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Practical News, Trends, and Analysis

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Conservative Care Management for Patients with CKD Who Forgo Dialysis

Patients with advanced stages of chronic kidney disease (CKD) face decisions regarding initiation of maintenance dialysis, including whether and when to begin treatment. Dialysis is considered a life-prolonging intervention for patients with advanced CKD; however, the therapy does not always deliver the anticipated effects of lengthening life and restoring health and patient quality of life. Particularly among older patients, the demands and potential burdens and complications may outweigh the benefits of dialysis therapy.

For patients with advanced CKD in Australia, Canada, and some countries in Europe and Asia who do not opt for dialysis treatment, care models to provide management of symptoms have been created. Data from such programs suggest that for patients ≥75 years of age who have a high burden of comorbid conditions and functional impairment, there is little difference in life expectancy and quality of life between initiation of dialysis and conservative care management.

Conservative care management is relatively uncommon in the United States. There are few dedicated services for the support of patients who opt to forgo dialysis, and nephrologists in the United States have limited experience caring for that patient population. **Susan P.Y. Wong, MD, MS,** and

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Non-adherence to Dialysis and Utilization of the Emergency Department

Treatment in the emergency department (ED) accounts for nearly half of all hospital-associated care in the United States. Emergency departments treat more than 135 million patients annually. Interventions aimed at identifying patients at high risk for frequent, possibly preventable ED visits are designed to lower costs and ED crowding. Such patients include those on maintenance dialysis for the treatment of end-stage renal disease (ESRD).

The number of patients receiving dialysis for ESRD in the United States has risen substantially since 1980, as has the incidence of ED care for patients with ESRD, which is six to eight times greater than among the general population. Further, patients with ESRD experience up to twice the ED length-of-stay and significantly higher in-patient admission rates. Among patients who shorten or miss

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Timing of Recovery from AKI Predictor of Subsequent Loss of Kidney Function

The rates of acute kidney injury (AKI) are growing, resulting in an increase in the number of survivors requiring ongoing medical care. AKI, particularly severe AKI, is associated with increased risk for incident and progressive chronic kidney disease (CKD), cardiovascular disease, future hospitalizations, recurrent AKI, and death.

Available data suggest that few patients with AKI receive nephrology care after hospital discharge. Identification of which patients would benefit from post-discharge specialist care and which elements of nephrology-based care would be helpful has not been established. The majority of studies designed to examine risk factors for poor outcomes after AKI have concentrated on the severity of AKI or the degree of recovery. Results of these studies indicate an association between more severe injury and less recovery of kidney function and higher risk of death or development of CKD or kidney failure.

Another indicator of future risk may be the timing of recovery. **Edward D. Siew, MD, MSCI,** and colleagues conducted a retrospective cohort study to test

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Non-adherence to Dialysis

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dialysis treatments, the risk of care in the ED further doubles and the risk of rehospitalization quadruples. There is an association between missed dialysis treatments and all-cause mortality and worse health.

According to **Kamna S. Balhara, MA, MD,** and colleagues, there are few available data assessing ED use following missed dialysis treatments. The researchers conducted an interdisciplinary pilot study designed to identify social determinants of heath associated with missing hemodialysis and presenting to the ED; the study also aimed to describe the resource utilization associated with those ED visits. Results of the study were reported online in *BMC Nephrology* [doi.org/10.1186/s12882-019-1673-7].

The prospective observational study included patients who had missed at least one hemodialysis session prior to a visit to the ED who were recruited in the ED of a large academic center (site 1), and a control group that included patients deemed adherent by their nephrologist who were recruited from a population of those regularly attending a large outpatient hemodialysis clinic (site 2).

Both sites are located in the same large urban city and serve communities in the same urban setting. Site 1 is an ED at an academic, tertiary care center with ~70,000 visits per year and a 22% admission rate; site 2 is a large outpatient hemodialysis center in the same city with nearly 300 chronic outpatient hemodialysis patients.

A total of 32 eligible cases were identified; of those, four declined participation and three were not reachable, resulting in a case cohort of 25. Of the 28 controls identified, three declined to participate and one was hospitalized during the recruitment period for a non-hemodialysis related cause, resulting in a control cohort of 24. There were no significant differences between the two groups in sex, age, diabetic status, and dialysis vintage. Most participants were African American with a dialysis vintage of <5 years, 44.9% were women, and 32.7% were diabetic.

In the case group, the most common reasons for missing dialysis were not feeling well or issues with transportation. Three of the seven patients who reported issues with transportation had problems related to the state mobility program. Of the 25 patients in the case group, 56% (n=14) had missed one session of hemodialysis prior to presentation at the ED, 20% (n=5) had missed two sessions, and 24% (n=6) had missed three or more sessions. On presentation to the ED, the most common complaint was shortness of breath (six patients). Six of the patients were acuity level 2 on the Emergency Severity Index (ESI) scale and the remainder were level 3. (ESI level 1 represents highest acuity, level 5 represents the lowest acuity.) Most patients arrived by private vehicle (48%) or ambulance (36%).

All patients who presented to the ED had laboratory studies drawn, at least one radiographic study, and at least one specialty consulting service. Intravenous medications were needed in 52% and 32% required intravenous access placed via ultrasound guidance by an ED physician. Median length of stay in the ED was 14 hours; 24% were directly discharged for the ED; 76% subsequently had an in-patient stay. Nearly half of the admitted patients were placed in monitored units (48%) and 16% required admission to the intensive care unit during the in-patient stay. Median in-patient length-of-stay was up to 6 days.

There were no significant differences between the two groups in comorbidity burden by Charlson Comorbidity Index score. Patients in the case group were significantly less likely to be fully mobile ($P<.001$), had greater reliance on mobility adjuncts ($P=.015$), and had poorer scores in the healthcare limitations scale of the Kidney Disease Quality of Life scale ($P<.02$). Higher levels of pain were reported by patients in the cases group than in the control group; 64% of patients in the case group reported severe or very severe bodily pain in the preceding 4 weeks. Most controls reported having no depression; rates of moderate, moderately severe, or severe depression were higher among patients in the case group. There were no differences between the two groups in alcohol or drug use; current participation in methadone or suboxone programs trended toward significance in the case group.

There were no differences between the groups in economic stability, educational attainment, health literacy, family support, or satisfaction with nephrology care. Cases were more dependent on public transport for dialysis ($P=.03$). There were no significant differences in distance traveled from home to outpatient hemodialysis center between the groups; a larger proportion of cases lived more than 5 miles from their outpatient HD center, but this difference did not reach statistical significance.

In citing limitations to the study findings, the researchers noted the small sample size, the high proportion of African American participants, excluding risk factors such as tobacco use or marital status, and the possibility of recall and self-selection bias among the participants.

In conclusion, the researchers said, "ED visits after missed hemodialysis resulted in elevated length-of-stay and admission rates. Frequently cited social determinants of health such as health literacy did not confer significant risk for missing hemodialysis. However, pain, physical limitations, and depression were higher among cases. Community-specific collaborations between EDs and dialysis centers would be valuable in identifying risk factors specific to missed hemodialysis and ED use, to develop strategies to improve treatment adherence and reduce unnecessary ED utilization." ■

TAKEAWAY POINTS

- Utilization of the emergency department (ED) is twice as high among patients who miss dialysis treatments compared with adherent patients; researchers conducted a prospective observational study to identify social determinants of health associated with missing hemodialysis and presenting to the ED.
- Patients who missed at least one dialysis treatment (case group) had increased rates of hospital admission than patients who were adherent to their dialysis regimen (control group).
- Pain, physical limitations, and depression were higher among patients in the case group compared with the control group.

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Timing of Recovery from AKI Predictor

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the hypothesis that recovery from moderate to severe AKI may last weeks or months and that there would be an association between duration of recovery and a hastened rate of future loss of kidney function. The study was designed to examine the association between timing of recovery and future loss of kidney function among patients who survived moderate to severe AKI. Study results were reported in the *American Journal of Kidney Diseases* [2020;75(2):204-213].

> Median times until the primary outcome were 721, 506, 425, and 445 days in the 1- to 4-day group, 5- to 10-day group, 11- to 30-day group, and 31- to 90-day group, respectively.

The study was conducted among a national cohort of US veterans ≥18 years of age who were hospitalized with moderate to severe AKI. Data were collected from January 1, 2002, to December 31, 2014. Baseline data were obtained from 730 days prior to hospital admission to 90 days following hospital discharge. The cohort included 4,169,266 adults hospitalized in 116 Veterans Affairs hospitals between January 1, 2004, and December 31, 2011.

Exclusion criteria were non-VA follow-up, baseline estimated glomerular filtration rate (eGFR) <15 mL/min/1.73 m^2, kidney transplantation, or registry within the US Renal Data System prior to the index hospitalization. In-hospital exclusions were stage 1 AKI and an uncertain diagnosis of AKI. Post-hospital exclusions were patients who did not recover to within 120% of baseline serum creatinine and patients for whom the timing of recovery could not be well characterized. Other exclusions were patients with evidence of recurrent AKI or those whose final eGFR during the recovery window was <15 mL/,min/1.73 m^2.

The primary outcome of interest was a composite outcome of time to a sustained 40% decline in eGFR or kidney failure from the most recent serum creatinine/eGFR value prior to the end of the 90-day recovery window. Kidney failure was defined as having two outpatient eGFRs of <15 mL/min/1.73 m^2 greater than 90 days apart, receipt of two dialysis procedures more than 90 days apart, kidney transplantation, or registry in the United States Renal Data System, whichever came first.

The final cohort included 47,903 unique patient hospitalizations in which the patient experienced Kidney Disease Improving Global Outcomes stages 2 to 3 AKI, recovered to within 120% of baseline serum creatinine within 90 days, and survived to 90 days without an episode of recurrent AKI or receiving dialysis.

Of the 47,903 patients, 61% (n=29,316) recovered by 1 to 4 days following the peak serum creatinine level, 22% (n=10.360) recovered by 5 to 10 days, 9% (n=4520) recovered by 11 to 30 days, and 8% (n=3707) recovered in the 31- to 90-day period. During a median follow-up time of 42 months, the unadjusted incidence rates per 100 person-years for the primary outcome were 2.01 in the 1- to 4-day group, 3.55 in the 5- to 10-day group, 3.86 in the 11- to 30-day groups, and 3.68 in the 31- to 90-day group. Median times until the primary outcome were 721, 506, 425, and 445 days in the 1- to 4-day group, 5- to 10-day group, 11- to 30-day group, and 31- to 90-day group, respectively.

Following risk adjustment, the overall hazard ratios (HRs) were estimated per patient group identified by time to recovery using 1- to 4-day recovery as the referent group. The risk adjusted HRs were: for patients in the 5- to 10-day recovery group, 1.33 (95% confidence interval [CI], 1.24-1.43); for patients in the 11- to 30-day recovery group, 1.41 (95% CI, 1.28-1.54); and for patients in the 31- to 90-day recovery group, 1.58 (95% CI, 1.43-1.75). The same results were found in straight covariate-adjusted models.

In analysis of subgroups stratified by baseline CKD, there were similar associations between the risk-adjusted HRs and the overall cohort analysis. The greatest absolute increase in incidence rates associated with longer recovery was seen in the highest risk quintiles (81%-100%), with an increase in incidence from approximately six per 100 person-years to 10 to 13 per 100 person-years.

The predominately male study population and the potential for residual confounding were cited by the authors as limitations to the study findings. Also cited was the inability to make causal inferences due to the retrospective design of the study.

In conclusion, the researchers said, "Recovery from moderate to severe AKI is heterogeneous and can take up to several months. The timing of recovery is an independent predictor of future loss of kidney function and may be useful information to help further risk stratify survivors of AKI. Future studies to identify whether the trajectory of recovery can be modified to improve outcomes are warranted." ■

TAKEAWAY POINTS

- A retrospective cohort study was designed to examine the independent association between the timing of recovery from moderate to severe acute kidney injury (AKI) and subsequent loss of kidney function.
- In a large cohort of US veterans, 61% of patients with AKI recovered within 1 to 4 days, 22% within 5 to 10 days, 9% within 11 to 30 days, and 8% within 31 to 90 days.
- With the 1- to 4-day group as referent, recovery within 5 to 10, 11 to 30, and 31 to 90 days was associated with increased rates of a sustained 40% decline in estimated glomerular filtration rate during the 90-day recovery period or kidney failure.

CONFERENCE COVERAGE KIDNEY WEEK 2019

Verinurad Combination Therapy Reduces Albuminuria in Type 2 Diabetes

Washington, DC–One of the earliest indicators of kidney disease is new-onset albuminuria, which is predicted by an elevation in serum uric acid. **Austin G. Stack, MBBCh, MD, MSc, FASN FRCP,** and colleagues conducted a study designed to examine the effects of intensive lowering of uric acid on albuminuria by combining verinurad with febuxostat in patients with type 2 diabetes mellitus and albuminuria. Results of the study were reported during a presentation at Kidney Week 2019. The oral session presentation was titled *Verinurad Plus Febuxostat Rapidly Reduces Albuminuria in Type 2 Diabetes Independent of Preexisting Kidney Disease*.

The phase 2, parallel group, multicenter, randomized, double-blind, placebo-controlled trial included adults with type 2 diabetes, albuminuria, and hyperuricemia. Participants were randomized to verinurad 9 mg plus febuxostat 80 mg once daily, or placebo, and were followed for 24 weeks. The primary outcome of interest was a reduction in urinary albumin to creatinine ratio (UACR) at 12 weeks compared with baseline. Changes in UACR were calculated according to baseline characteristics, including UACR and estimated glomerular filtration rate (eGFR).

In the verinurad plus febuxostat group, baseline UACR was 459 mg/g (n=32), compared with 412 mg/g in the placebo group (n=28). In the verinurad plus febuxostat group, there was rapid and sustained improvement in UACR; the improvement met prespecified criteria for statistical significance. At weeks 1, 12, and 24, the reductions versus placebo were 39%, 39%, and 49% (week 12, 90% confidence interval, -62% to -4%; *P*=.0747). The reduction in UACR was consistent across subgroups, including those based on UACR and eGFR. Verinurad plus febuxostat was well tolerated.

In conclusion, the researchers said, "Intensive urate lowering with verinurad plus febuxostat significantly reduced UACR in patients with type 2 diabetes mellitus, albuminuria, and hyperuricemia. Reduction was rapid, sustained, and similar regardless of baseline eGFR and degree of albuminuria. A larger study is underway to determine which patient groups might benefit most from verinurad combination therapy."

Source: Stack AG, Dronamraju N, Parkinson J, et al. Verinurad plus febuxostat rapidly reduces albuminuria in type 2 diabetes independent of preexisting kidney disease. Abstract of an oral presentation at the American Society of Nephrology Kidney Week 2019 (Abstract SA-OR086), November 9, 2019, Washington, DC.

Funding for this study was provided by AstraZeneca.

Conservative Care Management

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colleagues recently conducted a qualitative study to gain a clearer understanding of emerging approaches to conservative care in the United States. The study population included US nephrologists with experience caring for patients with advanced CKD who had elected to forgo dialysis. Results of the study were reported in the *American Journal of Kidney Diseases* [2020;75(2):167-176].

The study used grounded theory methods; data collection and analysis occurred simultaneously and the concepts that emerged during the analysis were developed and refined to collect subsequent data that elaborated on the concepts. The researchers employed a purposive snowball sampling strategy that enabled the targeted recruitment of nephrologists in the United States with experience caring for patients with advanced CKD who decided not to initiate dialysis. Nephrologists were recruited from a range of geographic regions, practice settings, and educational backgrounds.

Participating nephrologists completed a survey that included questions on demographic characteristics and clinical practice. Following completion of the survey, participants were interviewed, either in-person or via telephone, by one of the researchers; the interviews were conducted between November 2017 and June 2018. The interviews used a semi-structured interview guide that was designed to elicit information regarding the nephrologist's approach to, experiences with, and perspectives on caring for patients with progressive advanced CKD who had chosen not to receive dialysis treatment.

Of the 31 nephrologists approached, 21 provided informed consent and participated in a semi-structured interview. The mean interview duration was 55.0 minutes. The participating nephrologists practiced in 16 different states and had been in practice for a mean of 20.2 years. Fourteen of the 21 worked in academic settings and 15 reported working in an urban area. Patients who opted to forgo dialysis were managed with ancillary services to varying degrees; services used included primary care, home health, social work, nutrition, palliative care and/or hospice, and chaplaincy.

Qualitative analysis of the interviews yielded two dominant and inter-related themes related to the nephrologists' approached to conservative care: (1) a person-centered approach to care, and (2) improvising a care infrastructure.

The person-centered approach included orienting decisions to the things that mattered most to each patient, describing dialysis as an explicit treatment choice, being mindful of sources of bias in medical decision-making, and being flexible in accommodating patients' changing needs, values, and preferences.

The participating nephrologists viewed decisions regarding dialysis within a broader context of patient goals and values rather than based on conventional biomarkers of kidney disease. The clinicians mentioned engaging patients in building a relationship and getting to know them as "people." The clinicians used what they learned through those conversations to help inform discussions about treatment options. They focused on supporting patient choices in the decision-making process, and looked to the patient to determine what was most important in formulating a treatment plan.

The clinicians stressed the importance of presenting dialysis as an explicit treatment choice, including informing the patient about both the harms and benefits of treatment, as well as ensuring that the patient was aware that dialysis could be declined. Various strategies for raising the option of forgoing dialysis were cited. Some clinicians presented the opt-out option routinely along with other options; others were more selective, and only mentioned opting out with select patients based on a sense of who might benefit from a conservative management approach.

The participating nephrologists described the need to improvise a care infrastructure that recognized the challenges of conservative care management within health systems not configured to support that model. All of the clinicians reported being committed to caring for patients for the duration of their illness and noted it was important not to abandon patients because they had opted not to receive dialysis.

In citing limitations to the current study, the researchers noted that the nephrologists interviewed did not comprise a representative sample of US nephrologists and likely did not reflect practices of the wider nephrology community; further, the results are based on self-reported practices.

The researchers said, "In conclusion, interviews conducted with a select group of US nephrologists who are early adapters of conservative care suggest that far-reaching cultural, practice, and infrastructural changes would be needed to support more widespread delivery of conservative care in this country and the diverse needs and changing goals of US patients with advanced CKD." ■

TAKEAWAY POINTS

- Researchers conducted a qualitative study to examine practice approaches of nephrologists who provide conservative care for patients with advanced chronic kidney disease (CKD).
- Semi-structured interviews with 21 nephrologists yielded two themes for delivery of conservative care: (1) person-centered practices; and (2) improvisation of a care infrastructure for this patient population.
- Managing patients with advanced CKD who opt to forgo dialysis presents a challenge within healthcare systems that are not configured to support those patients.

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Sodium Bicarbonate Therapy in Patients with CKD Stages 3 and 4

More than 16 million individuals in the United States are affected by chronic kidney disease (CKD). CKD is associated with numerous comorbidities as well as an increased risk for mortality. There are limited treatments known to slow or stop the progression of CKD.

Metabolic acidosis is a known complication of kidney disease; it is unclear whether metabolic acidosis causes further kidney damage. Results of previous observational studies have suggested an association between lower levels of bicarbonate and faster progression of kidney disease. Further, poor outcomes have been seen in patients with acid retention, even in the absence of overt metabolic acidosis. Results of several small randomized studies cited benefits of alkali therapy in progression of CKD.

Bone and muscles may also be affected in patients with CKD and chronic metabolic acidosis; muscle dysfunction and bone disease may be associated with metabolic acidosis in patients with CKD. **Michal L. Melamed, MD, MHS,** and colleagues recently conducted a multicenter, randomized, placebo-controlled clinical trial designed to examine whether treatment with sodium bicarbonate improves muscle and bone outcomes. Results of the trial were reported in the *American Journal of Kidney Disease* [2020;75(2):225-234].

Of 283 patients assessed for study eligibility, 149 met inclusion criteria and were randomly assigned to either sodium bicarbonate 0.4 mEq per kg of ideal body weight per day n=74) or identical appearing placebo (n=75). The dual primary outcomes of interest were muscle function assessed using sit-to-stand test and bone mineral density. Muscle biopsies were conducted at baseline and 2 months. Participants were seen at baseline and 2, 6, 12, and 24 months.

Mean age of the study cohort was 61 years, 54% were women, 58% were non-Hispanic blacks, 27% were non-Hispanic whites, and 13% were Hispanics. At baseline, 93% of participants had hypertension and 62% had diabetes mellitus. Mean baseline serum bicarbonate level was 24.0 mEq/L and mean baseline estimated glomerular filtration rate (eGFR) was 36.3 mL/min/1.73 m^2. There were no statistically significant differences in baseline characteristics between the intervention group and the placebo group.

Mean follow up was 1.35 years; there was no difference between the two study arms in mean follow-up time (1.29 years for intervention arm vs 1.42 for placebo arm). In the placebo arm, follow-up represented 106 person-years and in the intervention arm, follow-up represented 92 person-years on sodium bicarbonate treatment. During the course of the study, a total of 45 participants dropped out.

At baseline, serum bicarbonate levels were similar between the two arms. Subsequently, levels in participants in the sodium bicarbonate treatment arm increased significantly (*P*<.001).

At baseline, serum bicarbonate levels were similar between the two arms. Subsequently, levels in participants in the sodium bicarbonate treatment arm increased significantly (*P*<.001). At 2, 6, 12, and 24 months, mean serum bicarbonate levels in the intervention arm were 26.4, 25.5, 25.6, and 24.4 mEq/L. In the intervention arm, 44 participants achieved a >3 mEq/l increase in serum bicarbonate level at any follow-up time compared with 20 participants in the placebo arm (*P*<.001). Sodium bicarbonate treatment caused a decrease in serum potassium levels by ~0.1 mEq/L compared with placebo; this difference had borderline statistical significance (*P*=.05). There were no differences in eGFR between the two arms.

Participants in the intervention arm had similar bone density at 24 months compared with those in the placebo arm. In both groups, bone density at 24 months decreased from baseline (*P*=.03). The two groups were also similar in hand grip strength; over time, hand grip strength decreased in the placebo group and increase slightly in the intervention arm, but the difference was not statistically significant. During follow-up, sit-to-stand times decreased in both arms (*P*<.001), but there was no difference in rate of change. The two groups were similar in weight, blood pressure, physical function, physical composite score, or any other quality-of-life measurements.

A total of 12 participants underwent muscle biopsy (five in the intervention arm and seven in the placebo arm). Between baseline and the 2-month muscle biopsy, the median change in serum bicarbonate levels was +1 mEq/L in the intervention arm and –1 mEq/L in the placebo arm. There were no significant effects of sodium bicarbonate supplementation on insulin signaling (based on Western blotting of phosphorylated protein kinase B [Akt] and total Akt), an indicator of muscle protein breakdown, proteolysis mediators, or markers of inflammation.

There were no statistically significant differences between the two arms in the number of serious adverse events. During the course of the study, 14 patients in the intervention arm had a potassium level >5.0 mEq/L compared with 30 in the placebo arm (*P*=.006; odds ratio, 0.35; 95% confidence interval, 0.17-0.74). Participants in the sodium bicarbonate group experienced slightly more total adverse events compared with participants in the placebo arm (45% vs 32%, respectively). There were no other differences in adverse events.

The researchers cited some limitations to the study, including the inability to evaluate kidney function outcomes, the greater than expected number of participants who dropped out during the study, and the bicarbonate levels of the two groups not achieving consistently large separation during the 24-month study period. The participants also had fairly normal serum bicarbonate levels at baseline, possibly limiting the effect of the intervention.

In conclusion, the researchers said, "In this multicenter randomized placebo-controlled trial of sodium bicarbonate in participants with CKD stages 3 and 4, there was no significant difference between the randomly assigned groups in muscle function, as measured using sit-to-stand test, or bone mineral density. Although not powered for the outcome, there were no differences in kidney function over the 2 years. A larger randomized clinical trial of sodium bicarbonate therapy, possible with a larger dose of sodium bicarbonate, is required to evaluate whether treatment with sodium bicarbonate is beneficial for kidney function." ■

TAKEAWAY POINTS

- Results of a randomized, placebo-controlled clinical trial to determine whether treatment with sodium bicarbonate improves muscle and bone outcomes in patients with chronic kidney disease stages 3 and 4.
- Participants were randomized to either sodium bicarbonate 0.4 mEq/L per kg of ideal body weight per day (intervention arm) or placebo.
- During 24 months of follow-up, mean sodium bicarbonate levels in the intervention arm were significantly higher than in the placebo arm (*P*<.001).

Study Examines Prevalence of Arrhythmias in Patients on Maintenance Dialysis

The management of patients with kidney failure on maintenance dialysis is complicated by the high rate of cardiovascular disease in that patient population. Cardiovascular disease is the leading cause of death and sudden cardiac death, caused primarily by arrhythmias, and is the source of nearly 30% of all-cause mortality in dialysis patients. Arrhythmias are recognized as important in the management of dialysis patients, yet there are limited data available regarding the prevalence of both nonsevere and clinically significant arrhythmias in these patients.

Earlier studies have been conducted in selected populations of small patient groups, resulting in a large variation in reported prevalence of arrhythmias in patients on maintenance dialysis. **Jesper Moesgaard Rantanen, MD, PhD,** and colleagues recently conducted a cross-sectional study designed to add to existing knowledge by analyses of the prevalence of nonsevere and clinically significant arrhythmias in an unselected contemporary cohort of maintenance dialysis patients. The researchers also sought to describe the pattern of arrhythmic events in relation to the dialysis session and identify clinical characteristics and echocardiographic findings associated with arrhythmias. Study results were reported in the *American Journal of Kidney Diseases* [2020;75(2):214-224].

The study included 152 patients with kidney failure who were treated at Aalborg University Hospital in Denmark from October 2013 to November 2015. Inclusion criteria were ≥18 years of age, and receiving either in-center hemodialysis, home hemodialysis, or peritoneal dialysis for >3 months. Exclusion criteria included inability to give informed consent.

The outcomes of interest were the prevalence and pattern of arrhythmias on 48-hour Holter monitoring and the odds ratios for arrhythmias. Arrhythmia was defined as paroxysmal atrial fibrillation (AF), AF for longer than 30 seconds and not the entire recording; permanent AF, AF for the entire recording; supraventricular tachycardia (SVT), 5 or more ectopic supraventricular beats and heart rate >100 beats/min and not AF; bradycardia, heart rate ≤40 beats per minute for four or more beats; and nonsustained ventricular tachycardia, three or more ventricular beats with heart rate ≥100 beats per minute.

Of the 252 patients on maintenance dialysis screened, 26 did not meet eligibility criteria, 48 declined participation, and nine could not be examined due to concurrent diseases, resulting in a study cohort of 169 patients. Of those patients, six with pacemakers and 11 with incomplete recordings were excluded, resulting in a final cohort of 152 patients eligible for analysis. Mean age was 62.2 years, 67.8% were men, and 97.4% were white. The causes of kidney failure included diabetes (25.0%); glomerulonephritis (17.8%); obstructive nephropathy, reflux nephropathy, or chronic pyelonephritis (15.1%); autosomal dominant polycystic kidney disease (11.2%); hypertension or ischemic nephropathy (9.2%); chronic interstitial nephropathy (5.9%); and other or unknown causes (15.8%).

Forty-two patients (25%) had a medical history of palpitations at baseline; during the recordings, only five patients (3.3%) noticed palpitations. Only one of those cases was due to a clinically significant arrhythmia (AF with a high ventricular rate). In addition, during the recording, only five patients (3.3%) experienced chest pain; two patients (1.3%) experienced syncope; and five (3.3%) experienced symptomatic intradialytic hypotension. None of the episodes were accompanied or caused by clinically significant arrhythmias.

Nearly all patients had premature atrial complexes (PACs) and premature ventricular complexes (PVCs). Among patients receiving in-center hemodialysis, the median number of PVCs was higher and more patients experienced frequent PVCs and episodes of ventricular bigeminy or trigeminy on dialysis day (day 1) compared with nondialysis day (day 2). Complex ventricular arrhythmias were seen in 119 patients (78.3%). Forty-one percent had paroxysmal SVT; SVT was more common on dialysis day compared with nondialysis day among the patients receiving in-center hemodialysis. With the exception of one, all episodes were classified as ectopic atrial tachycardia and generally were of short duration with a median of eight beats and a mean heart rate of 136 beats per minute.

Nearly all patients had premature atrial complexes (PACs) and premature ventricular complexes (PVCs).

Clinically significant arrhythmias included persistent AF (8.6% of patients), paroxysmal AF (3.9%), nonsustained ventricular tachycardia (19.7%), bradycardia (4.6%), advanced second-degree atrioventricular block (1.3%), and third-degree atrioventricular block (2.6%). Patients more commonly experienced premature ventricular complexes on dialysis days; tachyarrhythmias were more common during dialysis and in the immediate postdialytic period.

There were independent associations between older age (odds ratio [OR] per 10 years older, 1.53; 95% confidence interval [CI], 1.15-2.03; *P*=.003), elevated preload (OR, 4.02; 95% CI, 1.05-15.35; *P*=.04), and lower cardiac output (OR per 1 L/min greater, 0.66; 95% CI, 0.44-1.00; *P*=.05) and clinically significant arrhythmias.

There were some limitations to the findings cited by the authors, including limiting monitoring of arrhythmias to 48 hours, the small sample size, the heterogeneous nature of the study population, and the risk for residual confounding.

"In conclusion," the researchers said, "patients receiving maintenance dialysis had a high prevalence of both nonsevere and clinically significant arrhythmias. PVCs were more common on dialysis day and tachyarrhythmias were more frequent during dialysis and the immediate postdialytic period. Several variables were associated with arrhythmias, but further studies are warranted to increase the understanding of these associations and clarify the extent to which arrhythmias predict outcomes in this high-risk population." ■

TAKEAWAY POINTS

- Researchers in Denmark conducted a cross-sectional study to examine the prevalence of arrhythmias and the associated clinical characteristics among patients on maintenance dialysis.
- Nearly all of the 152 patients in the study had premature atrial and ventricular complexes and 41% had paroxysmal supraventricular tachycardia.
- Tachyarrhythmias were more frequent during dialysis and in the immediate postdialytic period.

Variations by Race/Ethnicity in Risk of Death in Dialysis Patients in US Territories and US 50 States

Chronic kidney disease (CKD) is a major contributor to premature morbidity and mortality. There are variations in the estimated prevalence of CKD by racial and/or ethnic (racial/ethnic) group and by geographic location. Previous studies have identified ethnic subgroup differences for Hispanics, with a nearly two-fold difference across individuals of Cuban (12%), Mexican (13%), Puerto Rican (17%), and South American (8%) backgrounds. In the United States, racial/ethnic minorities are more likely to develop end-stage renal disease (ESRD) than nonminority groups, and are often treated with maintenance dialysis.

There are numerous data on the incidence of CKD and ESRD in the United States; however, data regarding kidney disease in United States territories are limited. The US Renal Data System (USRDS) focuses primarily on individuals in the 50 states. There are five US territories: Puerto Rico, the US Virgin Islands, Guam, the Northern Mariana Islands, and American Samoa.

The proportions of diabetes-related ESRD are high in those territories. There are few available data on mortality outcomes of patients undergoing dialysis in the territories. To test the hypothesis that mortality outcomes for patients in the territories may differ from those in the 50 states, **Guofen Yan, PhD,** and colleagues conducted a national population study to examine all-cause mortality by racial/ethnic group among patients with ESRD treated with dialysis in the US territories compared with patients treated in the 50 states. Results were reported in the *Clinical Journal of the American Society of Nephrology* [2020;15:101-108].

The outcomes of interest were mortality differences between patients undergoing dialysis in the US territories and those in the 50 states in the same racial/ethnic group.

The researchers used the USRDS Core Standard Analysis Files to identify all patients ≥18 years of age with no prior kidney transplantation who initiated maintenance dialysis between April 1, 1995, and September 28, 2012. Exclusion criteria were missing body mass index data and missing data on estimated glomerular filtration rate.

The final analysis cohort consisted of 1,547,438 patients, including 22,828 patients in the four territories (295 in American Samoa, 1507 in Guam [including the Northern Mariana Islands], 20,289 in Puerto Rico, 737 in the Virgin Islands) and 1,524,610 nonterritory patients (50 states).

Of those in the 50 states, 55% (n=838,736) were white, 29% (n=444,066) were black, 12% (n=182,994) were Hispanic, and 4% (n=58,814) were Asian. Of the 22,828 patients in the territories, 1% (n=321) were white, 3% (n=666) were black, 89% (n=20,299) were Hispanic, and 7% (n=1542) were Asian.

On average, white and Asian patients in the territories were 7 years and 4 years younger, respectively, compared with their counterparts in the 50 states; black and Hispanic patients in the territories were an average of 2 years older than their counterparts in the 50 states. The patients in the territory cohort had a higher prevalence of diabetes-related ESRD (64% vs 45%) and were less likely to have pre-ESRD erythropoietin use (20% vs 27%), a nephrology visit prior to dialysis initiation (50% vs 58%), or use of an arteriovenous fistula (10% vs 14%).

Average BMIs were similar among white, black, and Hispanic groups in both cohorts; Asians in the territories had higher BMIs compared with Asians in the 50 states (28 vs 25 kg/m^2). There were also some patient characteristics that varied across the four territories; Samoans tended to have higher BMIs and Puerto Ricans were more likely to have received predialysis erythropoietin compared with those in the other territories, for example.

Median follow-up time for the territory group was 23 months; for the 50 states median follow-up was 25 months. In the territories, white patients undergoing dialysis had a much lower crude mortality rate compared with their counterparts in the 50 states (14 vs 29 deaths per 100 patient-years). Mortality rates among black patients were similar: 18 per 100 patient-years in the territories versus 17 per 100 patient-years in the 50 states. In contrast, mortality rates among Hispanics in the territories were much higher than among their counterparts in the 50 states: 27 versus 16 per 100 patient-years (27 deaths per 100 patient-years for Puerto Rican Hispanics alone and 24 deaths per 100 patient-years for Virgin Island Hispanics alone). The mortality rate in the territories among Asians was also higher than among their counterparts in the 50 states.

In both the territories and the 50 states groups, the major cause of death was cardiovascular disease. Regardless of race and ethnicity, the percentages of death from infection were consistently greater in the territories than in the 50 states.

Following adjustment for demographic and clinical characteristics, the mortality risk for white patients in the territories remained lower than that among white patients in the 50 states (hazard ratio [HR], 0.75; 95% confidence interval [CI], 0.65-0.86; $P<.001$); there was no difference in the mortality risk between the two groups for black patients (HR, 1.04; 95% CI, 0.94-1.15; $P=.45$). In contrast, the risks for death among Hispanic and Asian patients in the territories remained higher (HR, 1.61; 95% CI, 1.58-1.63; $P<.001$ and HR, 1.95; 95% CI, 1.82-2.08; $P<.001$, respectively).

Limitations to the findings cited by the authors included differences in payer mix and structure in the territories and the 50 states, the lack of data to identify specific Hispanic and Asian subgroups in the USRDS, the relatively low number of dialysis patients in most of the territories other than Puerto Rico, and not including data from 2013-2016.

In summary, the researchers said, "To our knowledge, this study is the first to document important differences in dialysis mortality for various racial/ethnic groups in the territories versus the 50 states. We found notable higher mortality rates for Hispanic and Asian patients undergoing dialysis in the territories than their counterparts in the 50 states. Mortality risk did not appear to differ between the territories and the 50 states for whites or blacks. Further studies are needed to better understand the influence of issues such as genetic factors, insurance coverage, health infrastructure, health beliefs and behaviors, social networks, and other subtleties in the United States territories that may add critical insights to our observations." ■

TAKEAWAY POINTS

- Researchers conducted a retrospective cohort study to examine all-cause mortality by racial/ethnic group among dialysis patients in the United States territories versus dialysis patients in the 50 states.
- The crude mortality rate (deaths per 100 patient-years) was lower for white patients in the territories versus the 50 states (14 and 29, respectively) and similar for black patients (18 and 17, respectively).
- The crude mortality rate was higher for Hispanic and Asian patients in the territories than in the 50 states (27 and 16 per 100 patient-years, respectively, and 22 and 15 per 100 patient-years, respectively).

CKD Severity Is Associated with Likelihood of Vitamin D and Balance Deficits

Approximately 15% of the US population is affected by chronic kidney disease (CKD), creating a significant and costly health problem. In 2014, 118,000 individuals with end-stage renal disease (ESRD) initiated dialysis and 662,000 individuals were receiving chronic dialysis or had undergone kidney transplantation.

The risk of fracture is increased in patients with ESRD. Treatment of fractures in this patient population contributes to the total cost of care. Patients with CKD are at increased risk of fracture at all stages of disease, but the risk is exacerbated with disease progression, with the highest incidence among patients with ESRD receiving maintenance dialysis. Mortality and morbidity rates are high after fracture; a recent study found a 1-year mortality rate of 64% following hip fracture. Risk factors for fracture in these patients include older age, female sex, Caucasian ethnicity, and lower body mass index. Due to its effects on bone and balance, low vitamin D status may also be a contributing factor to the increased risk of fracture.

Fractures typically occur after a fall in this patient population; there is a correlation between increased rate of falls and increased risk of fracture. The relative risk of falls in patients at all stages of CKD is four to five times higher than that in the general population. In addition to fracture, falls are associated with head injury, wounds, and an enhanced fear of falling, leading to subsequent inactivity.

Vitamin D deficiency, measured by 25(OH)D, is estimated to be as high as 70% to 90% in the dialysis population. A meta-analysis suggested that vitamin D supplementation results in a decrease of 14% in the risk of falls in the general elderly population. Supplementation also improved gait speed in individuals >70 years of age.

Jordan F. Wickstrom, MS, and colleagues, recently conducted a study designed to examine data from the 1999-2004 National Health and Nutrition Examination Study (NHANES) to assess the prevalence of balance deficits and describe the relationships between stage and severity of CKD and vitamin D status, self-reported balance and falling problems, and measured gait speed in the CKD sample. Results of the study were reported in the *Journal of Renal Nutrition* [29(6):490-497].

The primary outcome measures were measured 25(OH)D levels, timed 20-feet walk, Romberg standing balance task, and self-reported balance and falling issues. The study included 8554 subjects >40 years of age. Participants were categorized into CKD stages based on glomerular filtration rate; participants with normal kidney function and CKD stages 1 and 2 served as the control group, those with CKD stages 3 and 4/5 served as the CKD groups.

In the Romberg standing balance test, following adjustment for age, in the measure when standing on a firm surface with eyes open, failure rates increased with severity of kidney disease: those in the control group failed 0% of the time, those in the CKD stage 3 a/b group failed 1% of the time, and those in the CKD stage 4/5 group failed 3% of the time. Compared with the 0% failure rate in the control group, the 3% failure rate in the stage 4/5 group was a significant increase (P=.02). In the most difficult measure (standing on a foam surface with eyes closed), the rates of failure again increased with severity of kidney disease: the control group failed 54% of the time, the CKD stage 3 a/b group failed 76% of the time, and the CKD stage 4/5 group failed 85% of the time. The stage 4/5 group has a statistically significant increased fail rate compared with that of the control group (P=.02).

The amount of time to complete the walking test increased with kidney disease severity, indicating slower gait speed. The mean times to complete the 20-feet walk for the control group, the CKD stage 3 a/b group, and the CKD stage 4/5 groups were 6.8 seconds, 8.3 seconds, and 9.8 seconds, respectively. The stage 4/5 mean time was significantly longer than the mean time for the control group and for the stage 3 a/b group (P<.001 for both). The stage 3 a/b group took significantly longer than the control group to complete the walk (P=.003).

Compared with controls, the odds of self-reporting of dizziness, difficulty in balance, or difficulty with falling in the past year were higher in the stage 3 a/b group (odds ratio [OR], 1.54; 95% confidence interval [CI], 1.29-1.83) and the stage 4/5 group (OR, 2.07; 95% CI, 1.26-3.40). The ORs in older subjects versus younger subjects were 1.02 (95% CI, 1.01-1.03); in females versus males, 1.73 (95% CI, 1.52-1.98); in former smokers versus never smokers, 1.35 (95% CI, 1.17-1.56); in current smokers versus never smokers, 1.53 (95% CI, 1.28-1.82); in those with lower levels of 25(OH)D versus higher levels, 0.99 (95% CI, 0.98-1.00); and in those with lower levels of albumin versus higher levels, 0.79 (95% CI, 0.65-0.98).

The amount of time to complete the walking test increased with kidney disease severity, indicating slower gait speed.

Increased odds of taking longer than 8 seconds to complete the 20-feet walk were seen in the stage 4/5 group (OR, 3.39 vs controls); older subjects (OR, 1.12 vs younger subjects); females (OR, 1.35 vs males); those with lower levels of 25(OH)D (OR, 0.97 vs those with higher levels); and those with lower levels of albumin (OR, 0.38 vs those with higher levels).

Study limitations cited by the authors included utilizing cross-sectional data resulting in a limited scope in examining the relationships between CKD severity and impairments in 25(OH)D levels, balance, and gait speed; using subjective measures to test balance and falling problems; and the possibility that patients receiving dialysis were included in the analysis.

In conclusion, the researchers said, "The unique finding of this study is that the likelihood of reporting more balance and falling issues (both perceived and measured) and having slower gait is higher in persons with increased CKD severity and those with lower 25(OH)D levels. Patients with moderate-to-severe CKD may benefit from screening and treatment of both balance and vitamin D status." ■

TAKEAWAY POINTS

- Patients with chronic kidney disease (CKD) face a high risk of fracture at every stage of their disease; the risk is exacerbated with disease progression, with the highest incidence rates in those with end-stage renal disease on dialysis.
- Researchers conducted an analysis of 1999-2004 NHANES data to examine the prevalence of balance deficits and the relationships between severity of CKD and vitamin D status, self-reported balance and falling issues, and measured gait speed in the CKD sample.
- The likelihood of more reporting of balance and falling issues (both perceived and measured) and having slower gait was higher in those with increased severity of CKD and in those with lower 25(OH)D levels.

Receipt of a Kidney from a Deceased Donor with AKI and Subsequent Graft Survival

The shortage of deceased donor kidneys continues to be a concern, and is associated with increased length of time on the waiting list for transplant. The shortage accounts for the recent increase in the use of kidneys with certain risk factors such as age of donor or donors with HIV or hepatitis C. There were approximately 95,000 patients with end-stage renal disease who cleared medical evaluation on the transplant waiting list as of October 2019. Each year, there are approximately 9000 patients removed from the waiting list, due to death or deteriorating health, suggesting the continuation of the organ shortage despite the increased use of high-risk donors.

One of the stated goals of the 2019 Advancing Kidney Health initiative is to increase the number of kidneys available for transplant and to "double the number of kidneys available for transplant by 2030." According to **Caroline Liu, MHS,** and colleagues, achievement of that goal may "require substantial changes to the organ procurement system."

The researchers conducted a registry-based, propensity score-matched cohort study to examine the association of deceased donor acute kidney injury (AKI) with recipient graft survival; they also sought to characterize recovery and discard practices for AKI kidneys by organ procurement organizations. Results were reported in *JAMA Network Open* [2020;3(1) e1918634].

The study was conducted from January 1, 2010, to December 31, 2013. The analyses were conducted from March 1 to November 1, 2019. From 2010 to 2013, a total of 6832 deceased donors with AKI and 15,310 deceased donors without AKI had at least one kidney transplanted. A 1:1 propensity score-matched analysis was used to match deceased donors with AKI to deceased donors without AKI and investigate outcomes in their corresponding kidney recipients.

The study utilized data from DonorNet from the Organ Procurement and Transplantation Network; the network registers deceased donors and communicates organ offers. The main outcome of interest was time to death-censored graft failure; secondary

CONFERENCE COVERAGE KIDNEY WEEK 2019

Predictive Value of Functional and Nutrition Status in Older Transplant Candidates

Washington, DC–Outcomes following kidney transplantation may be predicted by measures of functional and nutrition status at the time of the transplantation. There is no gold standard tool to optimally assess functional status. In older kidney transplant candidates, assessment of physiological reserve is particularly important, due to the possibility of the presence of additional risk factors such as malnutrition.

During a poster session at Kidney Week 2019, **Olivia A. Moss, MS, RD,** and colleagues at UC Davis Health, Sacramento, California, reported results of a study designed to identify the functional and nutrition status measures predictive of ineligibility for kidney transplant listing. The poster was titled *Evaluation of Functional and Nutrition Status in the Older Transplant Candidate*.

Patients >65 years of age who were evaluated for kidney transplant were recruited for the study. Participants completed the short physical performance battery (SPPB) and the Fried Frailty assessment (FFA). Standardized malnutrition criteria were used to assess nutrition status. Patients charts were reviewed to ascertain kidney transplant listing status (ineligible or listed). ANOVA, Chi-square and logistic regression analyses were used to test differences between the two groups in SPPB, FFA, nutrition status, and the components of each assessment.

Of the 105 participants enrolled, 73 had complete follow-up data at the time of the analysis. Scores for the SPPB and the FFA did not predict ineligibility or kidney transplant listing. However, slower chair stand time and slower walk time were predictive of kidney transplant ineligibility.

Participants in the ineligible group tended to report lower levels of physical activity, have lower handgrip strength, and were malnourished, compared with those who were listed for transplant. This difference did not reach statistical significance.

"Objective measures like walk and chair stand time may be more predictive of kidney transplant ineligibility than SPPB and FFA when used at the time of kidney transplant candidacy evaluation, but further investigations are needed," the researchers said.

Source: Moss OA, Friedman GG, Yerraguntala AS, Sockolov M, Chen L-X. Evaluation of functional and nutrition status in the older transplant candidate. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2019 (Abstract TH-P01135), November 7, 2019, Washington, DC.

outcomes included delayed graft function, primary nonfunction, and the time to all-cause graft failure.

Of the 6382 deceased donors with AKI, 98% (n=6722) were matched to deceased donors without AKI (total deceased donors=13,444). Mean age of the total cohort was 40.4 years and 63% (n=8259) were male. The analysis included 25,323 recipients; of those, 61% (n=15,485) were male and mean age was 52.0 years. Follow-up of recipients was a median of 5 years.

ents: 4.77 years for no AKI, 4.82 years for stage 1 AKI, 4.76 years for stage 2 AKI, and 4.77 years for stage 3 AKI. Duration of follow-up, sex of recipient, black race, and human leukocyte antigen mismatch level were comparable by deceased donor AKI status. Recipients of deceased donors with AKI were marginally older, experienced increased time on the wait list, were more likely to have undergone prior transplants, and had longer duration of ESRD. Kidneys from deceased donors with AKI were more

The incidence of death-censored graft failure was comparable by deceased donor AKI status. When examined by AKI stage, there was no substantial risk of death-censored graft failure.

There were insubstantial differences in deceased donor characteristics, consistent with the propensity score-match analysis. There were no meaningful differences in deceased donor characteristics of the propensity score-matched cohort and the entire study cohort. Deceased donors with and without AKI were balanced at baseline in age, body mass index, and admission serum creatinine level.

Sixty-nine percent of the 6772 deceased donors with AKI (n=4621) had stage 1, followed by 21% (n=1409) with stage 2, and 10% (n=692) with stage 3 AKI. Deceased donors without AKI were more likely to have both kidneys transplanted compared with deceased donors with AKI (91% [6088/6722] vs 86% [5792/6722]).

Regardless of deceased donor AKI status, follow-up time was similar among recipi-

often biopsied and/or pumped prior to transplant and had longer cold ischemia times. Biopsy and pumping was more likely in kidneys from deceased donors with stage 3 AKI compared with kidneys from deceased donors without AKI or deceased donors with lesser stages of AKI.

Among 12,513 recipients of kidneys from deceased donors, 29% (n=3643) developed delayed graft failure compared with 22% (2779/12,810) of recipients of kidneys from deceased donors without AKI (relative risk, 1.34; 95% confidence interval, 1.28-1.41; $P<.001$). Increasing stage of deceased donor AKI was associated with higher incidence of delayed graft function: stage 1, 25% (2157/8627); stage 2, 32% (838/2613); and stage 3, 51% (648/1273). Regardless of CKI stage, few recipients developed primary nonfunction.

The incidence of death-censored graft failure was comparable by deceased donor AKI status. When examined by AKI stage, there was no substantial risk of death-censored graft failure. There was also no difference in the incidence of all-cause graft failure by deceased donor AKI status; the results were consistent when analyzed by AKI stage.

During the study period, 85% of kidneys (17,468/20,550) from deceased donors were recovered; 12,711 kidneys from deceased donors were transplanted. A total of 3030 kidneys from deceased donors with AKI were never procured, and 4757 of 17,468 (27%) were discarded following recovery. Median proportions of recovery and subsequent discard were 87.7% and 26.1%, respectively. Rates of recovery and transplantation of AKI kidneys varied by organ procurement organization; most (39/58) had high recovery and high discard of AKI kidneys.

Limitations to the study cited by the authors included the results not representing the true strength of a randomized clinical trial, the lack of data regarding posttransplant kidney function beyond 6 months, and the calculations for recovery and discard only capturing data associated with AKI status.

In conclusion, the researchers said, "This study found that the AKI kidneys transplanted in the United States from 2010 to 2013 had comparable rates of recipient graft survival, even among the highest stages of injury. There was organ procurement organization-level variation in the allocation of practices of AKI kidneys. From our study's findings, we believe that the transplant community should continue to use deceased donor AKI kidneys and consider research to investigate whether currently discarded AKI kidneys from deceased donors without substantial comorbidities can be used more effectively." ■

TAKEAWAY POINTS

- Researchers conducted a registry-based, propensity score-matched cohort study to examine the association between transplant of kidneys from deceased donors with acute kidney injury (AKI) and recipient graft survival.
- There was no association between deceased donor AKI status and death-censored graft failure; this finding remained consistent after analysis by AKI stage and adjustment for recipient and transplant characteristics.
- There was a higher incidence of delayed graft function among recipients of kidneys from deceased donors with AKI; few recipients developed primary nonfunction regardless of deceased donor AKI status.

CONFERENCE COVERAGE KIDNEY WEEK 2019

Evaluation Process for Transplant Can Be Burdensome

Washington, DC–Increasing access to kidney transplant for patients with advanced kidney disease has strong public and professional support. Nevertheless, more liberal practices for referral for kidney transplantation may increase the number of patients who are evaluated for transplant but do not receive a kidney. Shared decision making about transplant referral would be supported with a deeper understanding of the implications of being referred for transplant evaluation but not receiving a kidney.

Catherine Butler and colleagues conducted a qualitative analysis of adults referred to a transplant coordinator with no receipt of a kidney. Results of the analysis were reported during a poster session at Kidney Week 2019 in a poster titled *Care Practices for Patients with Advanced Kidney Disease Who Were Evaluated for Transplant but Did Not Receive a Kidney*.

The analysis utilized data from the electronic medical record (EMR) for 148 patients with advanced kidney disease who were referred to the Veterans Affairs Puget Sound Health Care System's transplant coordinator from 2008 to 2018 who did not subsequently receive a kidney during the follow-up period. Patients were followed to their death date or January 1, 2018. The researchers conducted an inductive content analysis to determine dominant emergent themes related to transplant evaluation.

At the end of follow-up, 71% of the 209 adults evaluated for transplant during the study period had not received a kidney (n=148/209). Analysis of the EMR for this subset of patients revealed three dominate themes: (1) sources of forward momentum in the process of transplant evaluation; patients were commonly referred for transplant evaluation reflexively and the tendency was for the evaluation process to move forward until identification of an absolute contraindication or the patient passively withdrew; (2) the potential for transplant informs other medical decisions; engagement in the evaluation process may have far-reaching effects on other aspects of medical care; and (3) personal responsibility and psychological burden; patients felt personally responsible for their progress through the evaluation process, creating the possibility that the evaluation process could create a significant emotional toll on patients and families.

In summary, the researchers said, "Most patients evaluated for transplant at our center did not receive a kidney. The evaluation process could be burdensome and emotionally taxing for these patients and their families and could intrude on many other aspects of their care. These findings highlight the potential tradeoffs involved in being evaluated for kidney transplant and argue for engaging patients in a deliberate and shared approach to referral decisions."

Source: Butler C, Taylor JS, Reese PP, O'Hare AM. Care practices for patients with advanced kidney disease who were evaluated for transplant but did not receive a kidney. Abstract of a poster presented during the American Society of Nephrology Kidney Week 2019 (Abstract TH-P01150), November 7, 2019, Washington, DC.

Living Donor Navigator Program and Access to Living-donor Kidney Transplantation

Kidney transplant, the gold standard for treatment of end-stage renal disease, is associated with significantly improved long-term outcomes. In addition, there is a significant survival benefit associated with living-donor kidney transplant compared with deceased-donor transplantation. However, despite those benefits, living-donor kidney transplant has declined in the United States since 2004. According to **Jayme E. Locke, MD,** and colleagues, there are multiple factors contributing to the decline.

Results from a National Kidney Foundation survey found that one in four Americans would consider living kidney donation if they knew someone who needed a kidney; in a Mayo Clinic survey, 84% of respondents would donate to a friend or family member and 49% said they would donate to a complete stranger. Those results suggest that potential donors may not be aware that they are needed, highlighting the lack of knowledge among transplant candidates regarding how to ask someone to donate.

Programs designed to separate the advocacy role from the transplant candidate include the Johns Hopkins Live Donor Champion Program and Smartphone app, the Boston-based House Calls Program, and the Northwestern website, Infórmate. These programs have generated interest in living-donor transplant, yet gains in actual approved donors and subsequent living-donor kidney transplantation have been modest.

Dr. Locke and colleagues at the University of Alabama at Birmingham (UAB) developed and implemented the Living Donor Navigator (LDN) Program. To evaluate the impact of the program, the researchers recently conducted a retrospective cohort study. Results of the study were reported in *Transplantation* [2020;194(1):122-129].

The LDN program combines advocacy training adapted from the Johns Hopkins Live Donor Champion program with the systems training of the Patient Navigator Program developed at UAB to address factors related to transplant candidates as well as potential donors. The advocacy and systems training components are delivered by lay navigators from the local community. The program was available to all patients evaluated for kidney transplant beginning in February 2017.

The advocacy training component paired transplant candidates with a live donor advocate to combine education, advocacy, and instrumental support. The program included four educational sessions offered two weeks apart. The sessions incorporated didactic as well as hands-on interactive lessons taught by trained living donor navigators.

The systems training component was designed to educate potential donors on the details associated with testing and physician visits required during the evaluation process. Potential donors who completed initial screening and were scheduled for evaluation were contacted by the living donor navigators who

CONFERENCE COVERAGE KIDNEY WEEK 2019

Access to Transplantation Varies with Distance from Dialysis Facility

Washington, DC–There is no association between the distance between a patient's residence and a kidney transplant center and access to transplantation. However, according to **Adrian Whelan, MBBCh,** and colleagues, the distance from the dialysis facility to the transplant center may be an important factor for access to transplantation. Dialysis providers closer to the transplant center may allow for better communication between the two facilities and contribute to expediting of patient work-up.

The researchers conducted a study to test the hypothesis that there would be an association between longer distance from the dialysis facility to the transplant center and longer time to transplantation. Results were reported during a poster session at Kidney Week 2019 in a poster titled *Longer Distance from Dialysis Facility to Transplant Center Is Associated with Lower Access to Transplantation.*

The study participants were adults who initiated dialysis between 2005 and 2015, as identified in the US Renal Data System database. The primary predictor was distance from the dialysis facility to the transplant center ≥100 miles versus <100 miles (reference group). The outcome of interest was the time from initiation of dialysis to kidney transplantation. The study utilized adjusted Cox models and tested for interactions by region of the United States, calendar year, and dialysis modality.

A total of 172,995 patients were included in the study. Mean age was 51.6 years and 30.3% were black. The distance from the dialysis facility to the transplant center varied by region of the United States. Overall, there was an association between distance from the dialysis facility to the transplant center ≥100 (vs <100 miles) and lower access to transplantation, regardless of dialysis modality. The association was modified by region of the United States and calendar year (P<.05 for interaction).

There was an association between longer distance from the dialysis facility to the transplantation center and lower access to transplant among patients living in the South and the West. The association between distance and transplantation access has attenuated over time.

"Longer dialysis facility to transplant center distance was associated with lower access to kidney transplantation even after accounting for distance between patients and the transplant center. Our data suggest that system-level factors such as proximity between referring and transplant providers may contribute to access to transplantation, but this association varies across the United States," the researchers said.

Source: Whelan A, Johansen KL, Adey DB, Roll GR, Siyahian S, Ku E. Longer distance from dialysis facility to transplant center is associated with lower access to transplantation. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2019 (Abstract TH-P01143), November 7, 2019, Washington, DC.

provided the potential donors with additional resources. Telephone and email contact between the navigators and potential donors was frequent and included reminders about physician and testing appointments. The navigators also greeted the potential donors at the transplant center and guided them through the large academic medical systems at UAB, providing concierge style service at their physician visits.

The study population included 2099 adult patients evaluated at UAB for kidney-only transplant between January 1, 2016, and March 1, 2018. Following application of exclusion criteria, the potential cohort included 2004 patients. Patients evaluated in the beginning of February 2017 were approached regarding participation in the study. Of those, 111 completed an interest form and 56 of the 111 choose to participate. One hundred percent of those who declined to participate (n=55) cited distance to the transplant center as the reason.

Among the 56 participants in the LDN program, there were 113 donor screenings, for a rate of 2.02 screened donors per participant. In contrast, among 1948 nonparticipants, there were 955 donor screenings, for a rate of 0.49 screened donors per nonparticipant. In unadjusted analyses, participation in the LDN program and being married were associated with increased likelihood of donor screening (hazard ratio [HR], 7.39; 95% confidence interval [CI], 4.87-11.21; *P*<.001 and HR, 1.75, 95% CI, 1.44-2.13; *P*<.001, respectively).

Following multivariate adjustment, LDN program participation remained the strongest predictor of having a living donor screened; program participation increased the likelihood more than 9-fold compared with standard of care (adjusted HR [aHR], 9.27; 95% CI, 5.97-14.41; *P*<.001). The finding persisted independent of race: African Americans in the LDN program were 8-fold more likely to have a donor screened compared with African American nonparticipants (aHR, 8.47; 95% CI, 5.05-14.20; *P*<.001) and 3-fold more likely than white nonparticipants (aHR, 3.20; 95% CI, 1.90-5.38; *P*<.001).

> The systems training component was designed to educate potential donors on the details associated with testing and physician visits required during the evaluation process.

Participants and nonparticipants were similar in age and sex. The proportion of African Americans was greater in the participant group than in the nonparticipant group (80.4% vs 63.9%; *P*=.06, respectively). Duration of dialysis vintage was shorter among participants than nonparticipants (0.73 years vs 1.27 years, respectively; *P*=.006), and participants lived closer to the UAB than nonparticipants (22 miles vs 85 miles, respectively, *P*<.001).

Among the 56 program participants, nine living donors were approved to donate, for an approval rate of 16.1%; in contrast, among 1948 nonparticipants, 100 living donors were approved, for an approval rate of 5.1%. In unadjusted analyses, there were associations between LDN program participation (HR, 4.62; 95% CI, 2.33-9.26; *P*<.001), male sex (HR, 1.81; 95% CI, 1.19-2.74; *P*=.005), and being married (HR, 2.88; 95% CI, 1.88-4.42; *P*<.001) and increased likelihood of donor approval. There was also an association between increased dialysis vintage and decreased likelihood of donor approval (HR, 0.72; 95% CI, 0.54-0.95; *P*=.02).

Following multivariate adjustment, the strongest predictor of living donor approval was participation in the LDN program: program participation increased the likelihood of donor approval more than 7-fold compared with standard of care (aHR, 7.74; 95% CI, 3.54-16.93; *P*<.001). This finding persisted independent of race: African American participants were 8-fold more likely to have a donor approved than African American nonparticipants (aHR, 8.24; 95% CI, 3.05-22.27; *P*<.001).

Limitations to the findings cited by the authors included the single center design conducted in the rural, deep South, potentially limiting the generalizability to centers in other regions; the need for program participants to travel to the transplant center to participate in the advocacy training; and the lack of prospectively collected data that may have informed the results.

In conclusion, the researchers said, "The UAB LDN program is highly effective and has tremendous reach. It is the first program designed to promote living-donor kidney transplantation that has demonstrated sustained increases in both donor screenings and approvals, and, importantly, has proven effective among African Americans. This first-of-its-kind program has tremendous promise for mitigating disparities in access to living-donor kidney transplantation among African Americans. Future work designed to overcome geographic limitations in participation is needed, but in the setting of modern technology, geography is likely easily overcome with the advent of a telehealth approach to the UAB LDN model." ■

TAKEAWAY POINTS

- Researchers at the University of Alabama at Birmingham reported results of a program designed to promote advocacy and systems training among kidney transplant candidates and their potential living donors.
- There were 56 participants in the Living Donor Navigator (LDN) Program and 1948 nonparticipants (standard of care).
- Participation in the LDN program was associated with a 7-fold increase in the likelihood of living donor screenings and a 7-fold increase in the likelihood of having an approved living donor.

CONFERENCE COVERAGE KIDNEY WEEK 2019

Living Donor Kidney Volume Predictive of Donor and Recipient Graft Function

Washington, DC–The treatment of choice for patients with end-stage renal disease is kidney transplantation, and living donor kidney transplantation is the optimal model. There are few data available on the predictive value of renal volume measurement in predicting long-term donor and recipient graft outcome.

Chaudhry Adeel Ebad, MBBS, MRCPI, and colleagues at Beaumont Hospital, Dublin, Ireland, conducted a retrospective cohort study of living donor transplantation performed from 2010 to 2017. The researchers utilized data from the National Kidney Transplant Service of Ireland. TeraRecon USA was used to measure renal volume bilaterally in living kidney donors. Results of the study were reported during a poster session at Kidney Week 2019 in a poster titled *Donor Kidney Renal Volume Predicts Recipient and Donor Graft Function at 1 Year.*

Low estimated glomerular filtration rate (eGFR), defined as <60 mL/min/1.73 m^2, in recipients and donors was used in logistic regression models with donor volume stratified into tertiles. The models included donor and recipient characteristics as potential confounding variables.

During the study period, there were 166 living donor kidneys transplanted. Mean donor age was 44.8 years, mean body mass index was 25.5 kg/m^2, and mean kidney volume was 152.7 mls. The tertiles of donor kidney volume were: (1) 89.2 to 135 mls; (2) 136 to 164 mls; and (3) 165 to 240 mls. At 1 year post-transplant, median donor estimated glomerular filtration rate (eGFR) was 63.3 mL/min/1.73 m^2. Mean age of recipients of living donor kidneys was 43.5 years, and mean recipient eGFR at 1 year post-transplant was 58.3 mL/min/1.73 m^2.

There was a slight correlation between donor kidney volume and donor eGFR at 1 year post-transplant; using the kidney volume tertile categories, the correlation was marginally nonsignificant in logistic regression (odds ratio [OR], 0.65; 95% confidence interval [CI], 0.40-1.04; *P*=.075). There was a correlation between donor kidney volume and recipient eGFR at 1 year post-transplant; the correlation remained significant in multivariable logistic regression (OR, 0.48; 95% CI, 0.26-0.90; *P*=.021).

In conclusion, the researchers said, "Donor kidney volume predicts recipient graft function 1 year post-transplant but is less conclusive for donor kidney function. Cognizance of donor renal volume may help optimize potential kidney donor selection."

Source: Ebad CA, Chevarria JL, Sexton DJ, et al. Donor kidney renal volume predicts recipient and donor graft function at 1 year. Abstract of a poster presented during the American Society of Nephrology Kidney Week 2019 (Abstract TH-P01130), November 7, 2019, Washington, DC.

NDA Application for Drug to Treat HRS-1 Announced

Mallinckrodt has announced a rolling submission of a New Drug Application (NDA) to the US FDA for terlipressin, an agent being investigated for the treatment of hepatorenal syndrome type 1 (HRS-1). The global biopharmaceutical company has submitted its clinical data package to the FDA. The rolling submission will allow for submission of portions of the regulatory applications to the FDA as they are completed. Mallinckrodt expects to complete the NDA submission in the coming months.

According to a press release, HRS-1 is an acute and life-threatening complication characterized by acute kidney failure in patients with cirrhosis. If left untreated, median survival time among patients with HRS-1 is less than 2 weeks and the mortality rate is more than 80% within three months of diagnosis. Currently, there are no approved drug therapies for HRS-1 in the United States; HRS-1 affects an estimated 30,000 to 40,000 patients annually in the United States.

Steven Romano, MD, executive vice president and chief scientific officer at Mallinckrodt, said, "This is an important milestone that brings us closer to potentially delivering the first FDA-approved treatment in the US for HRS-1, a life-threatening, difficult-to-treat condition. We are grateful to the patients, their families and caregivers, and the researchers who made this achievement possible."

The NDA for terlipressin is based, in part, on results from CONFIRM, a phase 3 prospective study conducted among patients with HRS-1. The trial met its primary end point of verified HRS reversal, defined as improvement in renal function, avoidance

of dialysis therapy, and short-term survival. Serious adverse events were reported in 65% of participants in the terlipressin group and 60.6% of those in the placebo group; there were no new or unexpected adverse events reported. Initial results of the CONFIRM trial were reported at The Liver Meeting® 2019, the annual meeting of the American Association for the Study of Liver Diseases.

FMCNA Announces Telehealth Solution

In a recent press release, Fresenius Medical Care North America (FMCNA) announced the planned rollout of a new telehealth solution for its home dialysis patients. FMCNA is a leading provider of kidney care products and services and its telehealth program is designed to improve collaboration among patients, the clinical care team, and physicians to facilitate the rapid growth of home therapies for patients with end-stage renal disease.

Following implementation of a series of pilot programs in 2019, FMCNA signed an agreement to seamlessly integrate telehealth into theHub, the company's connect health platform.

Joe Turk, president of home and critical care therapies at FMCNA, said, "We are excited to bring this user-friendly telehealth solution to our home dialysis patients, part of our effort to improve the experience for patients managing their own treatments. This solution will help people living with kidney disease better connect with their care team, including nephrologists, nurses, social workers, and dietitians."

The press release noted that as a result of legislation at the federal level, under certain conditions, Medicare allows for a home dialysis patient to meet with their nephrologist and care team for their monthly visit via telehealth. Telehealth is also supported by many private insurers. Telehealth can improve access to care while reducing travel burden for patients, particularly for patients residing in rural areas. Telehealth also provides a more frequent visual touchpoint with the care team, increasing the rates of successful home therapies.

Ahmad Sharif, MD, chief medical information officer for FMCNA, said, "We have rapidly accelerated development of new connected health technologies to improve the patient, physician, and staff experience. When home patients are more connected to their care team through remote monitoring, recent studies show fewer hospital admissions and less technique failure. This new telehealth solution will be critical to expanding the adoption of home dialysis for people living with kidney failure."

The new telehealth program will launch initially in select markets and roll out more widely later this year, the press release said.

CONFERENCE COVERAGE KIDNEY WEEK 2019

Canagliflozin Benefits Consistent across Levels of Kidney Function

Washington, DC–Canagliflozin is US FDA approved for treatment of patients with type 2 diabetes and estimated glomerular filtration rate (eGFR) ≥45 mL/min/1.73 m^2. Researchers, led by **Meg J. Jardine, MB, BS, PhD,** conducted a secondary analysis of data from the CREDENCE trial to examine the efficacy and safety of canagliflozin according to strata based on eGFR, including patients with eGFR 30 to <45 mL/min/1.73 m^2. Results of the analysis were reported during an oral session at Kidney Week 2019; the session was titled *Renal, Cardiovascular, and Safety Outcomes of Canagliflozin (CANA) According to Baseline Kidney Function: A CREDENCE Secondary Analysis.*

A total of 4401 participants were enrolled in the CREDENCE study. Eligible participants had eGFR 30 to <90 mL/min/1.73 m^2 and urinary albumin-to-creatinine ratio <300 to 5000 mg/g. Study participants were randomized within eGFR-based strata to receive canagliflozin 100 mg daily or placebo. Cox proportional hazards regression models were used to analyze primary and prespecified secondary composites and safety outcomes within each screening eGFR stratum: 30 to <45 mL/min/1.73 m^2, 45 to <60 mL/min/1.73 m^2, and 60 to <90 mL/min/1.73 m^2.

At screening, 29.8% (n=1313) of participants had an eGFR 30 to <45 mL/min/1.73 m^2, 29.1% (n=1279) had eGFR 45 to <60 mL/min/1.73 m^2, and 41.1% (n=1809) had eGFR 60 to <90 mL/min/1.73 m^2. Overall, treatment with canagliflozin resulted in reduction of the primary outcome, the renal composite of end-stage renal disease, sustained doubling serum creatinine, or renal death; as well as a range of cardiovascular outcomes and serious adverse events. There were no associations between treatment with canagliflozin and fractures or amputations.

There was no difference in the impact of canagliflozin between eGFR subgroups (all *P* for interaction >.11). For the primary composite, renal composite, and composite of cardiovascular death or hospitalization for heart failure, the benefits of canagliflozin were individually significant in participants with a screening eGFR of 30 to <45 mL/min/1.73 m^2.

"Canagliflozin safely reduces the risk of renal and cardiovascular events in people with type 2 diabetes and substantial albuminuria, and these benefits are preserved across a spectrum of eGFR 30 to <90 mL/min/1.73 m^2, including eGFR 30 to <45 mL/min/1.73 m^2," the researchers said.

Source: Jardine MJ, Mahaffey KW, Agarwal R, et al. Renal, cardiovascular, and safety outcomes of canagliflozin (CANA) according to baseline kidney function: A CREDENCE secondary analysis. Abstract of a presentation at the American Society of Nephrology Kidney Week 2019 (Abstract SA-OR078), November 9, 2019, Washington, DC.

Funding provided by The Janssen Pharmaceutical Companies of Johnson & Johnson.

American Kidney Fund Grants Aid Patients with Kidney Failure

In 2019, the number of kidney transplants reached an all-time high: more than 24,000. Of those, according to a press release from the American Kidney Fund (AKF), more than one in 20 transplants were made possible with financial assistance from the AKF. The press release announced that 1400 of the AKF grant recipients living with kidney failure received a kidney transplant and post-transplant care in 2019.

Patients who received the life-saving transplants were living in 48 states and Puerto Rico and ranged from 13 to 80 years of age. More than 60% of the AKF grant recipients who received a transplant last year are members of racial and ethnic minority groups; racial and ethnic minorities are disproportionately affected by kidney disease, yet generally receive fewer kidney transplants than white Americans, according to the press release.

LaVarne A. Burton, president and CEO of AKF, said, "Patients face so many obstacles on the road to getting a transplant, and the American Kidney Fund helps them overcome one very significant hurdle—the financial barriers to maintaining comprehensive health coverage necessary for transplant. Our charitable premium assistance program is a lifeline that helps low-income patients access the full range of healthcare services needed to treat this complex condition and stay as healthy as possible—allowing them to qualify for the transplant waiting list, go through the transplant workup, have the surgery itself, and receive post-transplant care. Our assistance continues for the full insurance plan year post-transplant, providing support to patients as they recover and adjust to post-transplant living."

The press release noted that AKF is also working to make it easier to become a living kidney donor. In 2019, nine states enacted legislation spearheaded by AKF that will protect living kidney donors from insurance discrimination and make it possible for them to have job-protected leave. This year, efforts to champion such legislation in 15 additional states are being led by AKF; the Fund also actively supports the federal Living Donor Protection Act of 2019.

Public Awareness Campaign Launched

The National Kidney Foundation (NKF), the American Society of Nephrology (ASN), and the US Department of Health and Human Services (HHS) collaborated to create a nationwide public awareness campaign highlighting the risk for kidney disease. The campaign was launched as part of National Kidney Month in March. The campaign focused on the 33% of Americans at risk for kidney disease, including those with diabetes, heart disease, hypertension, obesity, and a family history of the disease.

In a joint press release, **Kevin Longino,** CEO of NKF and a kidney transplant recipient, said, "Look around the next time you're sitting in a school auditorium or even in a giant, professional sports stadium; one-third of every adult in there with you is at risk of developing kidney disease. We believe it's essential to reach the more than 80,000,000 American adults at risk, because if you can diagnose and treat kidney disease early, you can help stave off its life-threatening complications."

The Are You the 33%? Campaign, cosponsored by the NKF, HHS, and ASN, is part of a public awareness initiative of the Advancing American Kidney Health plan. ASN president, **Anupam Agarwal, MD, FASN,** said, "More than 90% of the 37,000,000 Americans and 850,000,000 individuals worldwide affected with kidney disease are unaware that they are even sick. This silent epidemic often strikes without symptoms. Millions of people won't know they have kidney disease until their kidneys stop working and it's too late."

The campaign seeks to change those odds by urging every American adult to take a simple, one-minute quiz at the website MinuteForYourKidneys.org. HHS Secretary **Alex Azar s**aid, "My own family has known the burdens of kidney disease, including how taxing dialysis can be. Helping Americans understand their risk for kidney disease and take steps to prevent it is and must be a top public health priority." ■

CONFERENCE COVERAGE KIDNEY WEEK 2019

Patient Perceptions of CKD Anemia Burden and Treatment

Washington, DC–Patients with chronic kidney disease (CKD) who develop anemia may have reduced quality of life and require additional treatment. **Eirini Palaka, MSc,** and colleagues at AstraZeneca and Yale University conducted a study to examine the perceptions of patients with CKD and anemia in the United States regarding quality of life, understanding of their disease, and management of their anemia. Results of the study were reported during a poster session at Kidney Week 2019 in a poster titled *Understanding Patient Perspectives of the Impact, Awareness, and Treatment of CKD Anemia: A US Patient Survey.*

From August through September 2018, a quantitative online survey was administered to 500 patients with self-reported CKD with or without anemia. Eligible patients were ≥18 years of age; patients with cancer were excluded. Patients were recruited via open requests to online communities and support groups, patient associations, and patient referrals. The survey was designed to explore patient knowledge of anemia and its management, the impact of anemia symptoms, and quality of life for patients with CKD and anemia. Patient confidentiality was protected by aggregation and anonymization of the data.

Of the total cohort, 69% were female, mean age was 52.2 years, 68% reported they had CKD stages 3 to 5, and 24% had CKD stage 1 or 2 (the remaining 8% did not know what stage they had). Fifty-seven percent of the total cohort (n=255) said they had been told they had anemia by a healthcare professional. However, of those 255, only 66% (n =168) were aware of the relationship between anemia and CKD.

Only 38% of the entire cohort (n=170) knew their hemoglobin levels. Most were aware of the key symptoms of anemia; 89% cited fatigue and 70% mentioned weakness. Symptoms reported by patients with anemia were lack of energy (82%), feeling sad/depressed (53%), noting pain (52%), difficulty sleeping (53%), and worry over anemia worsening (63%).

Sixty-seven percent of patients said their anemia was well managed: 55% of those treated were treated with iron; 30% were treated with erythropoiesis-stimulating agents; and 11% had received transfusions. Fewer than half of the respondents felt confident that they knew the adverse effects of their treatment.

In summary, the researchers said, "US patients with CKD perceived that anemia had a negative impact on their physical symptoms and emotional well-being; their knowledge and understanding of CKD anemia and its management varied. These findings emphasize the challenges healthcare providers and patients face concerning the need for further education on the association between CKD and anemia, symptoms associated with anemia, and the available treatment options for anemia.

Source: Palaka E, Guzman NJ, Dunn A, Wittbrodt ET, Grandy S, Finkelstein FO. Understanding patient perspectives of the impact, awareness, and treatment of CKD anemia: A US patient survey. Abstract of a poster presented during the American Society of Nephrology Kidney Week 2019 (Abstract SA-P0232), November 9, 2019, Washington, DC.

Funding for this study was provided by AstraZeneca.

CHRONIC KIDNEY DISEASE

Variability in eGFR and Risk of Adverse Outcomes

Nephrology Dialysis Transplantation. 2019;34(12):2066-2078

There are few available data on the association between variability in first-year estimated glomerular filtration rate (eGFR) and longitudinal change scales concomitantly to the risk of developing end-stage renal disease (ESRD), acute coronary syndrome (ACS), and death following pre-ESRD program enrollment of patients with chronic kidney disease (CKD).

Ching-Wei Tsai, MD, and colleagues conducted a prospective cohort study of 5092 patients with CKD receiving multidisciplinary care between 2003 and 2015. Incidence of ESRD, ACS, and death during follow-up were determined. Variability in first-year eGFR and longitudinal change scales were based on all first-year measurements, including coefficient of variation of eGFR (EGFR-CV), percent change (eGFR-PC), absolute difference (eGFR-AD), slope (eGFR-slope), and area under the curve (eGFR-AUC).

There were 786 incident ESRD events, 292 ACS events, and 410 deaths during follow-up. In multiple Cox regression, the fully adjusted hazard ratio (HR) of progression to ESRD was 1.03 (95% confidence interval [CI], 1.02-1.04) for each unit change in eGFR-CV, 1.04 (95% CI, 1.03-1.04) for eGFR-PC, 1.16 (95% CI, 1.14-1.18) for eGFR-AD, 1.16 (95% CI, 1.14-1.17) for eGFR-slope, and 1.04 (95%CI, 1.03-1.04) for eGFR-AUC.

The adjusted HRs for incident ESRD comparing the extreme with the reference quartiles were 2.67 (95% CI, 2.11-3.38) for eGFR-CV, 8.34 (95% CI, 6.33-10.98) for eGFR-PC, 19.08 (95% CI, 11.89-30.62) for eGFR-AD, 13.08 (95% CI, 8.32-20.55) for eGFR-slope, and 6.35 (95% CI, 4.96-8.13) for eGFR-AUC.

In the 2 x 2 risk matrices, the risk of all outcomes was highest in patients with the highest quartile of eGFR-CV and concomitantly with the most severely declining quartiles of any other longitudinal eGFR change scale.

In conclusion, the researchers said, "The dynamics of eGFR changes, both overall variability and longitudinal changes, over the first year following pre-ESRD program enrollment are crucial prognostic factors for the risk of progression to ESRD, ACS, and death among patients with CKD. A risk matrix combining the first-year eGFR variability and longitudinal change scales following pre-ESRD enrollment is a novel approach for risk characterization in CKD care. Randomized trials in CKD may be required to ascertain comparable baseline eGFR dynamics."

Sodium Bicarbonate and Kidney Function: The BASE Pilot Trial

Journal of the American Society of Nephrology. 2020;31(10:161-174

Kidney function in patients with chronic kidney disease may be preserved with treatment with oral sodium bicarbonate ($NaHCO_3$); the benefit may be present even in patients with normal serum bicarbonate level. In part because the optimal dose for testing is unknown, there have not been adequately powered trials to test this hypothesis.

Kalani L. Raphael, MD, MS, and colleagues conducted a multicenter pilot trial designed to assess the safety, tolerability, adherence, and pharmacodynamics of two doses of $NaHCO_3$ over 28 weeks in adults with estimated glomerular filtration rate 20 to 44 or 45 to 40 mL/min/1.73 m^2 with urinary albumin-to-creatinine ratio (ACR) ≥50 mg/g and serum bicarbonate 20 to 28 meq/L.

A total of 194 patients from 10 clinical sites were randomly assigned to receive higher dose (HD-$NaHCO_3$; 0.8 meq/kg of lean body weight per day; n=90) or lower dose (LD-$NaHCO_3$; 0.5 meq/kg of lean body weight per day; n=52) $NaHCO_3$ or matching placebo (n=52). Dose was adjusted based on side effects. The primary outcome of interest was the prescribed dose at 28 weeks; an acceptable dose was identified as acceptable for a full-scale trial if ≥67% of participants were on full dose and ≥80% were on ≥25% of the per-protocol dose.

At baseline, mean eGFR was 36 mL/min/1.73 m^2, serum bicarbonate was 24 meq/L, and median ACR was 191 mg/g. Both doses of $NaHCO_3$ were well tolerated; there were no significant changes in blood pressure, weight, or serum potassium level. Both groups had similar proportions of adverse events and hospitalizations. At week 28, 87% of participants in the HD-$NaHCO_3$ group, 96% in the LD-$NaHCO_3$ group, and 87% in the placebo group were on full dose; in addition, 91% in the HD-$NaHCO_3$ group, 98% in the LD-$NaHCO_3$ group and 92% in the placebo group were on ≥25% of the per-protocol dose.

At week 28, compared with the LD-$NaHCO_3$ group, mean urinary ammonium excretion was 25% lower and serum bicarbonate concentration was 1.3 meq/L higher in the HD-$NaHCO_3$ group. However, mean ACR increased by 12% in the LD-$NaHCO_3$ group and 30% in the HD-$NaHCO_3$ group.

In conclusion, the researchers said, "Both $NaHCO_3$ doses were well tolerated over 28 weeks with no significant difference in adverse events or hospitalization, compared with placebo. The higher dose lowered urinary ammonium excretion and increased serum bicarbonate more than the lower dose but was associated with a greater increase in ACR. The higher 0.8 meq/kg of body weight per day dose of $NaHCO_3$ may be a reasonable choice for future trials."

Slowing CKD Progression in Patients with HCV Infection

Kidney International. doi.org/10.1016/j.knit.2019.04.030

Hepatitis C virus infection (HCV) is a common comorbidity of chronic kidney disease (CVD) and may lead to accelerated CKD progression. Rates of sustained viral remission have been seen with direct-acting antiviral (DAA) therapies against HCV; however, the effect on kidney function is unknown. **Meghan E. Sise, MD,** and colleagues conducted a retrospective, observational cohort study to compare the slopes of estimated glomerular filtration rate (eGFR) decline in the 3 years prior to DAA therapy with the slope after the therapy. Pre- and post-treatment albuminuria values were also compared.

HCV-infected patients receiving DAA therapies from 2013 to 2017 were eligible for the study. A total of 1178 patients were included. Mean age was 56 years, 64% were male, 71% were white, 21% were diabetic, and 42% had cirrhosis.

Among patients with eGFR <60 mL/min/1.73 m^2, the annual decline in eGFR in the 3-year prior treatment period was –5.98 mL/min per year (95% confidence interval [CI], –7.30 to –4.67) and improved to –1.32 mL/min per year (95% CI, –4.50 to 1.88) following DAA therapy. Among patients with eGFR >60 mL/min per year, the annual decline in eGFR in the pre-treatment period was –1.43 mL/min per year (95% CI, –1.78 to –1.08); following treatment with DAA therapies, the annual decline was –2.32 mL/min per year (95% CI, –3.36 to –1.03).

There was significant improvement in albuminuria in patients without diabetes. Predictors of improvement in eGFR were having CKD at baseline and being nondiabetic. Events of acute kidney injury (AKI) were rare and unrelated to antiviral therapy in 76% of the 29 patients who developed AKI.

"DAA therapy for HCV infection may slow CKD progression," the researchers said.

HYPERKALEMIA

Economic Impact of Management of Patients with CKD and Hyperkalemia

The International Journal of Clinical Practice. doi.org/10.1111/ijcp.13475

Hyperkalemia, defined as potassium level ≥5.0 mEq/L, is associated with poor clinical outcomes in patients with chronic kidney disease (CKD). **Michele Provenzano, MD,** and colleagues conducted a study to compare management costs of patients with CKD with normokalemia versus those with persistent hyperkalemia treated in renal clinics in Italy.

The researchers developed a Markov model over life-time horizon. An observational multicenter database was used to derive time to end-stage renal disease (ESRD) and time to death among 1665 patients with non-dialysis CKD stage 1 to 5 receiving nephrology care in Italy. Follow-up was 15 years.

In addition to delayed onset of ESRD by 2.29 years and increased survival by 1.79 years, management of patients with normokalemia versus persistent hyperkalemia was associated with a cost-savings of €16,059. Total survival and dialysis-free survival in patients with normokalemia decreased incrementally from early to advanced disease. The cost-savings associated with normokalemia increased at more advanced CKD; however, cost-savings were seen at early stages (€3388.97 at stages 1-3a). The cost-savings associated with normokalemia were confirmed across all parameter variations.

The researchers said, "This model is the first to simulate the impact of hyperkalemia in non-dialysis CKD patients on economic and clinical outcomes using real-world data from nephrology clinics. In these patients, persistent hyperkalemia results into higher lifetime costs, besides poorer clinical outcomes, that are evident since the early stages of CKD. Maintaining normokalemia should therefore be of main concern in CKD treatment planning to improve long-term economic and clinical outcomes."

Review of Trials and Guidelines in the Treatment of Hyperkalemia

Nephrology Dialysis Transplantation. 2019;34(Supplement 3):iii51-iii61

Stefano Bianchi, MD, and **Giuseppe Regolisti, MD,** recently conducted a review of pivotal clinical trials, meta-analyses, and current guidelines in the treatment of hyperkalemia. Hyperkalemia, an electrolyte disturbance in patients with advanced chronic kidney disease (CKD), is associated with an increased risk of fatal arrhythmias and has a significant impact on patients' prognosis and quality of life. In patients with heart failure and diabetes mellitus, treatment commonly includes renin-angiotensin-aldosterone system (RAAS) inhibitors. RAAS inhibitors are cardio-nephroprotective drugs; however, treatment with RAAS inhibitors per se increases serum potassium values.

The onset or recurrence of hyperkalemia is frequently associated with not starting, titrating down, or withdrawing RAAS inhibitor therapy and may be an indication to initiate renal replacement therapy in patients with end-stage renal disease.

Treatments that include restriction of dietary potassium, the use of sodium bicarbonate or diuretics, withdrawal or down-titration of RAAS inhibitors, or the administration of old potassium binders have limited efficacy and are poorly tolerated.

"The development of new potassium binders may change the treatment landscape. This review summarizes the current evidence on the treatment of chronic hyperkalemia in cardio-renal patients," the researchers said.

LUPUS NEPHRITIS

Biopsy-based Management May Reduce Lupus Nephritis Flare Rate

Kidney International. doi.org/10.1016/j.kint.2019.07.018

Currently, there is no consensus on the optimal duration of maintenance immunosuppression therapy for patients with lupus nephritis who have achieved clinical remission. In addition, according to **Ana Malvar, MD,** and colleagues, "Clinical and histologic remission are often discordant."

Dr. Malvar et al. recently conducted a prospective cohort study to test the hypothesis that continuing therapy for patients with persistent histologic activity on kidney biopsies done during maintenance and discontinuing therapy only for patients without histologic activity would minimize subsequent lupus nephritis flares.

The study included a cohort of 75 patients with proliferative lupus nephritis who were managed using kidney biopsies performed during maintenance therapy. Eligible patients had been on immunosuppression therapy for a minimum of 42 months, had responded, and maintained clinical response for a minimum of 12 months prior to a repeat of the kidney biopsy. If the biopsy showed an activity index of zero, maintenance was withdrawn. If the biopsy showed an activity index of one or more, maintenance was continued.

Seven patients experienced a lupus nephritis flare during the average 50 months from the third biopsy and the final clinic visit, for a flare rate of 1.5 per year (significantly less than reported flare rates).

Baseline clinical parameters (serum creatinine, proteinuria) and serologic parameters (complement C3, C4, and anti-dsDNA) were not predictors of activity index of zero in the third biopsy or who would experience a lupus nephritis flare. Four patients developed *de novo* chronic kidney disease; no patient developed end-stage renal disease. There were no serious biopsy-related adverse events.

In conclusion, the researchers said, "Thus, at an experienced center, biopsy-informed management of maintenance immunosuppression is safe and may improve the lupus nephritis flare rate compared to conventional clinical management."

TRANSPLANTATION

Long-term Outcomes of Acute Rejection

Journal of the American Society of Nephrology. 2019;30(9):1697-1707

Amid declining rates of acute rejection, the 1-year graft survival rate among patients with acute rejection is high, prompting a re-examination of acute rejection as an outcome of transplantation in trials and in clinical practice. However, there are few data available on the possible direct or indirect effects of acute rejection on longer-term outcomes for recipients of kidney transplantation.

Philip A. Clayton, MD, and colleagues conducted an analysis of data from the Australia and New Zealand Dialysis and Transplant Registry to examine the long-term effect of acute rejection on transplant outcomes. The analysis included data on 13,614 recipients of a primary kidney-only transplant between 1997 and 2017, with a minimum of 6 months of graft function. Cox models adjusted for baseline donor, recipient, and transplant characteristics were used to determine associations between acute rejection within 6-months post-transplant and subsequent cause-specific graft loss and death.

Acute rejection occurred in 21.4% of the recipients (n=2906); there were associations between acute rejection and graft loss attributed to chronic allograft nephropathy (hazard ratio [HR], 1.39; 95% confidence interval [CI], 1.23-1.56) and recurrent acute rejection beyond month 6 (HR, 1.85; 95% CI, 1.39-2.46). There was also an association between early acute rejection and death with a functioning graft (HR, 1.22; 95% CI, 1.08-1.36) and with death due to cardiovascular disease (HR, 1.30; 95% CI, 1.11-1.53) and with cancer (HR, 1.35; 95% CI, 1.12-1.64). Results were similar in sensitivity analyses restricted to subgroups with either biopsy-proven, antibody-mediated, or vascular rejection, or stratified by treatment response.

In conclusion, the researchers said, "Acute rejection is associated with increased risks of longer-term graft failure and death, particularly death from cardiovascular disease and cancer. The results suggest acute rejection remains an important short-term outcome to monitor in kidney transplantation and clinical trials." ■

Sarah Tolson

Chronic Care Management Services, Part One

Earlier this year, I received correspondence from several readers of this column expressing appreciation for some of the editions of From the Field featuring an educational theme. Additionally, the reimbursement landscape is changing from fee for service to pay for performance. With this in mind, this edition of From the Field will focus on the ins and outs of one of the newer programs geared toward patient-focused care, Chronic Care Management. As this is a large topic with many points to consider, the next edition of From the Field will cover implementation, billing, and reimbursement questions surrounding Chronic Care Management.

WHAT IS CHRONIC CARE MANAGEMENT?

Chronic Care Management (CCM) is the provision of care management and coordination services to patients with two or more chronic conditions expected to last at least 12 months or until death, that place the patient at significant risk of death, acute exacerbation/decompensation, or functional decline. Generally, primary care physicians provide CCM services. However, in many cases, the nephrologist becomes the equivalent of a primary care provider for patients with chronic kidney disease. Additionally, nephrologists and their staff are already accustomed to providing some of the components of CCM services.

Examples of chronic conditions:

- Diabetes
- Hypertension
- Cardiovascular Disease
- Depression
- Heart Failure
- Chronic Kidney Disease
- Osteoporosis
- Hyperlipidemia
- Alcohol Abuse
- Asthma
- Drug/Substance Abuse
- COPD

WHO CAN PROVIDE CCM SERVICES?

Physician or non-physician practitioners (physician assistants, nurse practitioners, clinical nurse specialists and/or certified nurse midwives) and their clinical staff can provide CCM services. CCM services that are not provided personally by the billing practitioner are provided by clinical staff under the direction of the billing practitioner (as an integral part of services provided by the billing practitioner), subject to applicable state law, licensure, and scope of practice.

ELEMENTS OF CCM SERVICES

CCM Services are comprised of several elements. The very first of those is the initiating visit. This visit can occur during an annual wellness visit, preventive physical exam, or any other face-to-face visit with the billing practitioner.

Patient consent is one of the integral components of CCM services, as obtaining consent provides an opportunity to ensure the patient is engaged in their own care and is aware of possible cost sharing associated with CCM services. Many patients receiving CCM services have coverage through Medicare. As with most Medicare services, CCM services are subject to Medicare deductibles and coinsurances.

The initial conversation with the patient regarding consent is a great time to educate the patient that while many providers may be involved in the patient's care, only one provider can furnish CCM services each month. Patients should also be aware they can stop CCM services at any time they choose (effective at the end of the calendar month).

Recording patient health information such as demographics and medications using certified Electronic Health Record (EHR) technology and developing a comprehensive care plan for the patient are also building blocks of CCM services. Comprehensive care plans may include things such as a problem list, medication management, measurable treatment goals, and a schedule for periodic review and applicable revision of the care plan.

Additional elements of CCM services are access to care and care continuity. Patients receiving CCM services should have 24-hour-a-day, 7-day-a-week access to physicians or other qualified healthcare professionals or clinical staff and a method to contact healthcare professionals in the practice to address urgent needs. Enhanced methods of communication via telephone, secure messaging, or secure electronic patient portals may help to facilitate access to a patient's care team. Continuity of care can be ensured by designating a member of the patient's care team with whom the patient is able to schedule successive routine appointments.

The final two elements of CCM services are comprehensive care management and transitional care management. Comprehensive care management may include an assessment of the patient's needs, medication reconciliation,n and care coordination with home and community-based services providers. Transitional care management may include managing the transitions between and among home health care providers and the timely exchange of continuity of care documents with other practitioners and providers. ■

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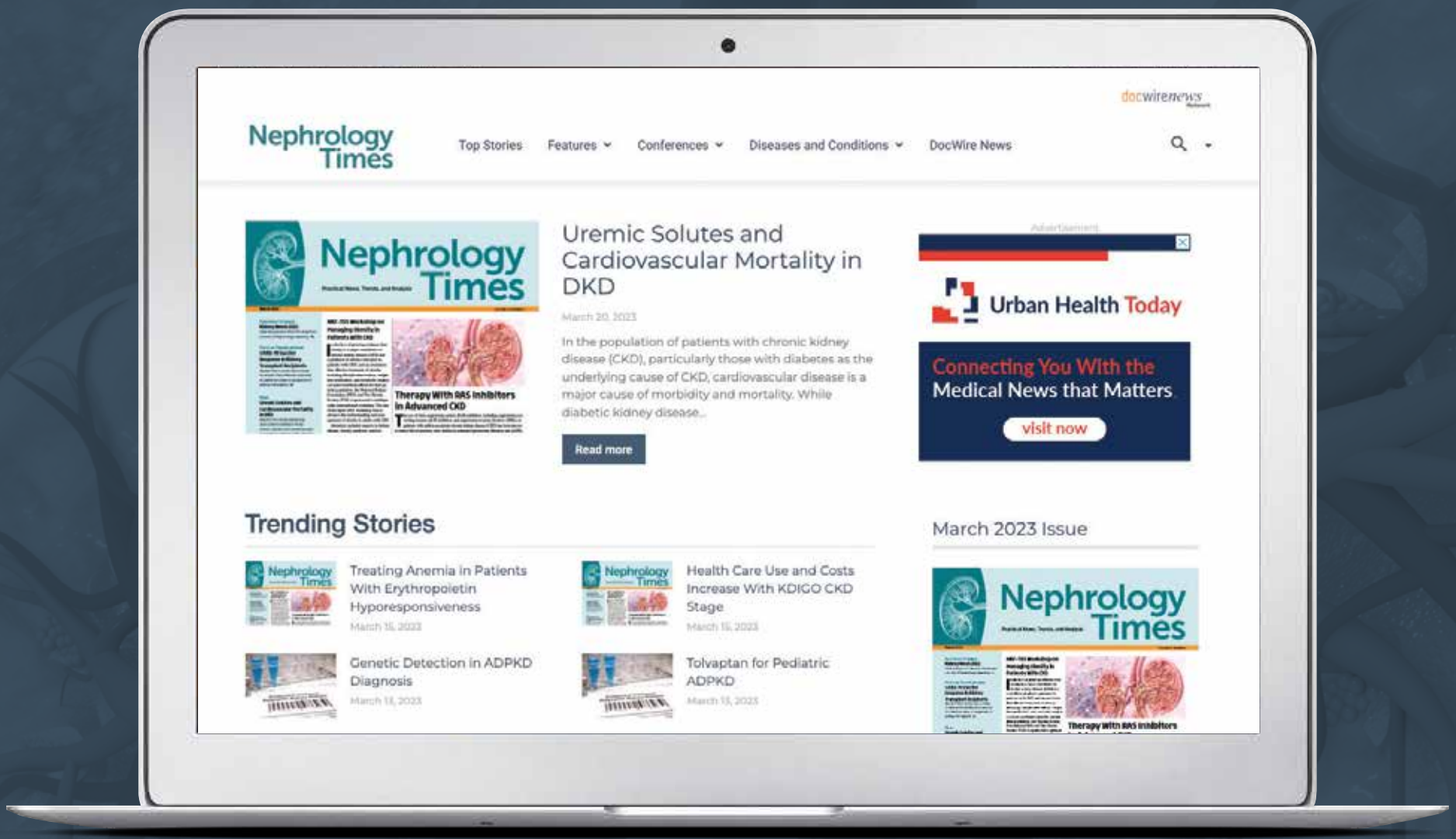

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