, 1957). In the roxadustat arm, the primary end point of mean hemoglobin change from baseline at weeks 28 through 52 was 1.21 g/dL versus 0.95 g/dL in the epoetin alfa arm (difference, 0.26 g/dL; 95% CI, 0.20-0.33) in pooled analysis. Roxadustat was noninferior and superior to epoetin alfa (P<.0001). Patients in the roxadustat arm received fewer transfusions compared with patients in the epoetin alfa arm: 9.5% versus 12.8% (HR, 0.82; 95% CI, 0.679-0.997).

In comparisons of roxadustat and epoetin alfa, the HR for MACE was 0.95 (95% CI, 0.81-1.12); the HR for MACE+ was 0.84 (95% CI, 0.73-0.97), P=.02) in the dialysis dependent cohort. In a subgroup of incident dialysis patients (dialysis vintage <4 months), the HRs for MACE and MACE+ were 0.70 (95% CI, 0.51-0.97; P=.03) and 0.66 (95% CI, 0.50-0.89; P=.005).

In conclusion, the researchers said, "These integrated Phase 3 analyses provide evidence for roxadustat superiority in anemia correction with transfusion reduction and acceptable cardiovascular safety profile."

Source: Provenzano R, Fishbane S, Wei L-J, et al. Pooled efficiency and cardiovascular (CV) analyses of roxadustat in the treatment of anemia in CKD patients on and not on dialysis. Abstract of an late-breaker oral presentation at the American Society of Nephrology Kidney Week 2019 (Abstract FR-OR131), November 8, 2019, Washington, DC.

Electronic Patient-Reported Outcome Measures in Renal Care Settings

Health-related quality of life (HRQoL) is substantially affected among patients with chronic kidney disease (CKD). Patients with CKD report clusters of nonspecific symptoms, including pain, fatigue, and pruritus, that adversely affect their physical, emotional, and psychological well-being.

Measures such as estimated glomerular filtration rate are established indicators of health status; however, these hard parameters may not represent the impact of CKD on patients' symptoms and HRQoL. Gathering patient-reported outcome measures (PROMs) using validated self-reported questionnaires has been on the increase, including in routine renal clinical practice.

Collection of electronic PROMs (ePROMs) using computers, smartphones, and tablets is also on the rise. Use of these real-time data could be beneficial in tailoring treatment to individual patient needs and reducing clinical appointments in stable patients. Further, ePROMs may promote patient-centered care by identifying health-related issues important to patients, facilitating patient-clinical communication and shared decision making.

TAKEAWAY POINTS

- Electronic patient-reported outcome measures (ePROMs) may be of use in management of chronic kidney disease (CKD). Researchers in Great Britain conducted a qualitative study to examine patient and clinician perspectives on renal ePROMs.
- Despite clinician concerns about patient burden, patients indicated they were willing to complete ePROMs on a regular basis as part of their care.
- Clinicians felt the extent of adoption of renal ePROM systems in renal care should be based on evidence of significant impact on patient outcomes.

Olalekan Lee Aiyegbusi, MBChB, and colleagues recently conducted a qualitative study designed to examine the perspectives of patients and clinicians on the use of a renal ePROM in development by the Centre for Patient Reported Outcomes Research at the University of Birmingham and University Hospitals Birmingham NHS Foundation Trust (UHB) in the United Kingdom. The researchers sought to gather insights that would help inform the design, implementation, and delivery of such a system in routine clinical practice. Results of the study were reported in the *American Journal of Kidney Diseases* [2019;74(2):167-178].

Participants at the host site (UHB) were recruited and data were collected and analyzed between August 2017 and May 2018. Patients with non–dialysis-dependent CKD stages 4 and 5 were recruited to test the hypothesis that a cohort with high symptom burden and risk for rapid progression to end-stage renal disease would benefit most from the ePROM system. The study cohort included 12 patients with stage 4 or 5 CKD, and 22 clinicians (six CKD community nurses, one clinical psychologist, 10 nephrologists, three specialist registrars, and two renal surgeons).

Participants were given information sheets that outlined the study aims and objectives and also outlined the UHB ePROM system being developed. Patients who agreed to be interviewed were provided with advance copies of the Kidney Disease Quality of Life-36 and Integrated Patient Outcome Scale-Renal questionnaires. Interviews with patients were conducted either face-to-face or on the telephone, depending on patient preference. Clinicians participated in semi-structured interviews and focus groups.

Of the 12 patients, 11 were ≥50 years of age, five were women, seven were British-white, four were British-Asian, and one was Irish-white. Seven were retired, four were employed, either full- or part-time, and one was unemployed. Examination of the saturation data throughout the study suggested that: (1) saturation was reached at the 10th patient and 12th clinical interviews; (2) there were no appreciable differences in the views held by nurses and doctors; and (3) there were no sex differences in the views held by participants.

Four themes were highlighted in the interviews/focus groups: (1) general opinions of PROMs; (2) possible benefits and applications of ePROMs; (3) practical considerations; and (4) concerns, barriers, and facilitators.

Despite clinical concerns regarding patient burden, patients indicated they were willing to complete ePROMs on a regular basis as part of their care. In general, patients had favorable assessments of the questionnaires. Patients felt that ePROMs could improve or open lines of communication between patients and clinicians and would provide clinicians with insight into patient experiences and care priorities. Patients with stable CKD suggested that use of ePROMs could reduce the frequency of their hospital appointments and the need to take time off from work.

Clinicians felt that the extent of adoption of renal ePROM systems should be based on evidence of significant impact on patient outcomes. Clinicians felt that ePROMs would be useful adjuncts to traditional clinical management, but would be insufficient on their own for obtaining research funding or changing health policy. Clinicians also expressed concerns that ePROMs would raise patient expectations to unrealistic levels and expose clinicians to the risk for litigation.

There was no clear consensus on the optimal frequency of use of ePROMs; however, both patients and clinicians felt it would become burdensome if an ePROM were administered more than once a month. Both groups agreed the best time to complete an ePROM was at home prior to a clinical appointment. The groups also agreed that everyone involved in a patient's care, including the patient, should have access to ePROM data.

Patients' feelings regarding potential barriers to an ePROM system included a lack of interest in the system, a dislike of information technology, and limited abilities and/or access to electronic devices and the internet. Potential barriers cited by the clinicians included alert fatigue, limited financial resources, and time pressures during clinical consultations.

Citing limitations to the study, the researchers named the possible limited transferability of the findings because only English-speaking participants were recruited to the study.

In conclusion, the researchers said, "The use of a renal ePROM system has the potential to enhance routine clinical practice by facilitating patient engagement and involvement in their care and providing clinicians with timely information that may guide clinical management. The rapid developments in information technology may also assist with the integration of ePROM data with other routinely collected electronic health data, thus facilitating its impact. However, patients and clinicians need to be involved at every stage in the development of ePROM systems. Patient and clinician views should be sought, considered, and appropriately used to facilitate their subsequent engagement with ePROM interventions. The degree of patients and clinician engagement may crucially influence the usefulness of ePROMs postimplementation." ■

Extended Hours Dialysis Reduced Serum Phosphate Levels in Patients with CKD-MBD

Patients with chronic kidney disease (CKD) commonly experience abnormalities of mineral and bone metabolism, contributing significantly to increased rates of mortality and morbidity, including cardiovascular disease and fracture. The term chronic kidney-disease-mineral and bone disorder (CKD-MBD) encompasses disturbances of mineral metabolism, renal bone disease, and vascular calcification in combination with patient-level outcomes of fracture, cardiovascular disease, and mortality in patients with CKD.

Phosphate binders, vitamin D analogues, and parathyroidectomy are standard of care for CKD-MBD. Treatment is complex and is not firmly evidence-based; further, there is potential for harm with current treatments. Conventional three times a week dialysis is often insufficient to attain negative phosphate balance and fewer than half of dialysis patients achieve levels suggested by several clinical practice guidelines. Low dietary protein intake and malnutrition can result from aggressive adherence to a low-phosphate diet and the large number of phosphate binder tablets required to control hyperphosphatemia creates high pill burden, increased disease intrusion, abdominal symptoms, and potential conflict with other medications.

> Over the duration of the study, achievement of serum phosphate levels within the target range was more common in the extended arm (relative risk [RR], 1.21; 95% CI, 1.04-1.43; *P*=.016).

In the ACTIVE Dialysis (A Clinical Trial of Intensive Dialysis) study, extended hours dialysis reduced serum phosphate but did not cause changes in parathyroid hormone (PTH) or serum calcium. Researchers, led by **Zhipeng Zhan, MD,** and **Brendon Smyth, MD**, conducted a secondary analysis of data from the ACTIVE Dialysis trial to examine the impact of extended hours dialysis on CKD-MBD markers in prespecified patient groups, accounting for concurrent changes in non-dialytic CKD-MBD therapies. Results of the secondary analysis were reported online in *BMC Nephrology* [doi.org/11.1186/s12882-019-1438-3].

The primary outcome of interest was the mean difference in each parameter between the extended (n=100) and standard dialysis arms (n=100), adjusted for confounding participant characteristics and for changes in associated non-dialytic therapies: total number of phosphate binders, use of calcitriol/alfacalcidol, dose of cinacalcet, and dialysate calcium. Secondary outcomes included interactions between subgroups derived from six pre-defined criteria and the unadjusted mean difference in parameters between treatment arms.

A total of 200 participants were recruited from China (62.0%), Australia (29.0%), Canada, (5.5%), and New Zealand (3.5%). The groups were similar in concentrations of serum phosphate, corrected calcium, and intact PTH. In the standard arm, median total weekly dialysis hours during the study period was 12, compared with 24 in the extended arm. In the standard arm, use of hemodiafiltration was more common during the study period than in the extended arm (22.2% vs 14.2% of sessions); the difference did not reach statistical significance. There were no significant differences in dialysate concentrations of sodium, potassium, or calcium.

During the study period, blood flow rates were lower in the extended arm compared with the standard arm (250 mL/min vs 280 mL/min). At 90.6% of study visits, dialysate flow rate was 500 mL/min and median flow rates did not differ (500 mL/min) (a small number of outlying values resulted in mean dialysate flow rates being lower in the extended arm). In the standard arm, one participant had a fracture and two had parathyroidectomies; in the extended arm, there was one fracture and one parathyroidectomy.

Extended hours dialysis resulted in reduction in use of phosphate binders (–0.83 tablets per day; 95% confidence interval [CI], –1.16 to –0.04; *P*=.04). In adjusted analyses, there were no differences in type of phosphate binder, use of vitamin D, dose of cinacalcet, or dialysate calcium.

Over the duration of the study, achievement of serum phosphate levels within the target range was more common in the extended arm (relative risk [RR], 1.21; 95% CI, 1.04-1.43; *P*=.016). There were no differences between the two groups in the proportion of patients who achieved target ranges for serum calcium (RR, 1.03; 95% CI, 0.93-1.14; *P*=.61) and PTH (RR, 1.09; 95% CI, 0.89-1.34; *P*=.40).

Across the tested subgroups, the impact of extended hours dialysis on serum phosphate, calcium, and PTH was generally consistent. Exceptions were the significant interaction between the effect of treatment allocation on phosphate and both baseline level of PTH (*P* for interaction=.043) and dialysis location (*P* for interaction=.046), such that participants with high baseline PTH and dialyzing at an institution experienced a greater reduction in serum phosphate with extended hours dialysis. There was also a significant interaction between the effect of treatment allocation on PTH and baseline phosphate (*P* for interaction=.019); participants with low baseline serum phosphate had a small increase in PTH if assigned to extended hours dialysis.

There were some limitations to the findings, including the relatively small cohort size, limiting the power of the study to detect subgroup differences; the short study duration; and the lack of serum levels of calcidiol (25-hydroxyvitamin D).

In conclusion, the researchers said, "The improvement in serum phosphate associated with extended hours hemodialysis was independent of changes in other CKD-MBD therapies and was consistent across a range of important patient subgroups. The observed differences in the impact of extended hours dialysis on phosphate seen in those with high baseline PTH or dialyzing in an institution, or on PTH in those with low phosphate require confirmation in larger studies." ■

TAKEAWAY POINTS

- Chronic kidney disease-mineral and bone disorder (CKD-MBD) is associated with changes in phosphate, calcium, and parathyroid hormone (PTH) in patients on hemodialysis. Researchers conducted an analysis of data from the ACTIVE Dialysis study that compared conventional dialysis (≤18 h/week) with extended hours dialysis (≥24 h/week).
- Phosphate binder use was reduced among patients assigned to extended hours dialysis; there was no difference in type of phosphate binder.
- In adjusted analysis, there was an association between extended hours dialysis and lower phosphate; there was no significant change in serum calcium or PTH among patients in the extended hours arm compared with the standard arm.

CRIC Study Subanalysis: Predictors of Net Acid Excretion

Due to an imbalance of acid load and excretion, metabolic acidosis is a common complication of chronic kidney disease (CKD). It is possible that higher acid load is the mechanism that links metabolic acidosis with poor kidney outcomes, due, in part, to associations between higher diet-derived acid load and faster progression of CKD.

The gold standard measure of acid load is net acid excretion (NAE). In unexpected results, higher NAE has been associated with slower CKD progression. Differences in NAE may reflect differences in diet-derived acid load in part; kidney and tubular function, body size, or metabolic acid production unrelated to dietary intake may also be involved.

Researchers have found that the associations between higher NAE and slower CKD progression are particularly pronounced in patients with diabetes mellitus, suggesting that excess acid may be produced during the altered energy metabolism characteristic of diabetes and its precursor, metabolic syndrome. **Landon Brown, MD,** and colleagues recently conducted a cross-sectional study to explore predictors of NAE in patients enrolled in the CRIC (Chronic Renal Insufficiency Cohort) study. Results of the current analysis were reported in the *American Journal of Kidney Diseases* [2019;74(2):203-212].

Candidate predictors were examined across a set of prespecified domains, including demographics, comorbid conditions, medications, laboratory values, diet, physical activity, and body composition. Each predictor was evaluated for an association with NAE in unadjusted and minimally adjusted linear regression models.

Participants for the current analysis were randomly selected from CRIC participants with 24-hour urine samples who participated in the CRIC mineral metabolism substudy (n=1000). Following obtainment of NAE measurements, 22 participants were excluded, resulting in an analysis cohort of 978 participants.

Mean age of the cohort was 58 years, 56.5% were men, 40.6% were non-Hispanic whites, and 43.5% were non-Hispanic blacks. Mean estimated glomerular filtration rate (eGFR) was 44 mL/min/1.73 m^2 and 51% had diabetes mellitus. Mean NAE was 33.2 mEq/d. NAE was higher among those with diabetes and greater levels of eGFR, insulin resistance, potential renal acid load (PRAL), and fat-free body mass.

In unadjusted analyses, characteristics associated with higher NAE included non-Hispanic white race, male sex, younger age, larger body size, greater physical activity and dietary intake, greater eGFR, higher serum albumin level, history of diabetes mellitus, increasing insulin resistance, and use of certain metabolically active medications. Following multivariable adjustment for age, sex, race, eGFR, and body surface area, the association between higher NAE and all measures of body composition remained.

There was a significant association between higher serum bicarbonate level and lower NAE, suggesting that low acid load was resulting in a higher steady-state bicarbonate concentration. There was no association between NAE and diuretics and other medications known to associate with steady-state bicarbonate concentrations. With the exception of metformin, there was no association between NAE and antidiabetic medications such as sulfonylureas, insulin, and thiazolidinediones.

Within the body composition domain, the largest effect size was observed for fat-free mass. Within the diet domain, PRAL and total dietary protein had similar effect sizes. The analysis examined serum uric acid level as a predictor post hoc, but there was no association between uric acid and higher NAE in univariate analysis.

To determine a full set of independent predictors, candidates from each of the domains were selected based on biologic rationale and strength of association in univariable, multivariable, and domain-specific models. Age, sex, race/ethnicity (non-Hispanic white, non-Hispanic black, and other), fat-free mass, homeostatic model assessment of insulin resistance, eGFR, 24-hour urine albumin excretion, presence of diabetes with and without use of metformin, and PRAL were included in the fully adjusted model.

Higher NAE remained directly associated with non-Hispanic white race, greater fat-free body mass, greater eGFR, higher insulin resistance, and higher PRAL. Among participants with diabetes, those using metformin had higher NAE compared with those not using metformin (*P*=.03).

Study limitations cited by the authors included the cross-sectional design; testing of urine specimens after long-term storage of up to 10 years, possibly affecting measurement accuracy; and basing urine measurements and inferences on a classic understanding of acid-base physiology.

In conclusion, the researchers said, "Overall, results from this study suggest that NAE is not only related to diet, but also body composition and metabolic factors, including metabolically active medications that could modify CKD risk. Interestingly, many of the established and emerging therapies that improve diabetic kidney disease outcomes also alter basal energy metabolism to increase acid production in diabetes mellitus. Metformin, a mainstay of diabetic therapy, is known to improve mortality, but also carries a rare risk for lactic acidosis. Newer therapies including sodium-glucose cotransporter 2 inhibitors also improve CKD outcomes while inducing subtle or frank ketosis. Sodium bicarbonate therapy may also promote augmented endogenous acid production, in part to protect against the development of metabolic acidosis, but effects on outcomes in diabetes are not known. We propose that differences in basal energy metabolism resulting in greater diet-independent acid production could explain our prior findings of improved kidney outcomes in diabetic patients with higher NAE and could be a unifying feature of kidney protective therapies in diabetes. Further studies are needed to validate this paradigm." ■

TAKEAWAY POINTS

- Researchers conducted an analysis of data from the CRIC study to examine independent predictors of net acid excretion (NAE) across multiple domains (demographics, comorbidities, medications, laboratory values, diet, physical activity, and body composition).
- In adjusted models, there were associations between NAE and insulin resistance, dietary potential renal acid load, and a variety of metabolically active medications.
- Higher NAE was also independently associated with body size, race/ethnicity, and estimated glomerular filtration rate.

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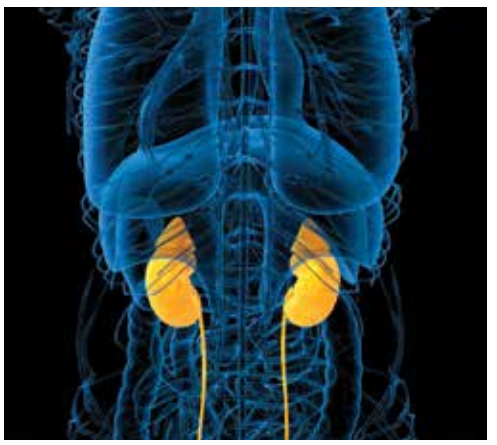
Kidney Transplant Center Volume and 3-Year Clinical Outcomes



For patients with kidney failure, kidney transplantation prolongs survival, improves quality of life, and reduces costs compared with dialysis. However, according to **Elizabeth M. Sonnenberg, MD,** and colleagues, there is a large gap between the demand for transplantation and supply of organs available. Identification of centers that are associated with the best outcomes of transplantation and encouraging patients to utilize those centers is a potentially valuable strategy for maximizing the benefit of transplantation.

Previous studies have shown an association between improved outcomes and high-volume centers in a variety of surgical fields. However, there are few data revealing an association between kidney transplantation volume and survival. Dr. Sonnenberg et al. conducted a retrospective cohort study to examine whether a center volume-outcome relationship exists for contemporary kidney transplantation, specifically for recipients with diabetes, recipients ≥65 years of age, and recipients of high kidney donor profile index (KDPI ≥85) kidneys. The researchers sought to test the hypothesis that compared with low-volume centers, high-volume centers would have decreased graft failure and patient mortality. Results were reported in the *American Journal of Kidney Diseases* [2019; 74(4):441-451].

The researchers utilized data from the Organ Procurement and Transplantation Network to identify a cohort of adults ≥18 years of age who underwent kidney-only transplantation between January 1, 2009, and December 31, 2013. Transplantation centers were stratified into quartiles: Q1, low (annual range, 2-65); Q2, medium (annual range, 66-110); Q3, medium-high (annual range, 111-195); and Q4, high (annual range, 198-315). Centers performing <10 transplantations during the study period were excluded. The primary outcomes of interest were all-cause graft failure and mortality within 3 years of transplantation. Recipients of living and deceased donor organs were analyzed separately.

The final cohort included 79,581 kidney transplantations performed at 219 centers. Deceased donor transplantations constituted a lower proportion of transplantations at Q4 centers compared with Q1 centers (57.1% vs 67.1%; *P*<.001). Of their total deceased donor volume, Q4 centers used a greater proportion of high-KDPI kidneys compared with Q1 centers (12.5% vs 8.3%; *P*<.001).

There were slight variations in patient characteristics among the volume quartiles. Deceased donor grafts at Q4 centers had longer cold ischemia times: 10.8% of grafts at Q4 centers had ≤36 hours compared with 1.1% of grafts at Q1 centers. There were also variations in donor characteristics across volume quartiles. Deceased donor kidneys at Q4 centers had higher median KDPI score compared with those used at Q1 centers (53 vs 44; *P*<.001). Q1 centers used a larger proportion of donation after cardiac death donors compared with Q4 centers (16.4% vs 13.6%; *P*<.001).

There were significant differences in unadjusted 3-year all-cause graft failure and mortality rates across volume quartiles. There were also significant differences across volume quartiles in unadjusted Cox models. The differences were small in absolute terms. Unadjusted rates of all-cause graft failure were 14.9% in Q1, 15.3% in Q2, 14.9% in Q3, and 16.7% in Q4. Rates of mortality were 9.1% in Q1, 8.8% in Q2, 8.4% in Q3, and 9.8% in Q4.

In analyses of graft failure, center volume had a borderline statistically significant interaction with recipients with diabetes (interaction term *P*=.05) and high-KDPI kidney recipients (interaction term *P*=.05). There was no interaction between recipient age and center volume for either outcome.

A total of 5128 recipients with diabetes who received a deceased donor transplant (38.1% of all deceased donor transplants) received care at a Q1 center; 3973 recipients with diabetes who received a deceased donor transplant (35.3% of all deceased donor recipients) were treated at a Q4 center. While not clinically meaningful, there were significant differences across volume quartile in unadjusted 3-year all-cause graft failure and mortality rates. The highest unadjusted rates of all-cause graft failure were in Q4 centers (19.7% vs 18.4%, 18,1%, and 17.7% in Q1, Q2, and Q3 centers, respectively; *P*=.02); rates of mortality were also highest in Q4 centers (13.8% vs 13.2%, 12.6%, and 11.7% in Q1, Q2, and Q3 centers, respectively; *P*=.01).

Because low-volume centers transplanted a larger proportion of deceased donor organs, all quartiles used a substantial number of high-KDPI kidneys: 1117 at Q1 centers versus 1401 at Q4 centers. In unadjusted analysis of 3-year all-cause graft failure and mortality rates of high-KDPI kidneys, the rates were lowest for Q3 centers: all-cause graft failure in Q3 centers, 23.3% versus 26.5% for Q1 centers, 28.0% for Q2 centers, and 26.5% for Q4 centers; mortality in Q3 centers, 13.0% versus 16.0% at Q1 centers, 17.5% at Q2 centers, and 15.0% at Q4 centers. There was no significant effect of center volume on all-cause graft failure and mortality in multivariable Cox frailty models.

There were some limitations to the study, including unmeasured confounding from patient comorbid conditions and organ selection and the potential for measurement errors in registry data.

In conclusion, the researchers said, "This study found no evidence that increased center volume was associated with improved outcomes for kidney transplant recipients. Importantly, this finding remained consistent among increased-risk recipients and increased-risk donors. For nephrologists, who influence where patients seek a transplantation evaluation, these results would argue against referral to larger centers based on volume alone. Other patient-specific considerations, such as proximity to center, may matter more than center volume when selecting a center. Additional research is needed to understand qualities and practices of transplantation centers that generate superior outcomes for patients." ■

TAKEAWAY POINTS

- Researchers conducted a retrospective cohort study to test the hypothesis that high-volume kidney transplantation centers would generate superior outcomes compared with low-volume centers.
- In multivariable Cox regression models, there was no significant association between center volume and all-cause graft failure or mortality within 3 years post-transplantation.
- Transplant recipients with diabetes had slightly lower 3-year mortality rates at centers with medium-high volume compared with centers with low volume (adjusted hazard ratio, 0.85; 95% confidence interval, 0.73-0.99).

Pretransplant Weight Loss and Poorer Posttransplant Outcomes

In patients with end-stage renal disease or earlier stages of chronic kidney disease, weight loss may signal protein-wasting malnutrition and progressive sarcopenia, as well as increased risk for mortality. Wasting measured by unintentional weight loss is a factor in physical frailty. Frailty in recipients of deceased donor kidney transplantation is associated with increased risk for delirium, early hospital readmission, longer transplant hospitalization length of stay, and post-transplant mortality.

However, according to **Meera Nair Harhay, MD, MSCE,** et al., there are few data available on pre-deceased donor kidney transplantation weight loss as an independent predictor of posttransplant outcomes. Dr. Harhay and colleagues conducted a retrospective cohort study to examine whether there is an independent association between weight change while awaiting deceased donor kidney transplantation and differences in transplant hospitalization length of stay and in posttransplant all-cause graft loss and risk of mortality. The researchers also sought to determine whether the association of pretransplant weight change with posttransplant outcomes was modified by patient characteristics. Results of the study were reported in the *American Journal of Kidney Diseases* [2019;74(3):361-372].

The outcomes of interest were (1) transplant hospital length of stay in days; (2) all-cause graft failure; and (3) mortality. The study exposures were relative pretransplant weight change as a continuous predictor and characterized as (1) <5% weight changes from wait-listing to transplant (stable weight); (2) weight loss ≥5% and <10% of listing body weight; (3) weight loss ≥10% of listing body weight; (4) weight gain ≥5% and <10% of listing body weight; and (5) weight gain ≥10% of listing body weight.

The study included 94,465 recipients of a deceased donor kidney transplant between December 4, 2004, and December 3, 2014. Median age was 54 years, 32% were black, and 60% were male. Median follow-up posttransplantation was 5.0 years. Median change in weight from listing to transplantation was 0 kg.

Weight change pretransplant was more common among recipients in the later years of the study period. Fifty-two percent (n=49,366) of recipients underwent transplant with stable weight (<5% weight change from listing to transplant); 12% (n=10,921) of recipients had lost ≥5% and <10% of their listing weight, 11% (n=10,779) had gained ≥5% and <10% of their listing weight; 14% (n=12,785) had gained ≥10% of their listing weight, and 11% (n=10,614) had lost ≥10% of their listing weight.

Those with ≥10% pretransplant weight loss were more likely to be younger than 45 years than those with <5% pretransplant weight change (33% vs 29%), more likely to be of black race (37% vs 31%), female (41% vs 37%), and have longer waiting times (median, 3.0 vs 1.8 years) (P<.001 for all comparisons). Those with <5% pretransplant weight change had similar rates of delayed graft function as those with ≥10% relative weight loss (24% vs 25%; P=.05).

There was a nonlinear unadjusted association between relative pretransplant weight change and transplant hospitalization length of stay, with a steep increase in length of stay among those with >20% relative pretransplant weight loss compared with those with no pretransplant weight change. In the complete gamma regression model, those with ≥10% pretransplant weight loss had 0.66 (95% confidence interval [CI], 0.23-1.09) days longer average transplant hospitalization length of stay compared with those with <5% pretransplant weight change (P=.003).

The association between pretransplant weight loss and transplant hospitalization length of stay was modified by pretransplant dialysis exposure, time on the transplant wait list, and listing body mass index (BMI). Age was not an effect modifier. Weight loss of ≥10% was associated with greater increased in length of stay among those with <3 years of dialysis exposure, shorter time on the wait list, and overweight or obese listing BMIs.

There was a nonlinear unadjusted association between relative pretransplant weight change and all-cause graft failure, with steep increases in graft failure among those who lost or gained ≥10% of their listing weight compared with recipients with no pretransplant change in weight. The unadjusted cumulative incidence of graft loss was highest among those who lost ≥10% of their listing weight.

In the complete case multivariable Cox model for all-cause graft loss, compared with recipients with <5% pretransplant weight change, those who lost ≥10% of their listing weight had 11% higher posttransplant graft loss (adjusted hazard ratio [aHR], 1.11; 95% CI, 1.06-1.17; P<.001); recipients who gained ≥10% of their listing weight had 6% higher graft loss (aHR, 1.06; 95% CI, 1.01-1.12; P=.02). The association between pretransplant weight loss and all-cause graft loss was not modified by recipient age, dialysis vintage, time on wait list, and listing BMI category.

There was a nonlinear association between relative pretransplant weight change and mortality, with a steep increase in mortality among those who lost ≥10% of their listing weight compared with recipients with no pretransplant weight change. In the complete case multivariable Cox model for mortality, compared with those with <5% pretransplant weight change, those who lost ≥10% of their listing weight had 18% higher posttransplant mortality (aHR, 1.18; 95% CI, 1.11-.1.25; P<.001). The association between pretransplant weight loss and mortality was not modified by recipient age, dialysis vintage, time on wait list, and listing BMI category.

The main study limitations cited by the authors were unmeasured confounders and the inability to identify volitional weight change.

In summary, the researchers said, "Among recipients who underwent deceased donor kidney transplantation in the United States from 2004 to 2014, we found that substantial pre-deceased donor kidney transplant weight loss was associated with longer transplant hospitalization length of stay and higher risks for all-cause graft loss and death. Because these associations were not modified by higher recipient listing BMI, our study suggests the need to closely monitor volitional weight loss among deceased donor kidney transplant candidates for evidence of worsening nutritional status and sarcopenia. More intensive monitoring strategies for deceased donor kidney transplant recipients who have experienced substantial pre-deceased donor kidney transplant weight loss may also be warranted." ■

TAKEAWAY POINTS

- Researchers conducted a retrospective cohort study to examine whether weight change while on the kidney transplant wait list is independently associated with differences in transplant hospitalization length of stay and in posttransplant all-cause graft loss and mortality.
- There was an association between ≥10% pretransplant weight loss and longer transplant hospitalization length of stay compared with <5% pretransplant weight change; the association was modified by pretransplant dialysis vintage, listing body mass index category, and time on wait list.
- There was also an association between ≥10% pretransplant weight loss and 1.11-fold higher graft loss and 1.18-fold higher mortality, compared with <5% pretransplant weight change; the association was not modified by pretransplant dialysis vintage, listing body mass index category, and time on wait list.

ASN Announces Endowed Lectureship Series

American Society of Nephrology (ASN) has announced the establishment of the Burton D. Rose, MD, Endowed Lectureship. Dr. Rose is an internationally recognized clinician, scientist, and educator, known for developing groundbreaking education and information resources for nephrologists and other clinicians.

The lecture will be presented each year during ASN's Kidney Week. The inaugural lecture was delivered at Kidney Week 2019 by **Bertram L. Kasiske, MD**. The 2019 lecture was titled "Educating Patients and Practitioners about the Benefits of Transplantation."

The Lectureship series is endowed with support from Wolters Kluwer, the Beth Israel Deaconess Medical Center Department of Medicine Foundation, the Rose family, and several of Dr. Rose's colleagues.

KidneyIntelX™ Covered for Reimbursement for Qualified CDPHP Members

Capital District Physicians' Health Plan, Inc. (CDPHP®), has adopted coverage determination policies that will provide KidneyIntelX™ for qualified CDPHP members who have type 2 diabetes and chronic kidney disease (diabetic kidney disease [DKD]).

In a press release from Renalytix AI, a developer of artificial intelligence enabled clinical diagnostics for kidney disease, **John D. Bennett, MD,** president and CEO of CDPHP, said, "At CDPHO, we have been on a mission to support our members with diabetes to the best of our ability, offering programming and services to meet their lifestyle choices and needs. Coverage of KidneyIntelX for qualified members is a proactive step toward identifying and treating fast-progressing kidney disease."

James McCullough, chief executive officer at Renalytix AI, said, "This CDPHP coverage determination is an important milestone for opening market access to the predictive value and data assessment capacity of KidneyIntelX in this critical medical indication. CDPHP is a progressive thinking physician led payor group that is offering advanced technology solutions to help patients experiencing rapid kidney function decline to slow or prevent the devasting effects of end-stage renal disease and dialysis."

In an April 2019 study, patients with DKD who scored high risk by KidneyIntelX were 10 times more likely to experience kidney failure than those who scored low risk. Patients identified as high risk can be managed with strategies and proven therapeutic options to slow the rate of disease progression and/or halt its progress. In the study, more than 95% of patients with a low KidneyIntelX score did not experience any progression of kidney disease over the subsequent 5 years, and remained at a primary care physician level for monitoring.

New Water Purification Systems Announced

In a press release, the Renal Therapies Group of Fresenius Medical Care North America announced the launch of AquaB*plus* and AquaC UNO H water filtration systems. The systems will be available to all dialysis centers and hospitals in North America in the first quarter of 2020. The systems are designed to reduce water and power usage.

AquaB*plus* and AquaC UNO H use reverse osmosis to remove organic and inorganic substances and microbial contaminants for the water required for hemodialysis and other therapies.

Mark Costanzo, president of the Renal Therapies Group of Fresenius Medical Care North America, said, "These new water treatment systems demonstrate our commitment to delivering the latest innovations for renal care providers. This technology helps ensure patients undergoing hemodialysis receive safe, clean water while reducing energy use and operational costs."

The AquaB*plus* system is a modular platform allowing components to be combined in multiple configurations, including single or double stage, while offering the option for automated heat disinfection. AquaC UNO H is a portable water treatment system that features a compact footprint, making it useful when space is limited.

"Providing clean, purified water is an essential part of delivering high quality dialysis therapy," **Rob Klossmann, MD,** chief medical officer for Fresenius Medical Care North America, said. "We are proud of our effort to improve the tools that drive quality care and advance our commitment to all patients living with kidney failure."

National Universal Living Donor Kidney Registry Created

In a recent press release, Donate Life America and Fresenius Medical Care Foundation announced a partnership created to launch a national, universal living donor kidney registry as well as an at-home testing kit. The effort aims to improve access to living donation for the 95,000 people on the national transplant wait list. The Foundation is a separately operated 501©(3) nonprofit arm of Fresenius Medical North America.

The $500,000 donated from the Foundation to Donate Life America will create two initiatives designed to encourage living donation:

- The National Donate Life Living Donor Registry will provide the opportunity to register interest in becoming a living donor. The platform will partner with the United Network for Organ Sharing and transplant programs nationwide to allow potential living donors and recipients to find matches. The new registry will build on the secured and trusted National Donate Life Registry that included deceased organ, eye, and tissue donor registrations.

- The First-Ever At-Home Living Donor Testing Kits will create a faster, more accessible screening option to identify and register potential living donors for kidney transplant. The process will convert testing results to a potential match as quickly and safely as possible.

Bill Vale, chief executive officer of Fresenius Medical Care North America, said, "We are committed to ensuring that every eligible person who is seeking a kidney transplant receives one. Kidney transplant is the best life-saving option for people living with kidney disease. We are committed to partnering with organizations like Donate Life America to raise visibility of the need for transplants while streamlining the living kidney donation process. By creating these innovative, first-ever resources, we expect to nearly double the number of successful matches within one year of launch, leading to reduced average transplant waiting times for people living with kidney disease."

David Fleming, president and CEO of Donate Life America, said, "We are excited to partner with the Fresenius Medical Care Foundation to reduce barriers to living donation, grow generosity, and save more lives."

The National Donate Life Living Donor Registry is expected to be live by spring 2020. For more information, visit www.fmcna.com/foundation.

CONFIRM Study Results Reported at The Liver Meeting 2019

Results for the phase 3 CONFIRM study were reported at The Liver Meeting® 2019, the annual meeting of the American Association for the Study of Liver Diseases in Boston, Massachusetts. The CONFIRM study was designed to test the efficacy and safety of terlipressin in adults with hepatorenal syndrome type 1 (HRS-1), a life-threatening condition involving acute

kidney failure in patients with cirrhosis. The study met its primary end point of verified HRS-1 reversal (*P*=.012). Verified HRS-1 reversal includes three components: improvement in renal function, avoidance of dialysis, and short-term survival.

In a press release from Mallinckrodt, a global biopharmaceutical company, presenting author **Florence Wong, MBBS, MD, FRACP, FRCPC,** said, "HRS-1 is estimated to affect between 30,000 and 40,000 patients in the United States annually. It is a rapidly progressing and devasting condition, and many patients don't live beyond a few weeks if left untreated. I am encouraged by the results of the CONFIRM trial of terlipressin, which, if approved, may make a difference in this difficult-to-treat population."

Terlipressin is an investigational product and its safety and effectiveness have not yet been established by the US FDA or Health Canada. Mallinckrodt plans to submit a New Drug Application to the US FDA in early 2020.

FDA Grants Breakthrough Device Designation to Endexo®

The US FDA has granted breakthrough device designation to a hemodialysis system in development that is designed to prevent blood clotting without the use of blood thinner medication in most patients. In a press release from Fresenius Medical Care North American (FMCNA), the company describes the antithrombogenic additive, Endexo®, that is being incorporated into the manufacturing process of dialyzers and bloodlines. The additive is a polymer of surface modifying molecules that inhibit the adsorption of protein and platelets, reducing clot risk and increasing hemocompatibility.

Olaf Schermeier, MD, chief executive officer for global research and development at Fresenius Medical Care, said, "Harnessing our innovational expertise, we continuously strive to make significant advances in our products and provide new solutions for people with chronic kidney disease worldwide. Receiving this designation, we are right on track with a new dialysis system that will directly benefit our patients' well-being."

The new technology aims to reduce the need for blood thinners that can have dangerous side effects. Fresenius Medical Care holds an exclusive worldwide license from Interface Biooogics to apply the Endexo technology to various hemodialysis components, including dialyzers and blood lines, according to the press release.

Robert Klossmann, MD, chief medical officer for FMCNA, said, "We are hopeful this new system will help eliminate the reliance on heparin during dialysis to improve treatments for most patients. The work to achieve this breakthrough has been years in the making and we are excited that the FDA has recognized the importance of bringing this technology to market as quickly as possible."

Topline Phase 2 Results of Praliciguat for Diabetic Nephropathy

Topline results for the phase 2 proof-of-concept study of praliciguat have been announced in a press release from Cyclerion Therapeutics, Inc. Praliciguat is a once daily, orally available systemic soluble guanylate cyclase (sGC) stimulator in patients with diabetic nephrology.

The study did not meet statistical significance on the primary endpoint of reduction in albuminuria from baseline compared with placebo, measured by urine albumin creatinine ratio. However, across the total intention-to-treat population, there was a tendency toward improvement. Further, there were improvements observed in patients in the praliciguat group in several secondary vascular and metabolic measures associated with cardiovascular risk and progression of kidney disease, including blood pressure, cholesterol, and hemoglobin A1c levels, compared with the placebo group.

Praliciguat was generally well tolerated and demonstrated a safety profile consistent with continued development.

"We believe praliciguat has the potential to be a first-in-category treatment for patients with diabetic nephropathy," **Mark Currie, PhD,** president and chief scientific officer at Cyclerion, said. "We look forward to sharing the data with prospective partners."

Cyclerion intends to out-license praliciguat for late-stage global development and commercialization.

FMCNA Announces Launch of TheHub

A new connected health platform, TheHub, has been launched by Fresenius Medical Care North America (FMCNA). The platform includes three integrated applications to enable improved collaboration among patients, care teams, and providers in monitoring patient treatments. FMCNA is the largest provider of kidney care products and services in the United States.

According to a press release, TheHub will further enhance FRCNA's remote monitoring capabilities for patients on home dialysis, encompassing all home modalities and technologies being used.

Jeff Burbank, chief strategy and transformation officer for FRCNA, said, "This best-in-class solution offers a technology hub that improves the experience for patients and the entire care team. This simple and streamlined experience supports our efforts to advance and accelerate the adoption of home therapies while ensuring our patients stay well connected to their care teams."

The three applications are PatientHub, helping patients manage their care and stay connected with their care team; CareTeamHub, helping home therapy nurses care for their patients via daily monitoring and clinical decision support; and ProviderHub, offering physicians and advanced practitioners real-time access to medical records.

Robert Kossmann, MD, chief medical officer for FMCNA, said, "This new suite of cloud applications is making our connected health technologies easier to use for providers and patients. We know these new tools are essential to helping patients succeed on home therapies and are committed to ongoing improvement of our remote monitoring capabilities." ■

Major Meetings 2020

Renal Physicians Association Annual Meeting 2020

March 19-22, 2020

Baltimore, Maryland

www.renalmd.org/page/calAnnualMeeting

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

CARDIOVASCULAR OUTCOMES

Increases in Creatinine after Initiation of RASi

Clinical Journal of the American Society of Nephrology. 2019;14(9):1336-1345

There have been conflicting results from observational and interventional studies on the relationship between creatinine increase following renin-angiotensin system inhibition (RASi) and adverse outcomes. Researchers, led by **Edouard L. Fu, MD,** conducted a retrospective analysis designed to compare health outcomes among patients with varying categories of increase in creatinine following initiation of RASi in a large population-based cohort.

The analysis utilized data from the Stockholm Creatinine Measurements database. The database includes complete information on diagnoses, medication dispensation claims, and laboratory test results for all Stockholm citizens accessing healthcare. The analysis included 31,951 adults with available pre- and postinitiation creatinine monitoring who initiated RASi during 2007-2011. Mortality, cardiovascular, and ESRD events were compared among individuals with varying ranges of creatinine increases within 2 months of treatment initiation using multivariable Cox regression.

Median follow-up was 3.5 years. There was an association of acute increases in creatinine and mortality (3202 events) in a graded manner: compared with creatinine increases <10%, a 10% to 19% increase showed an adjusted hazard ratio (HR) of 1.15 (95% confidence interval [CI], 1.05-1.27). For increases of 20% to 29%, the HR was 1.22 (95% CI, 1.07-1.40) and for increases of ≥30%, the HR was 1.55 (95% CI, 1.36-1.77).

There were similar graded associations between increases in creatine and heart failure (2275 events; $P<.001$) and ESRD (52 events; $P<.001$), and less, consistently, myocardial infarction (842 events, $P=.25$).

Among continuing users, when patients with decreases in creatine were excluded from the reference group and after accounting for death as a competing risk, results were robust across subgroups.

In conclusion, the researchers said, "Among real-world monitored adults, increases in creatinine (>10%) after initiation of RASi are associated with worse health outcomes. These results do not address the issue of discontinuation of RASi when plasma creatinine increases but do suggest that patients with increases in creatinine have higher subsequent risk of cardiovascular and kidney outcomes."

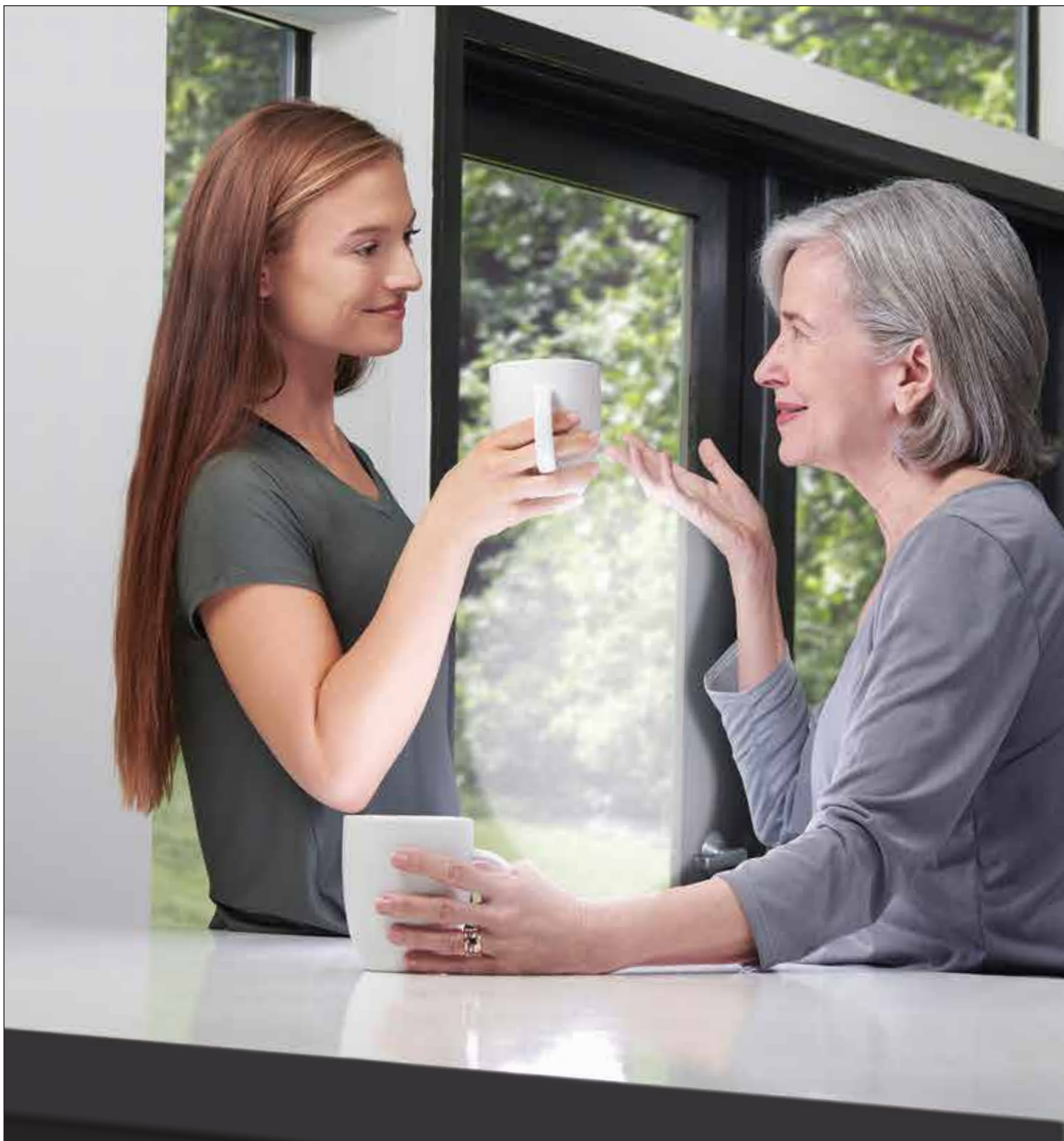
CHRONIC KIDNEY DISEASE

Prognostic Model to Predict 12-month Mortality in Advanced CKD

Nephrology Dialysis Transplantation. 2019;34(9):1517-1525

Advance care planning regarding future treatment for patients with advanced chronic kidney disease (CKD) requires a clear assessment of prognosis. Shared decision-making between clinicians and patients could be informed via a patient-specific integrated model designed to predict mortality. **Rebecca J. Schmidt, DO,** and colleagues developed and validated a prognostic model to predict mortality in patients with advanced CKD.

The process included patients from Massachusetts (n=749) and West Virginia (n=437) with stages 4 and 5 CKD. The patients were prospectively evaluated for clinical parameters, functional status (Karnofsky Performance Score [KPS]), and their provider's response to the Surprise Question. A predictive model for 12-month mortality was derived from the Massachusetts cohort; the West Virginia cohort provided external validation of the model. The model



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was created using logistic regression; model discrimination and calibration assessed using the c-statistic and Hosmer-Lemeshow statistic, respectively.

In the Massachusetts cohort, the most predictive factors of 12-month mortality were the Surprise Question, KPS, and age: odds ratio (OR), 3.29 (95% confidence interval [CI], 1.87-5.78) for a No response to the Surprise Question; OR 2.09 (95% CI, 1.19-3.66) for fair KPS, and OR, 1.41 (95% CI, 1.15-1.74) per 10-year increase in age.

The c-statistic for the 12-month mortality model for the Massachusetts (derivation) cohort was 0.80 (95% CI, 0.75-0.84); for the West Virginia (validation) cohort, it was 0.74 (95% CI, 0.66-0.83).

In conclusion, the researchers said, "Our integrated prognostic model for 12-month mortality in patients with advanced CKD had good discrimination and calibration. This model provides prognostic information to aid nephrologists in identifying and counseling advanced CKD patients with poor prognosis who are facing the decision to initiate dialysis or pursue medical management without dialysis."

DIALYSIS

Cost-Analysis of Dialysis Delivery Models in Hong Kong

Nephrology Dialysis Transplantation. 2019;34(9):1565-1576

Carlos K. H. Wong, PhD, and colleagues at the University of Hong Kong conducted an analysis to estimate the direct and indirect costs of patients with end-stage renal disease (ESRD) in the first and second years of initiating peritoneal dialysis, hospital-based hemodialysis, and nocturnal home hemodialysis. The cost analysis aimed to estimate the annual costs from both the health service provider's perspective and from a societal perspective.

The analysis included empirical data on use of healthcare resources, patient out-of-pockets costs, time spent on transportation and dialysis by patients, and time spent by caregivers. Costs were expressed in Hong Kong 2017 dollars. The analysis included 402 patients with ESRD on maintenance dialysis: peritoneal dialysis, n=189; hospital-based hemodialysis, n=170; and nocturnal home hemodialysis, n=43.

From the healthcare provider's perspective, hospital-based hemodialysis had the highest total annual direct medical costs in both the first and second year: hospital-based hemodialysis, $400,057 and $360,924; peritoneal dialysis, $118,467 and $80,796; and nocturnal home hemodialysis, $223,358 and $87,028 ($P<.001$).

From the societal perspective, the highest costs in both the first and second years were also hospital-based hemodialysis ($452,151 and $413,017), followed by peritoneal dialysis ($189,191) and nocturnal home hemodialysis ($242,03) in the first year. Costs for peritoneal dialysis and nocturnal home dialysis in the second year were $151,520 and $105,708, respectively.

In summary, the researchers said, "This study quantified the economic burden of ESRD patients, and assessed the annual healthcare and societal costs in the initial and second years of peritoneal dialysis, hospital-based hemodialysis, and nocturnal home hemodialysis in Hong Kong. From both perspectives, peritoneal dialysis

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is cost-saving relative to hospital-based hemodialysis and nocturnal home hemodialysis, except that nocturnal home hemodialysis has the lowest costs in the second year of treatment from the societal perspective. Results from this cost analysis facilitate economic evaluation in Hong Kong for health services and management targeted at ESRD patients."

FABRY DISEASE

Loss of Renal Function in Patients with Fabry Disease

Nephrology Dialysis Transplantation.
2019;34(9):1525-1533

Patients with Fabry disease often experience nephropathy. In previous studies, estimated glomerular filtration rate (eGFR) has been the most common measurement of renal function during enzyme replacement therapy. **Christoffer V. Madsen, MD,** and colleagues conducted a study to assess the attrition of renal function in patients with Fabry disease using measured GFR (mGFR) and urine protein excretion. The study also examined the influence of age.

The long-term observational study included a nationwide, family-screened cohort of patients with Fabry disease. All genetically verified Fabry disease patients in Denmark receiving enzyme replacement therapy, without end-stage renal disease at baseline and with three or more mGFR values were included.

A total of 52 patients with consecutive mGFR values (n=841) were evaluated over a median of 7 years (range 1-13 years). Throughout the evaluation period, blood pressure remained normal and there was no change in urine protein excretion. Plasma globotriaosylceramide (Gb-3) levels normalized while plasma lyso-Gb-3 remained abnormal in 34% of patients.

Baseline mGFR was 90 mL/min/1.72 m^2, and the rate of renal loss was 0.9 mL/min/1.73 m^2 per year. Baseline eGFR was 97 mL/min/1.73 m^2, and the rate of renal function loss was 0.8 mL/min/1.73 m^2 per year. Age-adjusted mGFR was compared with renal healthy non-Fabry disease individuals, giving a standard deviation score of –0.8 with an annual slope of –0.3; there were no differences between genders. Independent of baseline mGFR, age, and gender, there was an association between urine albumin-creatinine ratio >300 mg/g and faster renal function loss.

"Enzyme replacement therapy treated Fabry disease patients did not have faster attrition of renal function than healthy non-Fabry disease subjects (background population). The rate of renal function loss with age was independent of gender and predicted by high urine albumin-creatinine ratio. We suggest cautious interpretation of non-age-adjusted Fabry disease renal data," the researchers said.

GERIATRIC NEPHROLOGY

Patient-Centered Care for Older Adults with CKD

Journal of the American Society of Nephrology.
doi.org/10.1681/ASN.2019040385

Providing patient-centered care for older adults with advanced chronic kidney disease (CKD) requires patient-clinician communication about the patient's values, goals of care, and treatment preferences. Tools that patients are comfortable with that can enable effective communication about care preferences are needed.

Nicolas Awad Baddour, MD, and colleagues administered a questionnaire in a nephology clinic with patients ≥60 years of age with stage 4 or 5 nondialysis-dependent CKD. Patients were asked "If you had a serious illness, what would be important to you?" and given the option to select one of four possible responses: (1) live as long as possible; (2) try treatments, but do not suffer; (3) focus on comfort; or (4) unsure. The patients also completed a validated health outcome prioritization tool as well as an instrument that helped determine the acceptability of end-of-life scenarios. The researchers compared patient responses to the three tools.

There were 382 participants in the study. Of those, 134 (35%) selected try treatments, but do not suffer; 126 (33%) choose focus on comfort; 75 (20%) selected live as long as possible; and 47 (12%) opted for unsure. The patients' answers correlated with their first health outcome priority and acceptability of end-of-life scenarios.

A third of the patients who preferred focus on comfort reported that a life on dialysis would not be worth living, compared with only 5% of those who chose live as long as possible ($P<.001$). Nearly 90% of patients agreed to share their preferences with their healthcare providers.

"Older adults with advanced CKD have diverse treatment preferences and want to share them. A single treatment preference question correlated well with longer, validated health preference tools and may provide a point of entry for discussions about patients' treatment goals," the researchers said.

TRANSPLANTATION

Trends in Short-term Outcomes with HCV-viremic Kidney Donation

Journal of the American Society of Nephrology.
doi.org/10.1681/ASN.201905046

Pilot trials have established the safety of transplanting hepatitis C virus (HCV)-viremic kidneys into HCV-seronegative recipients. It remains unclear whether donor HCV-viremia or recipient HCV-serostatus are associated with allograft function. **Vishnu S. Potluri, MD, MPH,** and colleagues conducted an analysis of national US registry data to examine trends in use of HCV-viremic kidneys between April 1, 2015, and March 31, 2019. Advanced matching methods were used to compare estimated glomerular filtration rate (eGFR) for similar kidneys transplanted into similar kidney transplant recipients.

HCV-seronegative recipients received an increasing proportion of HCV-viremic kidneys over time. During the study period, the probability of HCV-viremic kidney discard declined, and kidney transplant candidates willing to accept a HCV-seropositive kidney increased (from 2936 to 16,809).

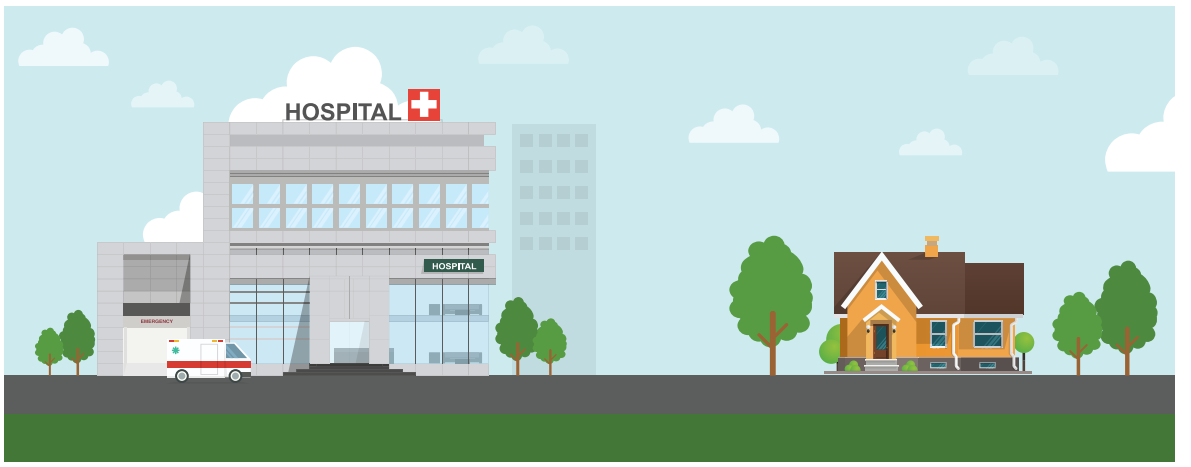
Despite the much worse kidney donor profile index scores assigned to HCV-viremic kidneys, HCV-seronegative recipients had similar 1-year eGFR compared with recipients of HCN-non-viremic kidneys (66.3 vs 67.1 mL/min/1.73 m^2). There was no clinically significant difference in 1-year eGFR associated with recipient HCV-serostatus after transplantation of HCV-viremic kidneys (66.5 vs 71.1 mL/min/1.73 m^2).

In conclusion, the researchers said, "By 2019, HCV-seronegative patients received the majority of kidneys transplanted from HCV-viremic donors. Widely used organ quality scores underestimated the quality of HCV-viremic kidneys based on 2-year allograft function. Recipient HCV-serostatus was also not associated with worse short-term allograft function using HCV-viremic kidneys." ■

Print-only Content

Sarah Tolson

Understanding Transitional Care Management



In recent years, the theme in healthcare reimbursement has been to find ways to pay for quality rather than quantity. Medicare has introduced several new programs with direct impact on the renal community, designed with the intent of producing better patient outcomes while driving cost savings. These programs can be complex, and some may argue they increase administrative burden. Effective January 1, 2013, Medicare began reimbursing providers for Transitional Care Management (TCM) services—a service that many nephrologists have been providing, to some extent, for patients with end-stage renal disease (ESRD) for many years. In this article we will discuss the basic components of TCM services, and in a subsequent article we will discuss several frequently asked questions about TCM services and the codes associated with TCM services.

TCM services were designed to reduce hospital readmissions of patients whose medical and/or psychosocial problems require moderate or high complexity medical decision making during the transition from the inpatient hospital setting to the patient's home setting. TCM services are only billable once per patient within 30 days of discharge. Additionally, the physician that bills for TCM services **may not** report care plan oversight services, medical team conferences, education and training, ESRD services, or complex chronic care coordination services, not to mention several other types of non–face-to-face and care coordination services during the time period covered by the TCM services. As nephrologists commonly see their ESRD patients in the hospital and continue to oversee the patient's care after discharge, TCM services are not billable by the same physician in the same time period as ESRD monthly capitation payment services.

There are several components that make up TCM services: initial, interactive patient contact, face-to-face visits, medication reconciliation and non–face-to-face services. Initial patient contact consists of some form of interactive contact with the patient and/or their caregiver within two business days following the patient's discharge. I have received several questions about the timing of the initial, interactive patient contact. To clarify, if a patient is discharged on Wednesday, the initial, interactive patient contact should take place by the end of the day Friday.

The initial, interactive contact can occur via telephone, email, or face-to-face. In the event you make two or more unsuccessful separate attempts to contact the patient and those attempts are documented in the patient's medical record, TCM services may still be billable. However, much of the Medicare documentation regarding TCM services indicates the expectation is that providers continue their attempts to communicate with the patient until the patient has been reached.

The complexity of medical decision making involved in a patient's TCM services determines when the face-to-face visit must take place. If a patient's condition requires medical decision making of at least moderate complexity, then the face-to-face visit should occur within 14 calendar days of the patient's discharge. In the event the patient's condition requires medical decision making of high complexity, the face-to-face visit should take place within seven calendar days of the patient's discharge. Billing staff should be advised that the TCM face-to-face visit should not be billed separately, as it is included in the TCM service bundle, and it may not take place on the date of discharge.

Medication reconciliation is the next component of TCM services and should occur no later than the date of the face-to-face visit. The last piece of the TCM package is the non–face-to-face services. Here are a few examples:

- Communication with the patient or family regarding the patient's care
- Communication with home health agencies and other community services utilized by the patient
- Patient and/or caretaker education to support self-management and independent living
- Reviewing need for or follow-up on pending diagnostic tests and treatments
- Interaction with other qualified health care professionals who will assume care of the patient's system-specific conditions

One important thing to remember about the non–face-to-face services is that some of the services must be performed by a physician, while others may be performed under the direction of a physician by clinical staff as long as the services are performed within the scope of license. ■

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.

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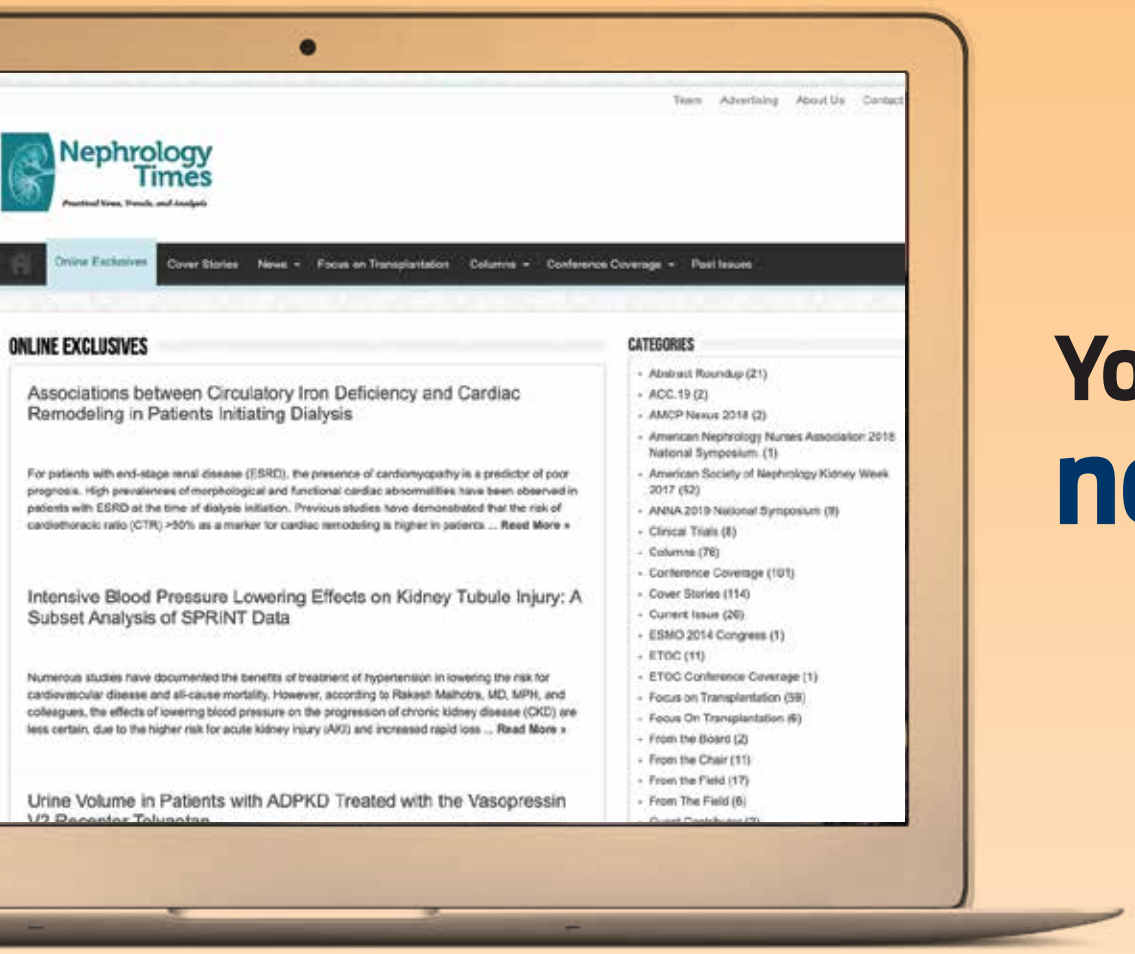

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