Nephrology Times

Practical News, Trends, and Analysis

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Conference Coverage

American Transplant Congress 2023

Selected posters and presentations from the June meeting. **9**

News

Prevalence and Risks of Anemia in Chronic Kidney Disease

A study assessed the burden of anemia by level of eGFR. **14**

Feature

Prescription Patterns of Newer Second-line Diabetes Medications in Underserved Populations

Prescribing patterns for SGLT2 inhibitors and GLP-1RAs, particularly among patient populations at high risk for disparities. **18**

Conference Coverage

European Renal Association 60th Congress

Nephrologists from around the world met in Milan, Italy, in June. **20**

From the Field

Improved Reimbursement in Dialysis Facilities: A Call for Action to Ensure Access to Care

Advocacy for improved reimbursement is crucial to ensuring continued access to care. **31**

AKI and Risk of Cardiovascular Events After PCI by Race, Diabetes, and Kidney Function

Patients undergoing percutaneous coronary intervention (PCI) may experience acute kidney injury (AKI) and face increased cardiovascular risk following the procedure. Compared with White patients, there is a disproportionate rate of AKI among Black patients. Black patients also have an increased overall risk of cardiovascular events compared with the general population. Further, diabetes and reduced kidney function are risk factors for AKI and are independently associated with increased cardiovascular risk in both PCI and non-PCI populations.

According to **Joseph Lunyera, MBChB, MSc,** and colleagues, there are few data available on the synergistic impact of AKI and AKI predisposition by race, diabetes, or reduced kidney function on the cardiovascular risk after PCI. The researchers conducted an observational cohort study to test the hypothesis that there would be a differential association between AKI and increased cardiovascular risk at 1 year after PCI, with a more pronounced association in Black patients than in White patients or those of other racial groups, and among patients with diabetes or reduced kidney function than in patients without those AKI risk factors. Results were reported in the *American Journal of Kidney Diseases* [2023;81(6):707-716].

The study utilized detailed clinical

continued on page 5

Kidney Outcomes in GRADE Study: Comparison of Glucose-Lowering Drugs

In the United States and in most of the world, diabetes is the leading cause of chronic kidney disease and kidney failure. Preventing or delaying the development of diabetic kidney disease (DKD) depends on achieving and maintaining glycemic control. Results of clinical trials in patients with type 1 diabetes and type 2 diabetes have consistently shown that the risk of developing albuminuria is reduced with intensive glycemic control. Long-term follow-up of some cohorts has suggested that intensive glycemic control

continued on page 4

Early Acetaminophen Exposure Reduces Severe AKI After Cardiac Surgery

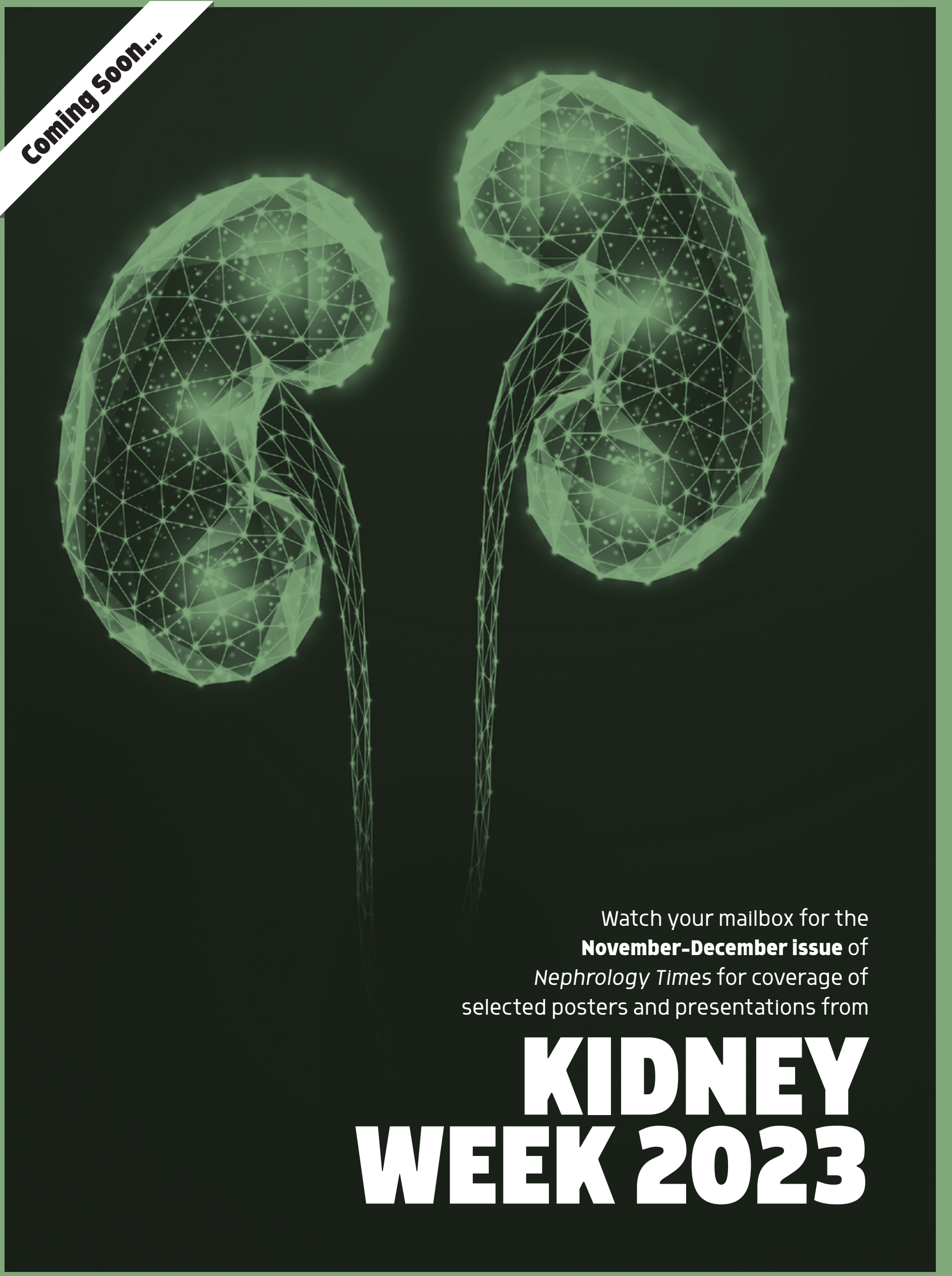
Patients undergoing cardiac surgery may experience postoperative acute kidney injury (AKI). The complication, known as cardiac surgery-associated AKI, is seen in 8% to 81% of cardiac surgery patients, and is associated with short- and long-term morbidity and mortality, prolonged stay in the intensive care unit (ICU) and hospital, and reduced quality of life. Patients who develop severe AKI face increased risk for worse outcomes, including an 8-fold increase in the odds of 30-day mortality.

According to **Chao Xiong, MD,** and colleagues, there is no specific pharmacologic prophylaxis for AKI subsequent to cardiac surgery. Acetaminophen is a commonly used postoperative analgesic, and evidence suggests that it protects against kidney damage mediated by free hemoglobin in both animals and humans. Because oxidative stress may be a contributing factor to the development of postoperative AKI, acetaminophen may be considered an antioxidant due to inhibition of hemoprotein-catalyzed lipid peroxidation.

The researchers conducted a retrospective, observational, cohort study to test the hypothesis that there is an association between perioperative administration of acetaminophen and reduced AKI after surgery. Results were reported in the *American Journal of Kidney Diseases* [2023;81(6):675-683].

The study utilized data from the Medical Information Mart for Intensive Care III (MIMIC-III) and the eICU Collaborative Research Database (eICU) on patients ≥18

continued on page 6



Watch your mailbox for the
November–December issue of
Nephrology Times for coverage of
selected posters and presentations from

KIDNEY WEEK 2023

UACR: Its Time Has Come

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The urine-albumin-creatinine ratio (UACR) is an estimate of urine albuminuria over a 24-hour timeframe and is expressed as the "excretion of albumin in milligrams per gram of creatinine." The UACR is a major predictor of both kidney progression and cardiovascular events.

Approximately 90% of patients with hypertension and/or diabetes undergo estimated glomerular filtration rate (eGFR) testing. However, UACR is majorly undermeasured.[1-3] Only about one-half of patients with diabetes undergo UACR testing. The rate is even lower (approximately 10%) among patients with hypertension. Why is UACR measurement important?

In the chronic kidney disease (CKD) Heat Map provided by the National Kidney Foundation (NKF), the UACR and GFR stages define risk in patients with CKD (Figure).[4] Estimating GFR and measurement of UACR allow for early detection of CKD among individuals at risk for CKD, especially those with diabetes or hypertension, and particularly among specific minority groups (eg, Black, Asian, and Latino patients). Measuring eGFR and UACR is now a key component of guideline-directed medical therapy for patients with CKD from type 2 diabetes (T2D).

Reports suggest that the underutilization of newer therapies for slowing progression of CKD in T2D may be due, in part, to under-recognition of CKD in patients with T2D.[5-9] Perhaps the 15% utilization of sodium-glucose cotransporter-2 inhibitors (SGLT2i) and 2% to 3% utilization of nonsteroidal mineralocorticoid receptor antagonists could improve if there is a major uptick in UACR measurement?

In a recent paper published in *JAMA Open Access,*[10] Chu and colleagues reported that among adults with hypertension or diabetes and albuminuria, approximately two-thirds did not undergo urine albumin testing. According to the authors, albuminuria testing was associated with higher adjusted odds of receiving angiotensin-converting enzyme inhibitor or angiotensin receptor blocker treatment (odds ratio [OR], 2.39; 95% CI, 2.32-2.46) or SGLT2i treatment (OR, 8.22; 95% CI, 7.56-8.94) and having blood pressure controlled to less than 140/90 mm Hg (OR, 1.20; 95% CI, 1.16-1.23). This paper reinforces the need for routine UACR testing, especially among high-risk patients.

The NKF, along with the National Committee for Quality Assurance (NCQA), developed the Kidney Health Evaluation for Patients With Diabetes (KED) as a measure in the Healthcare Effectiveness Data and Information Set (HEDIS). This resource is targeted for rollout later this year.

The consequences of UACR becoming a HEDIS measure are multifold. In 2023, the Centers for Medicare & Medicaid Services will make KED a measure in the Medicare Merit-based Incentive Payment System. Linking UACR measurement to payments for services covered by Medicare Part B creates a clear incentive. Also in 2023, as part of the Diabetes Recognition Program, the KED measure will contribute to crediting clinicians for providing high-quality ambulatory care to their patients with diabetes. The KED will be incorporated into the Medicare Star Rating system, a consumer-facing assessment of clinicians, in 2024.

The NKF and NCQA should be congratulated for their tremendous work on behalf of patients with CKD. Finally, for UACR, its time has come. ■

FIGURE | **CKD Heat Map**

				Albuminuria categories		
				A1	**A2**	**A3**
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-299 mg/g 3-29 mg/mmol	≥300 mg/g ≥30 mg/mmol
GFR Stages	**G1**	Normal or high	≥90			
	G2	Mildly decreased	60-90			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

KEY TO FIGURE

Colors: Represents the risk for progression, morbidity and mortality by color from best to worst.
Green: Low Risk (if no other markers of kidney disease, no CKD)
Yellow: Moderately Increased Risk
Orange: High Risk
Red: Very High Risk
Deep Red: Highest Risk

Source: www.kidney.org/content/kidney-failure-risk-factor-urine-albumin-to-creatinine-ration-uacr

REFERENCES

1. Alfego D, Ennis J, Gillespie B, et al. Chronic kidney disease testing among at-risk adults in the U.S. remains low: real-world evidence from a national laboratory database. *Diabetes Care*. 2021;44(9):2025-2032. doi:10.2337/dc21-0723

2. Shin JI, Chang AR, Grams ME, et al; CKD Prognosis Consortium. Albuminuria testing in hypertension and diabetes: an individual-participant data meta- analysis in a global consortium. *Hypertension*. 2021;78(4):1042-1052. doi:10.1161/HYPERTENSIONAHA.121.17323

3. Stempniewicz N, Vassalotti JA, Cuddeback JK, et al. Chronic kidney disease testing among primary care patients with type 2 diabetes across 24 U.S. health care organizations. *Diabetes Care*. 2021;44(9):2000-2009. doi:10.2337/dc20-2715

4. Kidney numbers and the CKD Heat Map. National Kidney Foundation. Accessed August 8, 2023. https://www.kidney.org/atoz/content/chronic-kidney-disease-quality-care-begins-measurement

5. Chu CD, Powe NR, McCulloch CE, et al; Centers for Disease Control and Prevention Chronic Kidney Disease Surveillance Team. Trends in chronic kidney disease care in the US by race and ethnicity, 2012-2019. *JAMA Netw Open*. 2021. doi:10.1001/ jamanetworkopen.2021.27014

6. Murphy DP, Drawz PE, Foley RN. Trends in angiotensin-converting enzyme inhibitor and angiotensin II receptor blocker use among those with impaired kidney function in the United States. *J Am Soc Nephrol*. 2019;30(7):1314-1321. doi:10.1681/ASN.2018100971

7. Chu CD, Powe NR, McCulloch CE, et al; Centers for Disease Control and Prevention Chronic Kidney Disease Surveillance Team. Angiotensin converting enzyme inhibitor or angiotensin receptor blocker use among hypertensive US adults with albuminuria. *Hypertension*. 2021;77(1):94-102. doi:10.1161/HYPERTENSIONAHA.120.16281

8. McCoy IE, Han J, Montez-Rath ME, Chertow GM. Barriers to ACEI/ARB use in proteinuric chronic kidney disease: an observational study. *Mayo Clin Proc*. 2021;96(8):2114-2122. doi:10.1016/j.mayocp.2020.12.038

9. Lamprea-Montealegre JA, Madden E, Tummalapalli SL, et al. Prescription patterns of cardiovascular- and kidney-protective therapies among patients with type 2 diabetes and chronic kidney disease. *Diabetes Care*. 2022;45(12):2900-2906. doi:10.2337/dc22-0614

10. Chu CD, Xia F, Du Y, et al. Estimated prevalence and testing for albuminuria in US adults at risk for chronic kidney disease. *JAMA Network Open*. 2023. doi:10.1001/ jamanetworkopen.2023.26230

Kidney Outcomes in GRADE Study

continued from page 1

also prevents a decrease in estimated glomerular filtration rate (eGFR) and kidney failure.

Several classes of glucose-lowering drugs have been shown to have kidney benefits in patients with type 2 diabetes, independent of glycemic effects. The kidney benefit effect has been seen primarily in patients with DKD, atherosclerotic cardiovascular disease, or high atherosclerotic cardiovascualr disease risk. Dipeptidyl peptidase 4 (DPP-4) inhibitors, glucagonlike peptide-1 (GLP-1) receptor agonists, and sodium-glucose cotransporter-2 (SGLT2) inhibitors have all been shown to reduce albuminuria in DKD, compared with placebo or other glucose-lowering drugs. SGLT2 inhibitors have also been shown to slow the decrease in eGFR Over time and GLP-1 receptor agonists have shown potential benefits with regard to eGFR loss in short-term studies and secondary analyses of cardiovascualr outcome trials.

The GRADE (Glycemic Reduction Approaches in Diabetes: A Comparative Effectiveness) study was designed to compare glycemic and other outcomes among four commonly used classes of glucose-lowering medications added to metformin (NCT01794143). **Deborah J. Wexler, MD, MSc,** and colleagues reported in the effects of GRADE interventions on detailed kidney outcomes [*JAMA Internal Medicine.* doi:10.1001/jamainternmed.2023.1487].

The GRADE study was a randomized, clinical trial conducted at 36 sites across the United States. Eligible adult participants had type 2 diabetes for less than 10 years, a hemoglobin A1C level between 6.8% and 8.5%, and eGFR ≥60 mL/min/1.73 m^2 who were receiving metformin treatment. Between July 8, 2013, and August 17, 2027, 5047 participants were enrolled. Follow-up continued for a mean of 5.0 years. Data analysis was conducted from February 21, 2022, to March 27, 2023.

The main outcome of interest was chronic eGFR slope (change in eGFR between year 1 and trial end) and a composite kidney disease progression outcome (albuminuria, dialysis, transplant, or death due to kidney disease). Secondary outcomes were incident eGFR less than 60 mL/min/1.73 m^2, 40% decrease in eGFR to <60 mL/min/1.73 m^2, doubling of urine albumin-to-creatinine ratio (UACR) to 30 mg/g or greater, and progression of Kidney Disease Improving Global Outcomes stages. Analyses were intention-to-treat.

Of the 5047 participants, 63.6% (n=3210) were men, and 36.4% (n=1887) were women. Mean age was 57.2 years, mean body mass index was 34.3 kg/m^2, and mean blood pressure was 128.3/77.3 mm Hg. At baseline, 58.1% (n=2933) were treated with renin-angiotensin-aldosterone system (RAAS) inhibitors. Mean baseline eGFR was 94.9 mL/min/1.73 m^2 and 2.5% of participants (n=125) had a baseline eGFR <60 mL/min/1.73 m^2. In 14.2% of participants (n=716), UACR was moderately elevated; UACR was severely elevated in 1.7% (n=84). Mean duration of the diagnosis of diabetes was 4.2 years.

Due to missing data, 98 patients were excluded from the analysis. Over the course of the study, mean hemoglobin A1c was 7.2%, mean blood pressure was 128/76 mm Hg, 64.4% of participants (n=2510) were treated with RAAS inhibitors, and 82.2% (n=3201) were treated with any blood-pressure-lowering medications at year 4. There were minor differences across some treatment groups. Mean eGFR was measured 5.4 times per participant and UACR was measured 9.8 times per participant. The rates of permanent discontinuation of assigned study medication were 14% for glargine, 23% for glimepiride, 23% for liraglutide, and 19% for sitagliptin.

KIDNEY OUTCOMES

During the study period, mean eGFR decreased, with a chronic slope from year 1 to trial end of –2.01 (95% CI, –2.10 to –1.92) mL/min/1.73 m^2 per year among all study participants. Mean chronic eGFR slope was –2.03 (95% CI, –2.20 to –1.86) mL/min/1.73 m^2 for participants receiving sitagliptin; –1.92 (95% CI, –2.08 to –1.75) mL/min/1.73 m^2 for those receiving glimepiride; –2.08 (95% CI, –2.26 to –1.90) mL/min/1.73 m^2 for those receiving liraglutide; and –2.02 (95% CI, –2.19 to –1.84) mL/min/1.73 m^2 for those receiving insulin glargine.

There were no significant differences in slope among the treatment groups. Further, there were no significant differences in mean total slope starting from baseline, change in eGFR during the first year of the study, confirmed progression to eGFR less than 60 mL/min/1.73 m^2, or confirmed 40% decrease in eGFR.

A total of 592 patients experienced the composite kidney disease progression coprimary outcome: 135 (10.6%) in the sitagliptin group; 155 (12.4%) in the glimepiride group; 152 (12.0%) in the liraglutide group; and 150 (11.9%) in the insulin glargine group. Of the 592 events, 82.6% (n=489) consisted of progression from normal to moderately elevated albuminuria. Ninety-three patients (15.8%) developed severely elevated albuminuria, and 10 had dialysis, kidney transplant, or death from kidney disease.

By year 4, the Kaplan-Meier-estimated cumulative incidence of the coprimary outcome of progression of kidney disease was 10.3% in the glargine group, 10.4% in the glimepiride group, 10.1% in the liraglutide group, and 9.3% in the sitagliptin group. There were no significant differences across treatment groups for the duration of study follow-up. At 5 years, the 5-year cumulative incidence of the coprimary composite kidney disease progression was 11.7% overall.

There were no significant differences across treatment groups in secondary outcomes. There were no adverse kidney events attributable to medication assignment.

The researchers cited some limitations to the study, including the relatively short follow-up time and the lack of an SGLT2 inhibitor arm because at the time that GRADE was designed, SGLT2 inhibitors were not approved.

In summary, the authors said, "As a randomized clinical trial of next-step therapy after metformin, GRADE enrolled a low-risk cohort of participants with type 2 diabetes, largely free of cardiac and kidney disease at baseline. The results of GRADE suggest that, in people with type 2 diabetes predominantly without kidney complications at baseline, a DPP-4 inhibitor, sulfonylurea, GLP-1 receptor agonist, or basal insulin added to metformin are equivalent with respect to the development or progression of DKD over 5 years." ■

TAKEAWAY POINTS

- Researchers reported results of an analysis of kidney outcomes in the GRADE (Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness) study comparing four classes of glucose-lowering medications added to metformin.
- The study participants were adults with type 2 diabetes and without kidney disease.
- There were no significant differences across treatment groups in decreased estimated glomerular filtration rate, progression of albuminuria, dialysis, kidney transplant, or death.

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AKI and Risk of Cardiovascular Events

continued from page 1

data in the Duke Databank for Cardiovascular Disease. The database includes all patients who underwent cardiac catheterization at Duke University Medical Center in Durham, North Carolina, between 1974 and 2014. Patients who underwent PCI at Duke between January 1, 2003, and December 31, 2013, were included in the study.

The study exposure was AKI, defined as a ≥1.5-fold relative elevation in serum creatinine within 7 days from a reference value ascertained 30 days prior to PCI, or a 0.3 mg/dL increase from the reference value within 48 hours. The primary study outcome of interest was a composite of all-cause death, myocardial infarction, stroke, or revascularization during the first year after PCI. Secondary outcomes were each individual component of the composite cardiovascular outcome.

Cox regression models adjusted for potential confounders and with interaction terms between AKI and race, diabetes, or baseline estimated glomerular filtration rate (eGFR) were used to examine the association between AKI and increased cardiovascular risk at 1 year after PCI.

The analytic cohort included 9422 unique patients who underwent an index PCI procedure during the study period. Most patients self-identified as White (75%, n=7084), 20% self-identified as Black (n=1864), and 5% self-identified as Native American or other (n=484). Median age was 63 years, and median household income was $44,612.

Overall, 32% of PCI procedures (n=3027) were urgent/emergent. Among patients with AKI, 43% of the procedures were urgent/emergent, and among patients without AKI, 31% were urgent/emergent. Most patients had a previous diagnosis of hypertension (70% overall, n=6607). Median baseline eGFR was 74 mL/min/1.73 m^2, and 30% of the cohort (n=2804) had diabetes. Only 1.7% (n=179) had diabetes with end organ damage.

Nine percent of the cohort (n=865) developed AKI within 7 days after PCI. The incidence of AKI was highest among Black patients (14%, n=258) relative to White patients (8%, n=561) and Native American/other patients (10%, n=46).

Overall, 21% of patients (n=2017) met the definition of the primary composite outcome at 1 year after PCI. For secondary outcomes, the rates were 6% (n=579) for death, 8% (n=719) for myocardial infarction, 3% (n=26) for stroke, and 11% (n=1031) for revascularization. The event rate for the composite outcome was 2-fold higher for patients with AKI compared with those without AKI (41% vs 20%), which was driven by death (21% vs 5%) and myocardial infarction (17% vs 7%).

AKI, compared with no AKI, was associated with greater risk for the primary composite outcome (adjusted hazard ratio [aHR], 1.94; 95% CI, 1.71-2.20). There was also an association between AKI and greater risks for death, myocardial infarction, and stroke. There was no association between AKI and revascularization.

There were significant differences by race in risks for the primary composite outcome (P=.04): compared with White patients, risk was greater in Black patients (aHR, 1.09; 95% CI, 0.97-1.22) but lower in Native American/other patients (aHR, 0.81; 95% CI, 0.65-1.01). The difference in risk between White and Black patients was driven by greater myocardial infarction risk in Black versus White patients (aHR, 1.43; 95% CI, 1.19-1.71; P<.001). There were no significant differences by race in risks for the other individual components of the composite outcome.

There was an association between diabetes without reported end organ dysfunction compared with no diabetes, and a greater risk for the primary composite outcome (aHR, 1.18; 95% CI, 1.07-1.31). For diabetes with reported end organ dysfunction, the risk was even greater, although the subgroup was small. Reduced baseline eGFR was also associated with graded, higher risk for the primary outcome (P for trend <.001). With the exception of vascularization, the risks were evident for all secondary outcomes.

There was no significant modification to the association between AKI and risk for the composite outcome based on baseline eGFR. However, the associations of AKI versus no AKI with increased risk for all-cause death were significantly greater in the higher eGFR categories.

With White patients with no AKI as the reference, the risk for the composite outcome was highest in Black patients with AKI (HR, 2.27; 95% CI, 1.83-2.82), followed by White patients with AKI (HR, 1.87; 95% CI, 1.58-2.21). The risk was least in patients of other races with AKI (HR, 1.48; 95% CI, 0.88-2.48). The results were similar with individual components of the composite outcome, with the exception of revascularization.

Study limitations cited by the authors included the observational nature of the study, the single-center design, and the possibility that the study was underpowered.

In conclusion, the researchers said, "AKI compared with no AKI conferred greater risks for a composite cardiovascualr outcome comprising, death, myocardial infarction, stroke, and revascularization at 1 year after PCI, but this AKI-associated risk did not differ significantly by race, diabetes, or baseline kidney function. Despite the lack of differential AKI-associated risk by race, Black patients with AKI had qualitatively greater cardiovascular risk at 1 year after PCI than White patients with AKI. Thus, AKI prevention interventions to offset cardiovascualr risk after PCI should be prioritized in all patients undergoing the procedure." ■

TAKEAWAY POINTS

- Researchers conducted an observational cohort study to test the hypothesis that acute kidney injury (AKI) would be differently associated with increased cardiovascular risk at 1 year after percutaneous coronary intervention (PCI), with a more pronounced association in Black patients than in White patients.
- AKI was associated with a nearly 2-fold higher risk of a composite outcome of all-cause death, myocardial infarction, stroke, or revascularization, compared with no AKI.
- Black race and severely reduced estimated glomerular filtration rate, but not diabetes, had a cumulative impact with AKI on the risk for the composite outcome.

Early Acetaminophen Exposure

continued from page 1

years of age who had cardiac surgery. MIMIC-III (version 1.4) included deidentified clinical details from 46,476 patients who had 61,532 ICU admissions in 2001-2012 at Beth Israel Deaconess Medical Center in Boston, Massachusetts; eICU (version 2.0) included 139,367 patients who had 200,859 ICU admissions in 2014-2015 at 208 hospitals across the continental United States.

The study exposure was administration of acetaminophen in the first 48 hours following surgery. The primary outcome of interest was severe AKI in the first 7 days following surgery, defined as stage 2 or stage 3 AKI according to Kidney Disease Improving Global Outcomes (KDIGO) criteria. Secondary outcomes included any stage AKI in the first 7 days after surgery, any new-onset postoperative kidney replacement therapy (KRT) during the index surgical admission, and in-hospital mortality. Multivariable cause-specific hazards regression analysis was used to characterize the association between early acetaminophen exposure and severe AKI.

Following application of inclusion criteria, the study cohort included 5791 cardiac surgical patients in the MIMIC-III database, and 3840 in the eICU database. In both cohorts, most patients were White and male. In MIMIC-III, 53% of the surgeries were non-elective versus only 7.5% of those in the eICU cohort.

Early postoperative acetaminophen was administered to 72% of patients in the MIMIC-III cohort and 71% of patients in the eICU cohort. Using both serum creatinine and urine output criteria, the incidence of severe postoperative AKI stages 2-3 using the KDIGO definition was 58.5% in the MIMIC-III cohort and 37.3% in the eICU cohort. The proportion of patients who developed any stage AKI was 86% in the MIMIC-III cohort and 50% in the eICU cohort. In a post hoc analysis using only serum creatinine criteria to diagnosis severe AKI, there was a significant decrease in incidence: 14.9% in the MIMIC-III cohort and 8.0% in the eICU cohort.

In general, patients who were given acetaminophen were more likely to be White, have a lower baseline hemoglobin concentration, need more postoperative vasopressor support and more mechanical ventilation, and were more often given high-risk nephrotoxins following surgery.

In the MIMIC-III cohort, the incidence of severe postoperative cardiac surgery-associated AKI was lower in patients given acetaminophen within 48

Following adjustment for clinically relevant covariates, there was an association between early administration of acetaminophen and a lower hazard of postoperative severe AKI in both the MIMIC-III cohort (adjusted hazard ratio [aHR], 0.86; 95% CI, 0.79-0.94; *P*<.001) and the eICU cohort (aHR, 0.84; 95% CI, 0.72-0.97; *P*=.02).

hours after surgery compared with those who were not given acetaminophen within 48 hours (52% vs 75%, respectively; *P*<.001). In the eICU cohort, the incidence of severe AKI was also lower in patients administered acetaminophen compared with those not exposed to acetaminophen (36.0% vs 40.3%, respectively; *P*=.01).

In both cohorts, the incidence of serve AKI defined only by serum creatinine was also significantly lower in the acetamino-

continued on page 8

Print-only Content

continued from page 7

There were no statistically significant associations in either cohort between acetaminophen exposure and the proportion of patients requiring postoperative kidney replacement therapy or in the rate of in-hospital mortality.

phen group compared with the group not exposed to acetaminophen: MIMIC-III, 11.9% vs 22.7%, respectively; *P*<.001); eICU, 7.3% vs 9.7%, respectively; *P*=.02).

Following adjustment for clinically relevant covariates, there was an association between early administration of acetaminophen and a lower hazard of postoperative severe AKI in both the MIMIC-III cohort (adjusted hazard ratio [aHR], 0.86; 95% CI, 0.79-0.94; *P*<.001) and the eICU cohort (aHR, 0.84; 95% CI, 0.72-0.97; *P*=.02). In the multivariable logistic regression model, there was an association between acetaminophen exposure as a dichotomous variable and a significant reduction in the risk of severe AKI in both cohorts: MIMIC-III, adjusted odds ratio (aOR), 0.48; 95% CI, 0.42-0.56; *P*<.001, and eICU, aOR, 0.80; 95% CI, 0.69-0.93; *P*=.004.

There was an independent association between use of acetaminophen and lower odds of any stage AKI in both cohorts. Following adjustment for covariates, there were no statistically significant associations in either cohort between acetaminophen exposure and the proportion of patients requiring postoperative KRT or in the rate of in-hospital mortality.

The inability to evaluate dosing of acetaminophen was cited by the authors as a limitation to the study findings.

In summary, the researchers said, "In two large registries, we found that acetaminophen use in the first 48 hours after cardiac surgery was associated with a lower incidence of postoperative severe AKI in adults recovering from cardiac surgery. Our results are largely consistent with the experimental results and the limited clinical data, and they suggest that a trial of acetaminophen for prevention of kidney injury is warranted." ■

TAKEAWAY POINTS

- Researchers reported results of a study testing the hypothesis that administration of acetaminophen in the early postoperative period following cardiac surgery would be associated with reduced incidence of severe acute kidney injury (AKI).
- In multivariable regression models, there was an association between early postoperative use of acetaminophen and a lower risk of severe AKI.
- The benefit was consistent across sensitivity and subgroup analyses.

Conference Coverage

San Diego, California | June 3-7, 2023

AMERICAN TRANSPLANT CONGRESS 2023

The American Transplant Congress is the joint annual meeting of the American Society of Transplant Surgeons and the American Society of Transplantation. The Congress provides a forum for the exchange of new scientific and clinical information related to solid organ and tissue transplantation. Presentations and posters provide information on advances in research and care to transplant physicians, scientists, nurses, organ procurement professionals, pharmacists, and other transplant professionals.

The American Transplant Congress was held June 3–7 in San Diego, California, providing a showcase for the latest research and advances made by the transplant community in the past year.

Conference Coverage

San Diego, CA | June 3-7, 2023

Outcomes of Hemodialysis in Patients With Hepatorenal Syndrome

Patients with alcoholic hepatitis (AH) who develop hepatorenal syndrome (HRS) have poor prognosis and frequently require hemodialysis as renal replacement therapy. Hemodialysis in this patient population can result in electrolyte imbalances and volume overload. Hemodialysis to treat HRS generally is considered a bridge to eventual liver transplant. However, according to **U. Farooq** and colleagues, hemodialysis is frequently initiated in patients with AH without clear liver transplant plans.

The researchers conducted a study designed to describe outcomes of use of hemodialysis for HRS in patients with AH in 2019. Results of the study were reported during an oral abstract session at the American Transplant Congress 2023. The presentation was titled *A Nationwide Analysis of Utilization of Hemodialysis for Hepatorenal Syndrome in Alcoholic Hepatitis and Outcomes With Liver Transplant.*

Adult patients with AH and a concurrent diagnosis of HRS were identified using the National Readmission Database 2018, using *International Classification of Diseases, Tenth Revision* codes. Fisher exact test was used to compare proportions and adjusted *P* values were computed using multivariate regression analysis.

Of the 73,203 patients admitted with AH during 2019 in the data sample, 4.9% (n=3620) had an associated diagnosis of HRS. Inpatient mortality was significantly higher in patients with AH and concurrent HRS compared with those without HRS (25.5% vs 2.1%; *P*<.01). Of those with HRS, 14.7% received hemodialysis during the hospital stay. Inpatient mortality was higher in patients with AH and HRS who received hemodialysis compared with those who did not receive hemodialysis (adjusted odds ratio, 1.18; 95% CI, 1.3-2.6).

The initiation of hemodialysis was associated with greater use of resources: longer length of stay, higher costs, greater intensive care unit utilization for vasopressor, sepsis management, and mechanical ventilation. A monthly survival benefit was noted only in patients who underwent liver transplant. Among patients with HRS receiving hemodialysis, 13.6% underwent liver transplant, resulting in significantly lower mortality (31.8% vs 0%; *P*=.01).

In conclusion, the authors said, "The initiation of hemodialysis for HRS in AH patients is associated with higher mortality, except in those who underwent liver transplant. However, there is significantly higher utilization of resources without survival benefit when liver transplant is not an option in patients with AH. Therefore, candidacy for hemodialysis should be carefully considered in patients who will not be eligible for liver transplant. There is an urgent unmet need for medical therapies to reverse HRS and reduce hemodialysis needs in patients with AH."

Source: Farooq U, Tarar Z, El Alayli A, Jaan A, Qureshi K. A nationwide analysis of utilization of hemodialysis for hepatorenal syndrome in alcoholic hepatitis and outcomes with liver transplant. Abstract 177. Abstract of an oral presentation at the American Transplant Congress 2023; June 3-7, 2023; San Diego, California.

Discard Rate of Deceased Black Donor Kidneys

There is an association between Black donor race and a higher risk of transplant failure, an association that is incorporated into the Kidney Donor Profile Index (KDPI). There is also an association between Black donor race and the rate of kidney discard. Results of recent studies have suggested that independent of a novel race-free KDPI, kidneys from Black deceased donors had higher odds of discard.

O. Aiyegbusi and colleagues conducted an analysis to clarify the association between donor race and utilization of deceased donor kidneys. Results were reported during an oral abstract session at the American Transplant Congress 2023 in a presentation titled *Black Donor Race and Deceased Donor Kidney Utilization.*

The analysis included data from the Scientific Registry of Transplant Recipients from January 1, 2015, to December 31, 2018. The researchers sought to determine the proportion of kidneys discarded in Black and non-Black donors within KDPI deciles separately in neurological brain dead donors (NBD) and donation after circulatory death (DCD) donors.

During the study period, there were 169,638 kidneys recovered for transplantation. Overall, 18% of non-Black donor kidneys were discarded compared with 22% of kidneys from Black donors. Within KDPI deciles, the rate of kidney discard was lower among Black donor kidneys compared with non-Black donor kidneys. Results were similar in both NBD and DCD donor kidneys.

In summary, the authors said, "The findings show that within KDPI groups, there is lower discard of Black donor kidneys, and donor source does not impact kidney utilization independent of the KDPI. The higher overall discard of Black donor kidneys is observed due to the inclusion of a race coefficient in the KDPI, which systematically assigns a higher KDPI to Black donor kidneys. Therefore, more kidneys from Black donors are categorized as KDPI ≥85%, a threshold beyond which the majority of donated kidneys are discarded. The findings suggest that removing the race coefficient from the KDPI may increase the utilization of Black donor kidneys, which could increase the transplantation rate among Black donor wait-list candidates."

Source: Aiyegbusi O, Chang D, Fakhredine S, Gill J. Black donor rate and deceased donor kidney utilization. Abstract 310. Abstract of an oral presentation at the American Transplant Congress 2023; June 3-7, 2023; San Diego, California.

Using Glomerulosclerosis in KDPI to Predict Graft Survival

The Kidney Donor Profile Index (KDPI) is key in kidney transplantation, but may have some shortcomings such as a lack of postprocurement data, including biopsies. According to **S. Weiss** and colleagues, while biopsies are associated with the 20% to 25% kidney nonuse rate in the United States, the role of biopsies is not well defined.

Previous research has suggested that the dose-response relationship between glomerulosclerosis (GS) and 10-year survival attenuated for GS beyond 10%, yet the kidney nonuse rate has continued to risk substantially for kidneys with GS beyond 10%. To test the hypothesis that integrating GS into KDPI can provide context regarding the strength of the association between GS and graft survival relative to other factors, potentially increasing kidney usage, the researchers conducted a data analysis to examine the impact of adding GS to the KDPI model. Results were reported during an oral abstract session at the American Transplant Congress 2023 in a presentation titled *A Glomerulosclerosis-Informed KDPI to Better Predict Long-Term Kidney Graft Survival.*

The analysis utilized data from the Organ Procurement and Transplantation Network on 5997 extended criteria donor transplants from 2008 to 2012. GS was added to the KDPI formula using a two-piece linear spline (knot at 10%). Case-level predictions were made using two assumptions for the hazard rate slope for GS >10%: slope=0; slope=upper 95% confidence limit of the GS hazard ratio.

The C-statistic increase from adding GS was small (0.002) but comparable with other key variables such as creatinine. The GS slope change was significant (*P*=.0028). There was a slightly negative slope in the post-knot spline, due possibly to selection bias or data artifacts.

Across a range of observed and hypothetical GS values, clinical predictions varies for individual cases. For a kidney with 3% GS, the current KDPI of 88 would drop to 83 in a KDPI informed by GS. Had that same kidney had 15% GS, the decrease in the predicted graft half-life would be <1 year using a KDPI informed by GS (8.0 years) rather that the current KDPI (8.9 years).

"By showing that a low GS can reduce KDPI (sometimes to <85%) while a high GS can only moderately elevate an already high KDPI, a GS-informed KDPI provides a data driven framework for physicians to use GS in their decision making. Incorporating GS into KDPI or other predictive models has the potential to help clinicians 'rule-in' more and 'rule-out' fewer kidneys based on biopsy results, and ultimately, increase kidney utilization," the authors said.

Source: Weiss S, Foutz J, Kamal L, et al. A glomerulosclerosis-informed KDPI to better predict long-term kidney graft survival. Oral abstract 485. Abstract presented at the American Transplant Congress 2023; June 3-7, 2023; San Diego, California.

Age Disparities in Kidney Transplant and Repeat Transplant Access

Improved access to kidney transplantation as well as better rates of patient survival may be associated with an increase in older kidney transplant recipients experiencing graft failure. **Y. Chen** and colleagues conducted a study designed to examine age disparities in access to first and repeat kidney transplantation.

Results of the study were reported during a poster session at the American Transplant Congress 2023. The poster was titled *Age Disparities in Access to First and Repeat Kidney Transplantation.*

The study utilized data from the United States Renal Data System to identify 2.495,031 adult transplant naïve dialysis patients and 110,338 adult kidney transplant recipients who experienced failure of the first graft between 1995 and 2018. Survival analysis was used to compare the likelihood of waitlisting and receiving repeat kidney transplantation versus first kidney transplantation by patient age (18 to 64 years of age vs ≥65 years of age).

Compared with kidney transplant recipients 18 to 64 years of age, those ≥65 years of age with graft failure had a lower chance of being listed for repeat kidney transplantation (adjusted hazard ratio [aHR], 0.37; 95% CI, 0.36-0.39) as well as a lower chance of receiving repeat kidney transplantation (aHR, 0.75; 95% CI, 0.70-0.79).

Between 1995 and 2018, there was no significant difference in the magnitude of age disparities in access to repeat kidney transplantation among patients with graft failure. There were age disparities observed in access to first kidney transplantation: chance of being waitlisted, aHR, 0.24; 95% CI, 0.23-0.24; and chance of receiving a kidney transplant, aHR, 0.86; 95% CI, 0.84-0.89.

Age disparities in waitlisting for a first kidney transplant were greater among transplant-naïve older patients than among older patients with graft failure waitlisting for repeat kidney transplant ($P_{interaction}$<.001). Disparities in receipt of a kidney transplant were similar ($P_{interaction}$<.09).

In conclusion, the researchers said, "Age disparities exist in access to both repeat kidney transplantation and first kidney transplantation; however, some of this disparity is attenuated among older adults with graft failure, a population that already received kidney transplantation and [is] familiar with transplant procedures. Transplant centers should be aware of these age disparities and help identify appropriate older patients who would benefit from the first and repeat kidney transplantation, regardless of their age."

Source: Chen Y, Churilla B, Quint E, et al. Age disparities in access to first and repeat kidney transplantation. Poster B304. Abstract of a poster presented at the American Transplant Congress 2023; June 3-7, 2023; San Diego, California.

Use of SGLT2 Inhibitors in Kidney Transplant Recipients

In patients with chronic kidney disease (CKD), use of sodium glucose cotransporter-2 (SGLT2) inhibitors has been associated with improved renal and cardiovascular outcomes. However, there is concern regarding use of SGLT2 inhibitors due to the risk of acute kidney injury (AKI) and urogenital infections.

During a poster session at the American Transplant Congress 2023, **L. Liriano-Ward** and colleagues at the Montefiore Medical Center, Albert Einstein School of Medicine, Bronx, New York, reported on outcomes of kidney transplant recipients treated with SGLT2 inhibitors. The poster was titled *A Single Center Experience With SGLT-2 Inhibitors Treatment in Renal Transplant Recipients.*

The retrospective review included data on 85 of the 142 adult renal transplant patients who received treatment with an SGLT2 inhibitor. Exclusion criteria were combined organ transplant, missing data, or less than 1 month follow-up since initiation of treatment. Median age of the cohort was 65 years, 64.7% were male, 28.2% were Black, and 55.3% were Hispanic. The etiology of end-stage renal disease was diabetes in 56.5% of the cohort, hypertension in 24.7%, and glomerulonephritis in 9.4%. Sixty-seven percent received a deceased donor transplant and median dialysis vintage was 26 months.

Ninety-four percent of the patients had diabetes and treatment with an SGLT2 inhibitor was initiated at a median 73 months posttransplant. Of the overall cohort, 51.8% were started on dapagliflozin at a median starting dose of 5 mg daily, 45.9% were started on empagliflozin at 10 mg daily, and 2.3% were started on canagliflozin at 50 mg daily. By the end of the study period, 15.3% of the patients had discontinued the medication.

Median follow-up was 7.3 months. At follow-up, allograft survival was 97.6% and patient survival was 94.1%. AKI occurred in 11.8% of the cohort, urinary tract infection in 15.3%, hypoglycemia in 10.6%, and hypotension in 9.4%. None of the patients developed acute rejection.

Compared with prior to treatment, serum creatinine was higher at last follow-up (1.45 mg/dL vs 1.28 mg/dL; P=.04). There was no significant decrease in spot urine protein to creatinine ratio (822.6 mg/g vs 685.8 mg/g; P=.05). Following treatment, patients' metabolic profile was significantly improved: body mass index was lower (26.9 kg/m^2 vs 28.5 kg/m^2 before treatment; P=.04), systolic blood pressure was lower (131 mm Hg vs 139 mm Hg; P=.02), and hemoglobin A1c was lower (7.7 vs 8.4; P=.01), Magnesium levels also improved following treatment (1.8 vs 1.7; P=.006).

In conclusion, the authors said, "Renal transplant patients treated with SGLT2 inhibitors had improved metabolic profile and no major adverse events. The incidence of AKI and urinary tract infection is comparable to published data in the transplant population. Larger studies are required to evaluate clinical outcomes in this patient population."

Source: Liriano-Ward L, Azzi Y, Pynadath C, et al. A single center experience with SGLT2 inhibitor treatment in renal transplant recipients. C176. Abstract of a poster presented at the American Transplant Congress 2023; June 3-7, 2023; San Diego, California.

AI-Enabled Prediction Model May Increase Use of High-Risk Kidneys

At present, allocation of high-risk deceased donor kidneys requires organ procurement organizations (OPOs) to perform a prolonged manual process, resulting in extended cold ischemia time and potential harm to kidney quality. Researchers, led by **R. Threlkeld,** aimed to develop an interactive digital simulation tool to identify high-risk kidneys that are hard to place and justify starting an accelerated placement process sooner.

Results were reported during a poster session at the American Transplant Congress 2023. The poster was titled *AI-Enabled Digital Support to Increase Placement of Hard to Place Deceased Donor Kidneys.*

AnyLogic software was used to develop the digital simulation tool to test kidney allocation policies and their effect on acceptance of deceased donor kidneys. The tool estimates the increased likelihood of placement, improves the current allocation model, and quantifies the system-level performance of OPO efforts to increase utilization of hard-to-place kidneys. AI models were developed to inform probability of utilization and identify transplant centers likely to accept and transplant high-risk kidneys. Users have the ability to adjust or scale factors to observe the influence on final decision offerings and policies.

Key performance parameters (KPP) of kidney utilization and observed/expected kidney transplants are used to measure the effectiveness of the digital simulation tool. Other calculated measures include allocation time, out-of-sequence allocation, and anticipated ischemia time.

To analyze the effect of KPPs and likelihood of utilization at varying times during the kidney allocation process, kidney characteristics can be adjusted. KPPs include age, Kidney Donor Profile Index score, hepatitis C viremic positive on a nucleic acid amplification test status, serum creatinine level, pump metrics, diabetes, biopsy, glomerulosclerosis, glomerulicount, race, hypertension and cold ischemic times. Historical UNOS data with and without the AI model will be used to validate and verify the approach.

In summary, the authors said, "The digital simulation tool predicts an increased deceased donor kidney utilization from early engagement in accelerated placement for out-of-sequence allocation, hence supporting high-risk kidney allocation policy changes. Future work will include incremental updates to the simulation and AI models for data-supported aggressive transplant centers willing to transplant high-risk kidneys."

Source: Threlkeld R, Ashiku L, Dzieran R, et al. AI-enabled digital support to increase placement of hard to place deceased donor kidneys. Poster B133. Abstract of a poster presented at the American Transplant Congress 2023; June 3-7, 2023; San Diego, California.

Transplanted Recycled Kidney: A Case Report

The United States is facing an ongoing shortage of organs available for transplantation. There are few data available on outcomes of the use of recycling transplanted kidneys. During a poster session at the American Transplant Congress 2023, **K. Yadav** and colleagues at the University of Toledo, Toledo, Ohio, presented a case report of renal transplantation from a donor who had received a kidney transplant 3 years prior to his death. The poster was titled *Recycling Transplanted Kidneys*.

The primary donor was a 14-year-old male who was brain dead following a gunshot wound to the head; terminal creatinine level was 0.47 mg/dL, and the Kidney Donor Profile Index (KDPI) score was 17%. A 48-year-old patient with end-stage renal disease and type 1 diabetes mellitus received a simultaneous kidney-pancreas transplant from the donor. Three years following the kidney-pancreas transplant, the recipient succumbed to a hemorrhagic stroke and became a secondary donor for the case-report patient; terminal creatinine level was 1.12 mg/dL, KDPI score was 94%, and hemoglobin A1c was 5.5%.

The kidney was procured en-bloc with the right common and external iliac artery and vein; the ureter was procured with a bladder cuff. The contralateral common iliac artery was used for cannulation during procurement. Results of the kidney biopsy showed 5% glomerulosclerosis with mild interstitial fibrosis and no vascular changes. Virtual crossmatch was negative and acceptable between the recipient and both the primary and the secondary donor. The renal vessels and ureter were dissected on the back-table and donor iliac vessels were excised. The kidney transplant was done in standard manner to the external iliac vessels. Bladder patch was excised and standard ureteroneocystostomy was performed.

The kidney reperfused well and made urine on the table. The postoperative course was uneventful and graft function was excellent. The recipient developed early BK viremia, first detected on postoperative day 8. He continues to have stable low load BK viremia with stable graft function. His 7-month creatinine level is 1.3 mg/dL.

In summary, the authors said, "Recycling transplanted kidneys requires good procurement technique, meticulous back-table dissection, good recipient selection (thin, good bladder capacity), virtual crossmatch due to unavailability of primary donor sample for physical crossmatch, and close follow-up for early BK viremia. KDPI is not a good measure of kidney quality of these kidneys. Centers should be more open to recycling transplanted kidneys to reduce organ shortage."

Source: Yadav K, Bera T, Masih S, et al. Recycling transplanted kidneys. Poster D142. Abstract of a poster presented at the American Transplant Congress 2023; June 3-7, 2023; San Diego, California.

Use of Kidneys With High KDPI Score

Kidneys available for transplantation in the United States are in limited supply, yet organs with high Kidney Donor Profile Index (KDPI) scores are commonly discarded. **A. Shah** and colleagues at Thomas Jefferson University, Philadelphia, Pennsylvania, conducted an analysis to examine trends in kidney transplantation with kidneys with high KDPI score over the last decade.

Results were reported during a poster session at the American Transplant Congress 2023. The poster was titled *10-Year Trends and Patterns of Kidney Transplantation According to KDPI Score and Factors Associated With Allocation of Higher KDPI Score*.

The researchers utilized the United Network for Organ Sharing's Organ Procurement and Transplantation Network database to identify kidney transplantations from 2010 to 2019. The transplantations were stratified into three groups by KDPI score (<35, 35-85, >85), and data on patient demographic and clinical characteristics were collected. Correlations between patient characteristics and high KDPI kidney transplantations were assessed using logistic regression analyses.

The analysis included data from 106,448 kidney transplant recipients. Mean age was 53 years and 60% were male. Six point eight percent of the transplants during the study period included kidneys with KDPI score >85. Of the transplants with KDPI score >85, 23.8% were performed on recipients ≥70 years of age, 45.5% in recipients 60 to 69 years of age, 30.2% in recipients 30 to 59 years of age, and 0.5% in recipients <30 years of age. The trends over time in utilization of kidneys with KDPI score >85 by age group were largely unchanged.

Results of regression analysis identified associations between several recipient factors and receiving a kidney with KDPI score >85. Compared with recipients <30 years of age, the odds of receiving a kidney with KDPI score >85 among recipients ≥70 years of age were increased 30 fold (odds ratio [OR], 30.6; 95% CI, 22.06-42.39).

Recipients with diabetes were also more likely to receive a kidney with KDPI score >85 (OR, 1.2; 95% CI, 1.08-1.32), as were those who were Black or Hispanic (OR, 1.3; 95% CI, 1.20-1.36 and OR, 1.3; 95% CI, 1.22-1.42, respectively). Women and recipients with glomerulonephritis or congenital rare familial disease were at decreased odds of receiving a kidney with KPDI score >85.

"Contrary to current guidance and expanded criteria, utilization of KDPI kidneys >85 remained modest during 2010-2019," the researchers said. "Several recipient factors, including older age, female sex, and Black or Hispanic [race/ethnicity], were positively associated with utilization of higher KDPI kidneys. This study can inform discussions on resource allocation in kidney transplantation based on KDPI score, especially in the advanced age population."

Source: Shah A, Litvintchouk A, Amaefule A., et al. 10-Year trends and patterns of kidney transplantation according to KDPI score and factors associated with allocation of higher KDPI score. Poster B143. Abstract of a poster presented at the American Transplant Congress 2023; June 3-7, 2023; San Diego, California.

Donation After Circulatory Death: 6-Month Outcomes

In the United States organ donation following circulatory death (DCD) has become more common in recent years. There are two methods for DCD heart donation: (1) thoracoabdominal normothermic regional perfusion (TA-NRP) and (2) super rapid recovery (SRS) with ex-vivo heart perfusion. Both procurement methods are used in successful liver and kidney transplantation.

Researchers, led by **A. Wall,** conducted an analysis of 6-month outcomes of liver and kidney transplantation from DCD heart donors in the United States. Results were reported during an oral abstract session at the American Transplant Congress 2023 in a presentation titled *6-Month Outcomes of Liver and Kidney Transplantation From Donation After Circulatory Death Heart Donors in the US*.

Using the United Network for Organ Sharing database, the researchers identified all successful DCD heart donors from October 1, 2020, through May 20, 2022, with at least 6-month outcomes. Death to cross-clamp time was used to distinguish between TA-NRP DCD donors (>15 minutes) and SRR DCD donors (<15 minutes).

During the study period, there were 202 successful DCD heart donations; of those, 42.1% (n=85) were TA-NRP and 57.9% (n=117) were SRR. Ninety-two point three percent (n=157/170) of kidneys and 71.8% (n=61/85) of livers from TA-NRP heart donors and 94.4% (n=221/234) of kidneys and 58.1% (n=68/117) of livers from SRR donors were used for transplantation. The delayed graft function rate was significantly higher for SRR DCD donors than TA-NRP DCD donors (42.0% vs 12.7%).

Two liver recipients from each group had early graft failures that required retransplantation. Neither group reported ischemic cholangiopathy requiring retransplantation. The liver recipient groups were similar in 1-year patient and graft survival. In multivariate analysis, TA-NRP and use of kidney pump were associated with less risk of delayed graft function.

"TA-NRP DCD abdominal transplantation is showing similar, if not better, results than SRR DCD in the US," the researchers said. "There is further opportunity to expand the utilization of NRP using abdominal-organ-only protocols given these promising outcomes."

Source: Wall A, Gupta A, Martinez E, et al. 6-month outcomes of liver and kidney transplantation from donation after circulatory death heart donors in the US. Abstract 129. Abstract of a presentation at the American Transplant Congress 2023; June 3-7, 2023; San Diego, California.

Prioritization for Recipients of Deceased Donor Kidneys

According to K. L. King and colleagues, while deceased donor kidney allocation is intended to follow an algorithm-ranked match-run list of eligible candidates, organ offers are commonly declined for individual patients. Further, the frequency of transplant centers declining offers for their highest-priority candidates but accepting them for lower-ranked candidates is unknown.

The researchers conducted a retrospective cohort of organ offers to 11 US transplant centers that were the only local transplant center served by their Organ Procurement Organization from 2015 to 2019. Results of the study were reported during an oral abstract session at the American Transplant Congress 2023 in a presentation titled *List Diving to Allocate Kidneys to Lower Waitlist Priority Candidates*.

The study was designed to quantify the proportion of deceased donor kidneys transplanted to candidates who were not their center's highest-ranked candidate in the match-run among the centers with no competition for organs in their local organ pool. Placement of kidneys by quality, grouped by Kidney Donor Profile Index (KDPI) score, was examined, and comparison of estimated posttransplant survival of the skipped candidates versus the recipients was assessed.

Results of the study demonstrated that transplant centers skipped their highest-ranked candidate 68% of the time, going to a median of their fourth-ranked candidates. Kidneys with higher KDPI score were less likely to go to the highest-ranked candidate, with 24% of KDPI ≥85% kidneys going to the top-ranked candidate versus 44% of KDPI 0% to 20% kidneys. The most frequently cited reasons for declining offers to higher-ranked candidates were related to organ/donor quality (65%); the least frequently cited reasons were related to patient or immunologic reasons (16% and 11%, respectively).

In comparisons of estimated posttransplant survival between the skipped candidates and the ultimate recipients, kidneys were placed with recipients with both better and worse estimated posttransplant survival compared with the skipped candidates. Results were similar across all donor quality groups.

In summary, the authors said, "When able, transplant centers frequently skip their highest-ranked candidates to place kidneys with recipients further down the allocation list, even for the highest-quality organs. This suggests the rank list prioritization generated under the current allocation system is incongruent with centers' prioritization of recipients for a given kidney. Improved understanding of how centers determine the appropriate recipient for a given kidney could lead to the incorporation of novel donor and recipient factors into allocation algorithms, improving efficiency and transparency."

Source: King KL, Husain S, Yu M, Adler J, Schold J, Mohan S. List diving to allocate kidneys to lower waitlist priority candidates. Abstract 373. Abstract of an oral presentation at the American Transplant Congress 2023; June 3-7, 2023; San Diego, California.

Predicting Major Adverse Cardiovascular Events After Transplantation

During an oral abstract session at the American Transplant Congress 2023, researchers at the First Affiliated Hospital of Sun Yat-sen University, Guangzhou, Chine, leg by **G. Wu,** reported results of a study designed to develop and validate a nomogram based on preoperative data with NT-proBNP for predicting major adverse cardiovascualr events (MACEs) in kidney transplant recipients. The presentation was titled *A Nomogram for Predicting Major Adverse Cardiovascular Events After Kidney Transplantation*.

The single-center retrospective study utilized data from 782 kidney transplant recipients at the facility from January 2015 to September 2020. Potential predictors were identified using LASSO-Cox regression analyses. The nomogram was developed and evaluated for discrimination, calibration, and clinical usefulness. It was also compared with previous predictive models. NT-proBNP was added to previous models to evaluate model improvement.

During 2.8 years of follow-up. 9.9% (n=58) of patients developed MACEs. Five variables were incorporated into the nomogram: Log2NT-proNT (hazard ratio [HR], 1.43; 95% CI, 1.25-1.64); age (HR, 1.05; 95% CI, 1.03-1.08); body mass index (HR, 1.08; 95% CI, 1.02-1.15); and diabetes (HR, 3.00; 95% CI, 1.67-5.39). The area under the receiver operating characteristic curve was 0.864 at 6 months, 0.859 at 1 year, and 0.838 at 3 years.

Calibration curve analysis demonstrated good consistency and decision curve analysis demonstrated good clinical value. Compared with the previous models in this cohort, the nomogram had higher predictive capacity; previous models were improved when adding NT-proBNP.

"A nomogram was developed with good predictive ability for MACEs in kidney transplant recipients when incorporating NT-proBNP, which could also serve as an addible predictor for previous model enhancement," the authors said.

Source: Wu G, Wang C, Li Q, et al. A nomogram for predicting major adverse cardiovascular events after kidney transplantation. Presentation 390. Abstract of a presentation at the American Transplant Congress 2023; June 3-7, 2023; San Diego, California.

Incompatible Living Donor Kidney Transplant: Long-term Outcomes

For patients with donor-specific antibody (DSA) without a compatible living donor, incompatible living donor (ILD) kidney transplantation carries an increased survival benefit compared with dialysis. There are few data available on longer-term outcomes in patients undergoing ILD kidney transplantation.

To help inform treatment selection for patients with an incompatible willing living donor and counseling for recipients of ILD kidney transplantation, **J. D. Motter** and colleagues at New York University, New York, New York, conducted an analysis comparing long-term outcomes in ILD kidney transplant recipients with those in compatible living donor kidney transplant recipients. Results were reported during an oral abstract session at the American Transplant Congress 2023 in a presentation titled *20-Year Outcomes Following HLA-Incompatible Living Donor Kidney Transplantation*.

Using data from 25 transplantation centers across the United States linked to national registry data, the researchers identified 1406 ILD kidney transplant recipients and 17,542 compatible living donor recipients from 1997 to 2016. Participating centers classified ILD kidney transplant recipients as positive Luminex, negative flow crossmatch (PLNF, n=376); positive flow, negative cytotoxic crossmatch (PFNC, n=687); or positive cytotoxic cross match (PCC, n=343). Multivariate Cox regression was used to quantify the risk of mortality and death-censored graft failure (DCGF), and multilevel mixed-effects linear regression was used to evaluate decline in estimated glomerular filtration rate (eGFR).

At 1-year posttransplant, the cumulative mortality risk for the compatible living donor group, the PLNH group, the PHNC group, and the PCC group was 1.6%, 1.9%, 3.2%, and 8.2%, respectively. The 10-year mortality risks were 22.5%, 18.4%, 29.4%, and 36.1%, respectively, and the 15-year risk was 39.1%, 36.1%, 45.4%, and 51.6%, respectively (P<.001). After adjustment, PLNF recipients had a mortality risk equivalent to that among compatible living donor recipients, while those in the PFNC and PCC groups had 1.48-fold and 1.66-fold higher risk compared with their compatible living donor recipients, respectively.

The cumulative risk for DCGF for the compatible living donor group, the PLNH group, the PHNC group, and the PCC group was 1.9%, 2.1%, 3.4%, and 11.1% at 1 year, respectively. The risk at 10 years was 16.8%, 20.5%, 33.1%, and 41.0%, respectively, and the risk at 15 years was 25.5%, 33.1%, 45.2%, and 52.5%, respectively (P<.001).

Average eGFR immediately following transplant was comparable in all groups. However, the ILD kidney transplant recipients had faster decline in eGFR per year compared with those in the compatible living donor recipient group.

"Patient and graft survival following ILD kidney transplantation is good through 15 years posttransplant, supporting this modality, but survival is worse compared with compatible living donor kidney transplant recipients," the authors said. "ILD kidney transplant recipients bear close monitoring to maximize graft life."

Source: Motter JD, Massie AB, Segev DL. 20-year outcomes following HLA-incompatible living donor kidney transplantation. Abstract 83. Abstract of an oral presentation at the American Transplant Congress 2023; June 3-7, 2023; San Diego, California.

Prevalence and Risks of Anemia in Chronic Kidney Disease

Patients with chronic kidney disease (CKD) frequently develop anemia, defined by the World Health Organization as a hemoglobin concentration of <13 g/dL in men and <12 g/dL in women. As estimated glomerular filtration rate (eGFR) declines, the prevalence of anemia increases, possibly via the development of erythropoietin deficiency and resistance and a heightened inflammatory state. Individuals with anemia are at increased risk for adverse cardiovascular outcomes and death.

Erythropoiesis-stimulating agents (ESAs) mitigate the need for blood transfusions in patients with anemia; however, the use of ESAs has been associated with increased risk of cardiovascular disease. Treatment targets have been scaled back to minimize risk, and ESAs are generally not considered unless for the treatment of severe anemia.

According to **Danielle K. Farrington, MD, MHS,** and colleagues, earlier studies regarding the burden of anemia by level of eGFR were based on older data and small sample sizes. There are few data available on the prevalence of iron deficiency as a cause of anemia or on the prevalence of vitamin B_{12} deficiency, both treatable causes of anemia in patients with CKD.

The researchers conducted a large cross-sectional and prospective cohort study to describe the burden of anemia by level of eGFR and to characterize the frequency of screening for low iron test results and vitamin B_{12} deficiency, the presence of both low iron test results and vitamin B_{12} deficiency by level of eGFR, and the receipt of ESAs in anemia. The study was designed to test the hypothesis that there is a strong association between severe anemia and low eGFR, and that iron deficiency is common when tested for but iron studies are not commonly conducted. Results were reported in the *American Journal of Kidney Diseases* [2023;81(2):201-208].

The outcomes of interest were incident kidney failure with renal replacement therapy (KRT), cardiovascular disease (coronary heart disease, stroke, or heart failure, whichever occurred first), and death. Data were extracted from the Optum Labs Data Warehouse that contains deidentified claims and electronic health record data from a wide range of health care centers in the United States.

The analysis included data from 5,004,957 individuals across 57 health care organiza-

tions. Forty-two percent of the cohort were men, the mean age was 54 years, and 10.1% were Black. Mean hemoglobin was 14 g/dL, and mean eGFR was 87 mL/min/1.73 m^2. Only 8.3% of individuals had available data on urinary albumin-creatinine ratio (UACR), but 35.6% had urine dipstick results. Men and women were similar in those baseline characteristics. Of the total population, 14.9% had diabetes mellitus, and 39.8% had hypertension.

In men, across eGFR categories of 60 to 74, 45 to 59, 30 to 44, 15 to 29, and <15 mL/min/1.73 m^2, the prevalence of severe anemia was 1.3%, 3.1%, 7.5%, 17.4%, and 29.7%, respectively. The corresponding values in women were 1.9%, 3.8%, 8.6%, 19.4%, and 37.6%.

There was a strong association between lower eGFR and increased prevalence of anemia across all categories of hemoglobin. The pattern was similar in men and women; however, across all categories of eGFR, anemia was more prevalent in women than in men. Hemoglobin <9 g/dL was present in 18.8% of women compared with 15.2% of men with an eGFR <15 mL/min/1.73 m^2.

Following adjustment for age, race, and health care organization, the prevalence of different categories of anemia remained very strongly associated with lower eGFR. Adjusted prevalence increased more sharply with lower eGFR for the lower hemoglobin categories such as <9 g/dL as compared with higher hemoglobin categories such as 12 to 13 g/dL. The pattern was similar in men and women. In the fully adjusted model (age, race, eGFR, prevalent cardiovascular disease,

continued on page 16

Print-only Content

continued from page 15

hypertension, UACR, diabetes mellitus, smoking, and health care organization), there were associations between older age and Black race and a higher prevalence of anemia. Extremes of higher eGFR were also associated with higher prevalence of anemia.

Among patients with anemia, iron studies and checks of levels of vitamin B_{12} were infrequent. Of the men with anemia, only 15.6% and 11.7% had iron studies and vitamin B_{12} levels available, respectively. The respective percentages in women were 19.6% and 13.9%. Among those tested, low iron test results were highly prevalent: 60.4% of men and 81.3% of women. In both men and women with anemia, the prevalence of low iron test results was lower with lower eGFR; low iron results were more common in women than in men.

Across all categories of eGFR, vitamin B_{12} deficiency was rare. Total prevalence was 3.0% in men with anemia and 3.5% in women with anemia. The average mean corpuscular volume values were normal across all categories of eGFR, indicating that anemia was most frequently normocytic. The prevalence of low iron test results in those with eGFR >60 mL/min/1.73 m^2 using an alternate ferritin cutoff for the general population demonstrated that even in severe anemia ESA use was extremely uncommon in all categories of eGFR.

Following adjustment for age, race, eGFR, prevalent CKD, hypertension, UACR, diabetes mellitus, smoking, and health care organization, there was an association between lower hemoglobin and an increased risk of KRT, cardiovascular disease, coronary heart disease, stroke, heart failure, and death. The adjusted hazard ratio for death was 2.91 (95% CI, 2.82-3.00) in men with hemoglobin <9 g/dL compared with men with hemoglobin 12 to 13 g/dL.

The presence of low iron test results in anemia was generally associated with a decreased risk of adverse outcomes compared with the absence of low iron test results in those tested.

The authors cited some limitations to the study, including reliance on *International Classification of Diseases* codes for medical diagnoses, obtaining data on mortality from claims data, and the observational design of the study.

In conclusion, the researchers said, "Overall, our study provides generalizable, precise estimates from a large clinical population on the full spectrum of anemia severity. We quantify the association of low eGFR with severe anemia in both men and women. We find that studies to detect iron deficiency are conducted in less than one in five patients with anemia regardless of eGFR level, suggesting a need for greater testing and potentially for iron supplementation. We document that the presence of anemia is consistently associated with incident KRT, cardiovascular disease, coronary heart disease, stroke, heart failure, and death in both men and women independent of other risk factors. Future studies should investigate safe strategies to mitigate the risks associated with anemia in CKD." ■

TAKEAWAY POINTS

- Researchers reported results of a study designed to characterize the burden, risk factors, and risks associated with anemia in chronic kidney disease.
- In fully adjusted models, there was a very strong association between lower estimated glomerular filtration rate and increased prevalence of anemia.
- Among those tested for iron and vitamin B_{12} levels, use of erythropoiesis-stimulating agents was uncommon.

Vaccine Hesitancy Among Parents of Children With Kidney Disease

Vaccine hesitancy is defined as delay in acceptance or refusal of vaccines despite availability of vaccination services. In May 2021, a COVID-19 vaccine was granted Emergency Use Authorization (EUA) by the FDA for children and adolescents ages 12 to 15 years; the authorization was extended to children ages 5 to 11 years in November 2021. However, as of December 16, 2021, just 52.5% of 12- to 17-year-olds and 11.3% of 5- to 11-year-olds had been fully vaccinated. In a national survey conducted in October 2021, 30% of parents with children 5 to 11 years of age said they would "definitely not" vaccinate their child.

Approximately 0.5% of children in the United States have chronic kidney disease (CKD) and are at increased risk for infection-related morbidity and mortality. Studies have demonstrated that adults with CKD are at increased risk of severe COVID-19, as well as for COVID-19-related complications and death. There are only limited data on COVID-19 in children with CKD. Children with CKD may have increased vulnerability to infection and severe disease associated with direct effects of CKD, use of immunosuppressive medications among kidney transplant recipients and glomerular diseases, comorbid conditions such as hypertension and diabetes, and unavoidable exposures at health care facilities (eg, hemodiaysis).

Vaccine hesitancy ranges from acceptance of some vaccines, to uncertainty and delays in vaccination, to complete refusal of all vaccines. **Chia-shi Wang, MD, MSc,** and colleagues in Atlanta, Georgia, conducted a sequential explanatory mixed-methods design study to examine COVID-19 vaccine hesitancy among parents of children with CKD or hypertension. Results were reported in the *American Journal of Kidney Diseases* [2023;81(1):25-35].

The researchers sought to assess the scope of vaccine hesitancy, identify subgroups that might benefit from targeted interventions, and recognize underlying factors that influence attitudes toward vaccines to aid future pragmatic COVID-19 vaccine promotion among parents of pediatric patients with kidney disease. The study cohort included parents of children <18 years of age with kidney disease or primary hypertension within a large pediatric practice.

The study exposure was parental attitudes toward general childhood and influenza vaccines assessed by the Vaccine Hesitancy Scale (VHS). Based on responses, select survey participants then participated in an in-depth interview to gather further understanding of the influences on vaccine attitudes. The outcome of interest was parents' willingness to vaccinate their child against COVID-19.

The study was conducted between December 2020 and October 2021, inclusive of the regulatory approval time points for the COVID-19 vaccine for children in the United States (December 2020 for those ≥16 years of age and May 2021 for those ≥12 years of age). The study period preceded the EUA approval in November 2021 for those ≥5 years of age.

Comparison of parental attitudes toward general childhood and influenza vaccination with attitudes toward COVID-19 vaccination was conducted with the analysis of variance (ANOVA) test. Willingness to vaccinate against COVID-19 was assessed using multinominal logistic regression. Influences on parental attitudes were characterized using thematic analysis of interview data.

A total of 207 surveys (39% of eligible, approached parents) were completed, representing 22% (39/176) of approached kidney transplant patients, 32% (12/38) of approached dialysis patients, and 50% (156/315) of approached CKD (non-kidney failure) or hypertension patients.

Thirty-six percent (n=75) of participants indicated they were willing to vaccinate their child with kidney disease or hypertension against COVID-19; 39% (n=80) were unsure; and 25% (n=52) were unwilling. There was moderate agreement between parents' willingness to vaccinate themselves versus their child with kidney disease or hypertension and versus other children without kidney disease. Parents were less willing to vaccinate their children than themselves. There was high agreement between willingness to vaccinate the child with kidney disease or hypertension and other children; however, there was low willingness to vaccinate the child with kidney disease or hypertension.

Hesitancy against general childhood and influenza vaccines was highest among the group unwilling to vaccinate against COVID-19 ($P<.001$).

In adjusted analysis, there was an association between having a child with glomerular disease versus congenital anomalies of the kidney and urinary tract and willingness to vaccinate. There was also an association between having a college or higher degree and willingness to vaccinate. Compared with White respondents, those who identified as Black were more likely to be unwilling to vaccinate. Results of analyses contrasting with the respondents who were unsure, parents with a female child were more likely to be willing to vaccinate, and parents of older age children were nominally more likely to be willing to vaccinate (this finding was of borderline statistical significance).

Three salient themes differentiated the participants who were willing, unsure, or unwilling to vaccinate their child with kidney disease or hypertension: (1) benefit versus harm; (2) what do the doctors think?; and (3) information still needed. Respondents expressed concerns about rushed development of the COVID-19 vaccine and fear of serious and unknown long-term side effects. The need for additional information on COVID-19 vaccines was greatest in the parents in the unwilling to vaccinate group and the unsure about vaccination group.

Limitations to the study findings cited by the authors include the inability to account for the various underlying kidney diseases and variations in clinical interaction frequencies and possibly communications about the vaccines. In addition, generalizability would be limited across different clinical settings and other institutions and contexts.

In summary, the researchers said, "We present novel information on the prevalence, predictive factors, and influences on vaccine hesitancy in this vulnerable patient cohort. We combined the strengths of quantitative and qualitative methodology for robust findings to help inform the kidney community on the scope of vaccine hesitancy and develop COVID-19 vaccine promotional campaigns." ■

TAKEAWAY POINTS

- Researchers reported results of a study examining COVID-19 vaccine hesitancy among parents of children with kidney disease or hypertension.
- Of the 207 parents who completed the study survey, 36% were willing to vaccinate, 39% were unsure, and 25% were unwilling to vaccinate their child against COVID-19.
- Parents with college or beyond were more likely to vaccinate their child. There was an association between Black race and being more likely to be unwilling.

Prescription Patterns of Newer Second-line Diabetes Medications in Underserved Populations

Results of numerous clinical trials have demonstrated that, in addition to glucose-lowering properties, newer second-line diabetes medications (glucagon-like peptide-1 receptor agonists [GLP-1RAs] and sodium-glucose cotransporter-2 [sGLT2] inhibitors) have cardiovascular and renal protective effects. Trials of cardiovascular outcomes have shown marked improvement in cardiovascular and renal outcomes with SGLT2 inhibitors and GLP-1RAs. Use of those agents reduced the risks of hospital admission due to congestive heart failure, mortality from cardiovascualr disease, and major adverse atherosclerotic cardiovascular disease, as well as the incidence and progression of chronic kidney disease (CKD).

Metformin is the preferred first-line agent for the treatment of most patients with type 2 diabetes mellitus. Clinical guidelines now advise the use of the newer second-line diabetes medications in patients with clinically established cardiovascular disease independent of glycated hemoglobin levels. According to **Deborah O. Ogunsanmi, BPharm,** and colleagues, despite strong evidence of benefits, there are few data available regarding prescribing patterns for SGLT2 inhibitors and GLP-1RAs, particularly among patient populations at high risk for disparities.

The researchers conducted a retrospective cohort study to examine the associations of cardio-renal and obesity comorbidities and neighborhood factors of prescribing factors of newer second-line diabetes medications compared with older second-line medications (dipeptidyl peptidase 4 inhibitors [DPP-4is] or sulfonylureas [SFUs] among patients with diabetes mellitus type 2 treated with metformin in medically underserved populations at high risk for disparities. Results were reported in the *Journal of Managed Care Pharmacy* [2023;29(6):699-711].

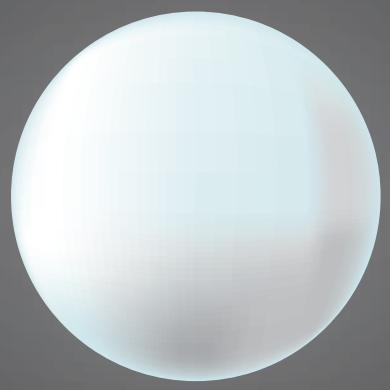
The study utilized data from three large secondary databases: (1) the Tennessee Population Health Data Network (TN-POPnet); (2) IPUMS National Historical Geographic Information Systems (NHGIS) database; and (3) Centers for Medicare & Medicaid (CMS) database. TN-POPnet includes electronic medical records data from a large health care delivery system, including five adult hospitals and more than 50 outpatient clinics. The system serves medically underserved populations in the Memphis metropolitan statistical area in the Mid-South region of the United States.

The researchers obtained patient-level data from January 2016 to August 2021 from TN-POPnet. Census tract-level data for 2016 to 2020 were extracted from the IPOMS NHGIS database. Zip code-level data on health professional shortage area (HPSA) designations were extracted from the CMS database of HPSA. Multilevel logistic regression models were used to examine the associations of comorbidities and neighborhood factors with the prescription of newer second-line diabetes medications.

A total of 7223 patients residing in 763 distinct census tracts and 196 zip codes met eligibility criteria. Of those, 45.0% (n=3477) were prescribed SFUs, and 28.1% (n=2168) were prescribed DPP-4is, compared with 15.8% (n=1223) who were prescribed GLP-1RAs and 11.1% (n=855) who were prescribed SGLT2 inhibitors. On average, patients who were prescribed newer second-line diabetes medications (GLP-1RAs or SGLT2 inhibitors) were younger than those who received older second-line medications (DPP-4is or SFUs); (57.9 years vs 64.4 years).

The overall study cohort included more women than men, as did each of the newer (57.4%) and older (52.2%) second-line diabetes medication study groups. The overall study cohort also included more Black patients, as did each of the newer (52.2%) and older (53.9%) second-line medication study groups.

Following adjustment for patient demographics and patient clustering, results of multilevel logistic regression models showed that patients with cerebrovascular disease were significantly less likely to be prescribed newer second-line diabetes medications (odds ratio [OR], 0.65; 95% CI, 0.52-0.80). Those with obesity were more likely to be prescribed newer second-line diabetes medications (OR,



The odds of being prescribed newer second-line diabetes medications decreased with increasing age, women were more likely to be prescribed newer medications than men, and all non-White racial groups were less likely to receive newer second-line diabetes medications.

1.68; 95% CI, 1.48-1.90). There were no statistically significant associations between prescription of the newer medications and coronary artery disease, congestive heart failure, and CKD.

In analyses of neighborhood factors, patients living in census tracts with higher levels of those with bachelor's degrees (quartiles 3 and 4) had significantly higher odds of receiving newer second-line medications for diabetes compared with those living in census tracts with the lowest levels of those with bachelor's degrees (quartile 3 vs quartile 1: OR, 1.30; 95% CI, 1.06-1.59; and quartile 4 vs quartile 1: OR, 1.46; 95% CI, 1.13-1.88). There were no significant associations between living in HPSAs and poverty levels with the likelihood of being prescribed newer second-line diabetes medications.

The odds of being prescribed newer second-line diabetes medications decreased with increasing age, women were more likely to be prescribed newer medications than men, and all non-White racial groups were less likely to receive newer second-line diabetes medications.

In a subanalysis of prescription of GLP-1RA versus DPP41, patients with cerebrovascular disease and congestive heart failure were significantly less likely to receive GLP-1RAs ($P<.05$). Those with obesity were more likely to receive GLP-1RAs ($P<.05$). Those living in areas with higher levels of college graduates and in zip codes designated HPSAs were more likely to receive GLP-1RAs ($P<.05$). In subanalysis of GLP-1RA versus SFU, those with cardiovascualr disease and coronary artery disease were significantly less likely to receive GLP-1RAs ($P<.05$) and those with CKD and obesity were more likely to receive GLP-1RAs ($P<.05$).

Study limitations cited by the authors included the inability to ascertain the actual patient use of medications, and measuring socioeconomic factors at the census tract level.

In summary, the researchers said, "We found suboptimal prescriptions of GLP-1RAs and SGLT2 inhibitors in comparison with older second-line diabetes medications. Patients with cerebrovascular comorbidities were less likely to be prescribed newer second-line diabetes medications, and patients with obesity were more likely to be prescribed these diabetes medications. Furthermore, patients living in neighborhoods with higher education levels were more likely to receive newer second-line diabetes mediations. Future studies are needed to understand barriers to prescribing newer diabetes medications to address the inequalities in diabetes care. Our findings are important for policymakers and providers and can help improve care delivery among socioeconomically disadvantaged populations with diabetes." ■

TAKEAWAY POINTS

- Newer second-line diabetes medications have been shown to confer cardiovascular and renal benefits to patients with type 2 diabetes mellitus.
- Researchers reported results of a study examining the associations of neighborhood factors and comorbidities with the prescription of those medications.
- Analyses revealed substantial underprescribing of the newer second-line diabetes medications as well as significant clinical and neighborhood variation in the use of the newer second-line diabetes medications.

ERA 60TH CONGRESS

The European Renal Association Congress is the largest annual nephrology congress in Europe, welcoming thousands of attendees from all over the world. The program focuses on key learning features in the clinical field as well as the latest scientific innovations.

PPI Use and Uremic Toxins in Patients With CKD

Patients with chronic kidney disease (CKD) are commonly treated with proton-pump inhibitors (PPIs). PPIs and uremic toxins are eliminated by a kidney tubular organic anion transporter system.

Carolla El Chamieh and colleagues conducted analysis designed to examine the association between PPI prescription and serum concentrations of various uremic toxins. Results were reported during the ERA 60th Congress in a presentation titled *Proton-Pump Inhibitors and Serum Concentrations of Uremic Toxins in Patients With Chronic Kidney Disease*.

The analysis included a randomly selected subgroup of participants in the CKDREIN prospective cohort with available frozen samples collected at baseline. The CKDREIN cohort included adult patients with a confirmed diagnosis of CKD and estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2.

The researchers used a validated liquid chromatography tandem mass spectrometry technique to measure serum concentrations of 10 uremic toxins. Using the log uremic toxin concentration as the dependent variable, the researchers conducted multiple linear regression models.

A total of 680 patients were included in the analysis; median age was 68 years, and median eGFR was 32 mL/min/1.73 m^2. Thirty-one percent of the cohort had a prescription for a PPI at baseline.

Compared with patients not using a PPI, those in the PPI group had higher levels of certain uremic toxins, including total and free indoxyl sulfate (IS), total and free p-cresylsulfate, total and free pcresylglucuronide (PCG), phenylacetylglutamine (PAG), free kynurenine, and free hippuric acid. Following adjustment for baseline comorbidities, the number of coprescribed drugs, and laboratory data including eGFR, the associations between PPI prescription and elevated serum concentrations of free and total IS, free and total PCG, and PAG remained significant.

"Our results indicate that PPI prescription is independently associated with serum uremic toxin retention," the authors said. "These findings indicate a potential mechanism for side effect of PPIs in CKD patients that will need to be confirmed by longitudinal studies."

Source: El Chamieh C, Larabi IS, Laville S, et al. Proton-pump inhibitors and serum concentrations of uremic toxins in patients with chronic kidney disease. Presentation #3386. Abstract of a presentation at the European Renal Association 60th Congress; June 15-18, 2023; Milan, Italy.

Clinical Outcomes Among Hypertensive Living Kidney Donors

A possible solution for the imbalance between supply and demand for kidney transplantation is the use of kidneys from living donors with hypertension. However, according to **Jong Ho Kim** and colleagues in Korea, there are limited data on the safety of donors with hypertension following donor nephrectomy, and only a few studies comparing clinical outcomes of hypertensive donors with outcomes of normotensive donors.

The researchers conducted a study to examine the occurrence of proteinuria and the development of impairment in renal function in a cohort of living hypertensive kidney donors and normotensive donors. Results were reported at the ERA 60th Congress in a presentation titled *Comparisons of Clinical Outcomes Between Hypertensive and Normotensive Living Kidney Donors: A Nationwide Prospective Cohort Study*.

The cohort included 672 hypertensive donors and 5134 normotensive donors identified using data from the Korean Organ Transplantation Registry. Impairment of kidney function was defined as estimated glomerular filtration rate <60 or 45 mL/min/1.73 m^2.

The hypertensive donor group had lower eGFR prior to kidney donation and remained lower following donation. However, following adjustment for multiple variables, there was no increase in the risk for eGFR below 60 mL/min/1.73 m^2 (adjusted hazard ratio [aHR], 0.87; 95% CI, 0.70-1.09; *P*=.226) or below 45 mL/min/1.73 m^2 (aHR, 1.49; 95% CI, 0.77-2.896; *P*=.234) among donors with hypertension.

There was no significant difference between the two groups in the rate of decline in eGFR (adjusted unstandardized B, -0.19; 95% CI, -1.15 to -0.76; *P*=.691). There was an increase in the incidence of occurrence of proteinuria among the donors with hypertension; the incidence tended to increase even 4 to 5 years postdonation. Hypertensive donors had significantly more proteinuria than normotensive donors (aHR, 1.83; 95% CI, 1.13-2.96; *P*=.014).

In conclusion, the researchers said, "Our study indicated that the risk of proteinuria after donation was increased in hypertensive donors, while it was not translated into significant decline in renal function. The continuous and careful monitoring for proteinuria should be required in hypertensive donors after nephrectomy."

Source: Kim JH, Lee YH, Yoon SY, et al. Comparisons of clinical outcomes between hypertensive and normotensive living kidney donors: a nationwide prospective cohort study. Presentation #4343. Abstract of a presentation at the European Renal Association 60th Congress; June 15-18; 2023; Milan, Italy.

Transplant Waiting List Status of Patients With Diabetic Kidney Disease

As identified by the 24th Annual Renal Registry Report, the most common primary renal disease in patients initiating renal replacement therapy (RRT) is diabetes. The prevalence of diabetes in patients with kidney failure was 30.5% at the end of 2020, an increase from 27.0% in 2015.

Recommendations from the Renal Association and British Transplantation Society suggest that patients with a body mass index (BMI) >30 kg/m^2 are at heightened risk of complications and should be discouraged from kidney transplantation. The transplant center at St. James's University Hospital, at the Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom, accepts candidates with a BMI up to 35 kg/m^2 for kidney transplant alone transplantation.

However, according to **Maria Angela Gauci** and colleagues at the center, there is still a significant proportion of patients suspended from the deceased donor transplant waiting list due to an unacceptably raised BMI. The researchers conducted an analysis to examine barriers to transplantation in patients with diabetic kidney disease at the St. James's University Hospital transplant center. Results were reported at the ERA 60th Congress in a presentation titled *The Barriers to Transplantation in Our Diabetic Hemodialysis Population at the Leeds Teaching Hospitals NHS Trust*.

Data were collected using clinic letters or records uploaded to the Patient pathway Managed and the BHLY (Bradford, Hull, Leeds, and York) Renal Patient System. The study included patients with diabetic kidney disease who were receiving either home or in-center hemodialysis. The study was designed to examine the demographics of the diabetic hemodialysis population at the center, and to determine the reasons for suspension from the renal transplant waiting list, with a focus on obesity.

Of the 631 patients receiving hemodialysis from the Leeds renal services, 248 had diabetic kidney disease. Of those 248 patients, 66% were male and the mean age was 60 years. Just over 50% were White, and 30% were South Asian.

At the end of December 2022, nearly 20% (n=119) of all hemodialysis patients were active on the national deceased transplant waiting list. However, only 14% (n=35) of the subpopulation of patients with diabetic kidney disease on hemodialysis were active, 13% (n=31) were under assessment, and 14% (n=35) were declined and/or disengaged from assessment for transplantation, The remaining patients were either temporarily or permanently suspended. Ten percent (n=24) of all diabetic hemodialysis patients were suspended due to a BMI >35 kg/m^2.

"Our audit reveals that only 14% of the hemodialysis diabetic population is presently active on the deceased transplant waiting list," the authors said. "This remains suboptimal, as renal or simultaneous pancreas kidney transplantation is the gold standard for diabetes-induced end-stage kidney disease (ESKD). Obesity (BMI >35) was a reason for temporary suspension in 10% of our hemodialysis diabetic population. Therefore, we need to target this comorbidity in a timely manner in order to optimize patients for transplantation.

"NICE [National Institute for Health and Care Excellence] recommend pharmacological weight-lowering therapy for people who have failed to achieve a healthy BMI following conservative methods. Such medical therapy (eg, liraglutide) is still yet to be evaluated in depth in the ESKD-hemodialysis obese population. Only one patient in our cohort was being treated with liraglutide, while the rest [were] either on insulin, linagliptin, gliclazide, or nonpharmacological dietary modification.

"The authors of this study encourage the inclusion of CKD 5 patients on liraglutide, before they are started on hemodialysis, in order to pave their way to transplantation before it is too late."

Source: Gauci MA, Ahmed M, Gullapudi VRL, Wright M. The barriers to transplantation in our diabetic hemodialysis population at the Leeds Teaching Hospitals NHS Trust. Presentation #6884. Abstract of a presentation at the European Renal Association 60th Congress; June 15-18, 2023; Milan, Italy.

Conference Coverage

Milan, Italy | June 15-18, 2023

COVID-19 Vaccine Responses in Patients With CKD

Patients with chronic kidney disease (CKD) are at high risk for serious complications associated with SARS-CoV-2 infections and can benefit from vaccination. Researchers in Uzbekistan, led by **Sherzod Abdullaev,** conducted a study to examine the effectiveness of available COVID-19 vaccines in patients with CKD. Results of the study were reported at the ERA 60th Congress in a presentation titled *Evaluation of Antibody Responses to SARS-CoV-2 Vaccines in Patients With CKD.*

The study cohort included 198 consecutive adult patients with CKD in a single center in Uzbekistan. The patients were divided into four cohorts: (1) hemodialysis, n=116; (2) peritoneal dialysis, n=110; (3) kidney transplant recipients, n=22; and (4) nondialysis-dependent CKD (stage 4 and 5, estimated glomerular filtration rate [eGFR] <30 mL/min/1.73 m^2), n=49. All participants received complete vaccination with any of the available vaccines: Pfizer-BioNTech, Moderna, AstraZeneca, Sputnik V, or ZF-UZ-Vac2001. Antibodies were measured at baseline and on day 28 following the last vaccine dose, and compared between the cohorts. Factors associated with the development of antibodies were analyzed.

In the overall cohort, 55% (n=109) were male and the mean age was 54.3 years. Twenty-five patients (12.6%) received Pfizer-BioNTech vaccine, 42 (21.2%) received Moderna vaccine, 28 (14.1%) received the AstraZeneca vaccine, 36 (18.2%) received Sputnik V vaccine, and 67 (33.9%) received ZF-UZ-VAC2001 vaccine. The distribution of vaccine types differed across the four subgroups.

Of the 198 patients, 155 underwent testing for antibody response at 28 days after the final vaccination dose (97 in the hemodialysis group, 8 in the peritoneal dialysis group, 16 kidney transplant recipients, and 34 in the nondialysis-dependent CKD group). Of those, 137 patients (88%) presented antibody responses, three (2%) were doubtful, and 15 (10%) had a negative result.

Of the patients who did not develop antibody responses, three were in the hemodialysis group (2%), two were in the peritoneal dialysis group (1%), eight were in the kidney transplant recipient group (6%), and two were in the nondialysis-dependent CKD group (1%); $P<.01$.

Patients who received the Pfizer-BioNTech, Moderna, and AstraZeneca vaccines had higher antibody titers than those who received Sputnik V and ZF-UZ-VAC2001 vaccines ($P<.01$). The differences were significant across all four cohorts.

Increasing age ($P<.01$), history of cardiovascular disease ($P=.02$), and lower eGFR ($P<.05$) were associated with negative antibody response. There was an association between previous COVID-19 infection and higher antibody titers at 28 days ($P<.05$). There were no significant associations between antibody response and sex, ethnicity, body mass index, diabetes, or donor type.

In conclusion, the authors said, "Our study has shown a much lower seropositivity rate among the kidney transplant recipients after SARS-CoV-2 vaccine than other cohorts of CKD patients, suggesting that kidney transplant patients require persistent isolation measures and booster doses of a COVID-19 vaccine. Increasing age, history of CKD, and lower eGFR were factors associated with a nonresponse. Potential differences between COVID-19 vaccines should be explored in prospective long-term follow-up studies. These findings complement those of earlier studies and highlight the need for a tailored approach to the vaccination."

Source: Abdullaev S, Sharapov O, Igamberdieva R. Evaluation of antibody responses to SARS-CoV-2 vaccines in patients with CKD. Presentation #2765. Abstract of a presentation at the European Renal Association 60th Congress; June 15-18, 2023; Milan, Italy.

Symptom Perception Among Patients With IgAN and Their Nephrologists

The estimated prevalence of immunoglobulin A nephropathy (IgAN), the most common form of primary glomerulonephritis worldwide, is approximately 25/100,000,000. Clinical manifestations associated with IgAN include hematuria, proteinuria, and hypertension.

During a presentation at the ERA 60th Congress, **Nicholas R Medjeral-Thomas, MBBS, PhD,** and colleagues reported results of an analysis comparing perceptions of symptom burden, disease severity, and treatment satisfaction between patients with IgAN and their nephrologists in Europe, the United States, and Asia. The presentation was titled *IgA Nephropathy: A Real-World Comparison Between Disease Severity, Symptom Burden, and Treatment Satisfaction Reported by Patients and Nephrologists.*

The analysis utilized data from the Adelphi IgAN Disease Specific Programme, a point-in-time survey of nephrologists and their consulting IgAN patients. The survey was conducted in the United States, Europe (EU5: France, Germany, Italy, Spain, United Kingdom), Japan, and China from June to October 2021. Structured online patient record forms for successive patients presenting with IgAN were completed by participating nephrologists. Patients voluntarily completed questionnaires that corresponded with the nephrologists' records. Reported data included demographics, signs and symptoms of IgAN, disease severity, and treatment satisfaction.

Data on 991 patients with IgAN and matched nephrologists were collected. Mean patient age was 42.1 years and 57% were male. Perceived severity of disease was reported on a scale of mild, moderate, and severe. Overall, nephrologists and patients agreed on disease severity for 77% of patients (n=981) (United States, 82%; EU5, 77%; Japan, 70%; and China, 78%).

Where patients reported nausea/vomiting, it was not recognized by nephrologists in 85% of cases. Results were similar for appetite loss (80%), headaches/migraines (69%), and aching joints (67%). Overall, nephrologists and patients agreed on a fatigue score in 33% of cases (n=991). In comparison with fatigue reported by patients, nephrologists underreported fatigue in 46% of cases and overreported in 21% of cases. In 53% of cases, nephrologists agreed with patients' self-reported pain score (n=988). Pain was underreported by nephrologists in 26% of cases and overreported in 21% of cases.

Overall, there was a 65% agreement between nephrologists and patients on treatment satisfaction. The percentage agreement varied across countries: EU5, 76%; United States, 77%; China, 61%; Japan, 58%.

In summary, the researchers said, "Although there seemed to be a good level of agreement between nephrologists and patients on their overall IgAN severity, nephrologists underreported patients' symptoms, notably nausea/vomiting and appetite loss, and fatigue…Satisfaction with current treatment also differed in around a third of cases.

"This highlights that communication between nephrologists and their patients can be improved, especially when it comes to appreciating IgAN symptom burden. This could be combated through more investment in a holistic patient evaluation, Cultural differences may impact symptom perception and reporting, as evidenced by differences between nephrologists and patients in different countries/regions. An improvement in communications may lead to a better management of IgAN patients, including treatment, and, subsequently, a better quality of life for patients with IgAN."

Source: Medjeral-Thomas NR, Aldworth C, Kattlun J, Thomas George A, Decourcy J, Chatterton E. IgA nephropathy: a real-world comparison between disease severity, symptom burden, and treatment satisfaction reported by patients and nephrologists. Presentation #5514. Abstract of a presentation at the European Renal Association 60th Congress; June 15-18, 2023; Milan, Italy.

Late Referral of Migrant Patients With Kidney Disease in Italy

Among migrants in Italy, the prevalence of end-stage kidney disease (ESKD) is increasing. Migrant patients commonly present to a nephrologist with advanced kidney disease, limiting the possibility of preventing progression to ESKD. Barriers to referral to nephrology care include low literacy rates, language barriers, lack of medical insurance, and cultural diversity.

According to **Gaetano Alfano** and colleagues, there are few data available on the prevalence and clinical characteristics of migrant patients in dialysis clinics. The researchers conducted a study comparing data on demographics, clinical characteristics, and health-related quality of life (HRQoL) among that patient population with Italian patients undergoing hemodialysis. Results were reported at the ERA 60th Congress in a presentation titled *Epidemiological and Clinical Characteristics of Migrants on Chronic Hemodialysis Treatment*.

The retrospective, cross-sectional observational study included patients who underwent hemodialysis at the University Hospital of Modena, Italy, from December 2021 to August 2022. All patients ≥18 years of age who were receiving hemodialysis were enrolled. Electronic health databases and interviews with selected patients were used to collect relevant data.

HRQoL was evaluated using the EQ-5D questionnaire. Scores ranged from 5 (no problems) to 25 (extreme problems). A scale (EQ VAS) ranging from 0 (worst imaginable health) to 100 (best imaginable health) was used for global self-assessments of health. The study cohort was divided based on their origin: migrant patients or nonmigrant patients. Using criteria from the International Organization for Migrations, migrant patients were those who were born in a foreign country and came to Italy for work, family reunification, economic, or political reasons.

The overall cohort included 302 patients on hemodialysis. Of those, 18.2% (n=55) were identified as migrants: 62% from Africa, 20% from other countries in Europe, 16% from Asia, and 2% from Latin America. Seeking work and family reconciliation were the primary reasons for migrating to Italy (84.3% and 15.7%, respectively). A consistent percentage of the migrants (37.5%) were undocumented when they crossed the Italian border.

Compared with nonmigrant patients, migrant patients initiated hemodialysis at a younger age (48.1 years vs 70.7 years; P=.001). Sixty-nine percent of the migrant group were male, and those in the migrant group initiated hemodialysis a median of 12.3 years following their arrival in Italy. Median age of patients in the migrant group varied by country: sub-Saharan Africa, 44.7 years; Asia, 46 years; Europe, 53.9 years; and northern Africa, 54.5 years. Forty percent had kidney disease of unknown etiology.

Most of the patients in the migrant group (54.5%) initiated hemodialysis with a central vein catheter (CVC) and 53.0% had not been referred to a nephrologist prior to starting hemodialysis. At follow-up of 1.8 years, the rate of CVC use decreased to 26.3%. Only 14.5% had been educated regarding home dialysis. Using age criteria, 87.2% were potentially eligible for kidney transplantation, yet only 18.7% were active on the transplant waiting list.

Compared with the nonmigrant group, those in the migrant group had a better perception of HRQoL. Median EQ-5D scores were 5 in the migrant group compared with 7 in the nonmigrant group (P<.001). Scores on the global health self-assessment were 90 in the migrant group and 80 in the nonmigrant group (P=.028). When the EQ-5D score and the EQ VAS scale were adjusted for participant age, the differences did not remain statistically significant.

"Migrants were a consistent percentage of patients in our dialysis unit," the authors said. "This group of patients was formed by young people often unaware of their kidney disease. Late referral to the nephrologist had a profound implication on vascular access for hemodialysis. The language barrier and cultural diversity were the major limitations to entry into the kidney transplant waiting list."

Source: Alfano G, Fontana F, Magistroni R, Donati G. Epidemiological and clinical characteristics of migrants on chronic hemodialysis treatment. Presentation #6511. Abstract of a presentation at the European Renal Association 60th Congress; June 15-18, 2023; Milan, Italy.

Management of Symptom Burden in Patients on Peritoneal Dialysis

Kidney supportive care (KSC) is a standard of care in Australia for patients with advanced kidney failure where health systems work to help manage the high burden of patients' physical and psychosocial symptoms. According to **Holly Brand** and colleagues, while there have been studies examining the symptom burden among patients on hemodialysis, there are few data available on the symptom burden among patients on peritoneal dialysis.

The researchers conducted a study to describe the symptom burden experienced by patients on peritoneal dialysis and by patients on hemodialysis seen in a KSC clinic. Results were reported at the ERA 60th Congress in a presentation titled *Kidney Supportive Care for Patients on Peritoneal Dialysis: Are Symptoms Being Addresses? A Retrospective Study.*

The researchers analyzed data on patients who attended a multisite KSC clinic in Brisbane, Australia, between February 2016 and October 2022. Clinical records were used to extract patient demographic characteristics, dialysis modality, Charlson Comorbidity (CCI) scores, and Integrated Palliative Care Outcome Scale Renal (IPOS-Renal) scores. Intraperson physical symptom burden, determined by IPOS-Renal physical scores at baseline, was compared with the scores at a subsequent clinic visit where applicable. Descriptive and group analyses were performed.

The cohort included 232 participants. Of those, 201 were on hemodialysis and 31 were on peritoneal dialysis. Median age was 689 years, 57.3% were male, and 55.2% were referred to KSC primarily for symptom management. The two groups were similar in demographic characteristics and reasons for referral to KSC. Initial entry to the KSC clinic was considered baseline.

At baseline, median CCI was 9 and mean total IOPS score was 16.59. The groups were similar in symptom prevalence. Weakness was the most prevalent symptom (76.0%), followed by poor mobility (74.2%), pain (60.9%), drowsiness (55.8%), and dyspnoea (54.9%). The prevalence of severe or overwhelming rated diarrhea and pruritis were significantly higher in the peritoneal dialysis group than in the hemodialysis group (P=.01 and P=.03, respectively).

Of the 232 participants with baseline data, 145 attended a second clinic appointment. Of those, 122 were on hemodialysis and 23 were on peritoneal dialysis. The second visit occurred a median of 91 days after the initial visit. There were no significant differences in individual symptom burden at the second clinic appointment. However, there was a significant improvement in the subcategory of pruritis in the peritoneal dialysis group at the second clinic visit (mean change, 0.45; P=.02).

In summary, the authors said, "Our results show that patients on peritoneal dialysis have a similar burden of comorbidities and symptoms to patients on hemodialysis, as well as unique symptoms to address. In addition to the five most prevalent symptoms, pruritis and diarrhea were identified as experienced more severely by the peritoneal dialysis cohort. Of these, pruritus was shown to improve between KSC appointments, which may suggest that the interventions commenced at the first appointment were effective.

"These findings also indicate the need for further bowel assessment and management for patients on peritoneal dialysis by KSC clinicians in our health service. This KSC cohort had fewer patients on peritoneal dialysis than hemodialysis. Further studies are needed to elicit if there is a selection bias or if there is an underappreciation for the symptom burden of this cohort, especially given peritoneal dialysis is delivered outside of the hospital system."

Source: Brand H, Purtell L, Berquier L, et al. Kidney supportive care for patients on peritoneal dialysis: are symptoms being addressed? A retrospective study. Presentation #4315. Abstract of a presentation at the European Renal Association 60th Congress; June 15-18, 2023; Milan, Italy.

Predicting Risk for Rapid Progression of ADPKD

Patients with autosomal dominant polycystic kidney disease (ADPKD) commonly develop end-stage kidney disease (ESKD). ADPKD is characterized by the progressive development of bilateral renal cysts, which results in enlargement of the kidney volume, hypertension, and ESKD.

The ERK-NET [European Rare Kidney Disease Reference Network] recently published a position paper outlining indications for the use of tolvaptan for the treatment of patients with ADPKD based on three algorithmic criteria: (1) total kidney volume and the Mayo Clinic Imaging Class (MCIC); (2) rate of decline in estimated glomerular filtration rate (eGFR); and (3) the Predicting Renal Outcome in Polycystic Kidney Disease (PROPKD) score, combining clinical and genetic variables. The MCIC and PROPKD scores are alternatively used to identify patients at risk for rapid progression of disease.

Valeria Aiello and colleagues conducted a retrospective, multicenter cohort study to examine and improve the concordance of sensitivity and specificity of MCIC and PROPKD predictive abilities for rapid disease progression. Results were reported at the ERA 60th Congress in a presentation titled *Evaluation of the Predictive Ability and Concordance of Prognostic Scores for Rapid Progression in ADPKD: A Multicenter Cohort*.

The study utilized data on adult patients with ADPKD from three renal centers (Bologna, Italy; Dublin, Ireland; and Berlin/Leipzig, Germany). Rapid disease progression was defined as eGFR slope ≥3 mL/min/1.73 m^2 per year over 4 years (clinical score), or MCIC classes 1C-D-E (imaging score), or high-risk PROPKD score (7-9 points). Clinical parameters were summarized using descriptive statistics. Kappa statistics were used to assess the concordance between MCIC and PROPKD scores.

In participants with PKD1 missense variants, the REVEL score was obtained and treated as a continuous variable. Scores greater than 0.65 were considered pathogenic and regarded as PKD1-truncating variants for PROPKD score calculation.

The cohort included 298 patients with ADPKD. Following 4 years of follow-up, results of multivariate analysis demonstrated significant associations between disease progression and MCIC (P=.041), hypertension (P=.031). and urologic events (P<.001). Assessment of rapid disease progression using PROPKD and MCIC scores yielded kappa of Cohen of 0.149; 47.9% (n=143) were concordant, and 49.32% (n=148) patients identified as rapid progressor for MCIC were identified as nonrapid progressor for PROPKD. Seven patients (2.3%) considered rapid progressor using PROPKD score were considered nonrapid progressor using MCIC classes.

Following reclassification of PKD1 missense variants by REVEL score, kappa of Cohen improved to 0.174 and PROPKD became predictive of fast progression (P=.01).

In conclusion, the researchers said, "Concordance between scores results [were] low (kappa of Cohen, 0.149). The PROPKD is more selective compared with the Mayo. Nevertheless, PROPKD allows the identification of some rapid progressor patients excluded from using the Mayo score only. The combined use of scoring may increase the ability to identify progressive patients. REVEL score could improve the agreement."

Source: Aiello V, Elhassan E, Cristalli C, et al. Evaluation of the predictive ability and concordance of prognostic scores for rapid progression in ADPKD: a multicenter cohort. Presentation #55496. Abstract of a presentation at the European Renal Association 60th Congress; June 15-18, 2023; Milan, Italy.

ORIGIN: 24-Week Results of Phase 2b Trial of Atacicept in Patients With IgAN

Worldwide, immunoglobulin A nephropathy (IgAN) is the most common primary glomerulonephritis. Central in the pathogenesis of IgAN are galactose-deficient IgA1 (GD-IgA1), anti-GD-IgA1 autoantibodies (anti-Gd-IgA1), and IgA-IgA-containing immune complexes (ICs), all contributing to kidney damage. The phase 2a JANUS trial (NCT02808429) evaluating the safety and efficacy of atacicept in patients with IgAN demonstrated the potential of targeting the disease-causing species.

During a late-breaking session at the ERA 60th Congress, **Richard Lafayette, MD,** and colleagues presented preliminary results of the phase 2b ORIGIN trial (NCT04716231) in a presentation titled *ORIGIN Trial: 24-wk Primary Analysis of a Randomized, Double-Blind, Placebo-Controlled PH2B Study of Atacicept in Patients With IgAN*. Atacicept is a fusion protein that binds B-lymphocyte stimulator and a proliferation inducing ligand to inhibit maturation and class-switching of B-cells and plasma cells.

The ORIGIN cohort includes 116 patients with biopsy-proven IgAN, 24-hour urine protein >0.75 g per day or urine protein-to-creatinine ratio (UPCR) >0.75 g/g, and estimated glomerular filtration rate (eGFR) >30 mL/min/1.73 m^2 despite treatment with optimized renin-angiotensin system blockade. Patients were randomized to atacicept 150 mg, 75 mg, or 25 mg administered via subcutaneous injection once per week versus placebo (2:2:1:2) for up to 36 weeks. The primary end point was the change in 24-hour UPCR at 24 weeks in the pooled atacicept 150 mg and 75 mg arms compared with placebo.

Of the 116 patients in the intent-to-treat (ITT) population, 33, 33, and 16 received atacicept 150, 75, and 25 mg, respectively, and 34 received placebo. In the pooled 75 and 150 mg atacicept arms, mean UPCR at 24 weeks was reduced from baseline by 31% compared with a 7% reduction from baseline in the placebo arm. Results of the ITT analysis are supported by a prespecified per-protocol analysis: the atacicept 150 mg arm showed a 41% reduction from baseline in UPCR at 24 weeks compared with a 10% reduction in the placebo arm.

For the secondary outcome, eGFR showed stability at week 24 in the atacicept 150 mg arm. Safety results demonstrated that atacicept was generally well tolerated, with no increased rates of infection compared with placebo and a low rate (2%) of serious adverse events overall, with no serious adverse events in the atacicept 150 mg arm.

"The ORIGIN Ph2b study met its primary end point, demonstrating a favorable impact on disease biomarkers and a clinically meaningful reduction in proteinuria and demonstrated a favorable safety profile," the researchers said. "These promising results at Week 24 support atacicept 150 mg for further evaluation as a potential disease modifying treatment of patients with IgA nephropathy."

Source: Lafayette R, Maes B, Lin C, et al. ORIGIN trial:24-wk primary analysis of a randomized, double-blind, placebo-controlled ph2b study of atacicept in patients with IgAN. Presentation #3848. Abstract of a presentation at the European Renal Association 60th Congress; June 15-18, 2023; Milan, Italy. ORIGIN is supported by Vera Therapeutics, Inc.

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Major Meetings

American Society of Nephrology Kidney Week 2023
November 2-5, 2023
Philadelphia, Pennsylvania
www.asn-online.org/education/kidneyweek

American Nephrology Nurses Association 2024 National Symposium
April 14-17, 2024
Orlando, Florida
www.annanurse.org/education-events/events/national-symposium

National Kidney Foundation Spring Clinical Meetings 2024
May 14-18, 2024
Long Beach, California
www.kidney.org/spring-clinical

American Transplant Congress 2024
May 31-June 5, 2024
Philadelphia, Pennsylvania
www.myast.org/american-transplant-congress/american-transplant-congress-information

Interwell Health Expands Its Kidney-Care Network

Interwell Health has announced the addition of more than 20 nephrology practices and nearly 100 physicians to its nationwide network. The Interwell Health provider network now totals 1700 nephrologists across the United States who are aligned with the mission to reimagine kidney care and help individuals with chronic kidney disease (CKD) live healthier lives. Interwell Health practices range from large to small, and rural to urban.

In a recent press release, **George Hart, MD,** chief medical officer at Interwell Health, said, "We believe it's essential to keep physician practices independent, strong, and at the center of new models of care for people living with kidney disease. In the shift from volume to value, our network practices receive the resources, tools, and support needed to succeed in new value-based care agreements and improve outcomes for our patients. We are honored to be the partner of choice for these providers."

Dave Koeper, MD, of Fox Valley Nephrology in Wisconsin, said, "Interwell is making us better nephrologists by supporting our important transition to value-based care. They are providing us with the resources and expertise we need to improve the lives of our patients, including data-driven insights and an unmatched educational platform built for nephrologists, while also driving down the total cost of care. We believe value-based care is the future of kidney care and are thrilled to partner with the leading network of kidney care providers nationwide."

Bhajan Dara, MD, president of Metro Renal in St. Louis, Missouri, added, "I have been fortunate to apply the principles of value-based care throughout my nephrology career, combined with more than a decade of successful participation in both upside and downside value-based contracts as a primary care physician. I am pleased to see value-based programs formally make their way to the nephrology arena to address the unsustainable cost of CKD care. Metro Renal is proud to be a part of the Interwell family, which is leading the way with its extensive network of payers, strategic business partnerships, data-driven value-based model, and especially its unique and unwavering support to independent nephrology practices." ■

Unanimous Passage of Organ Procurement Transplant Act Is a Good Day for Patients

Statement from Kevin Longino, CEO of the National Kidney Foundation (NKF) and a transplant recipient, on the Senate's unanimous passage of the Securing the U.S. Organ Procurement and Transplantation Network (OPTN) Act

"There are more than 800,000 Americans living with kidney failure, and more than 100,000 of them are on the transplant waiting list. Fourteen people will die each day before they get the lifesaving call that a kidney is available. Yesterday's bipartisan and unanimous passage of the Securing the U.S. Organ Procurement and Transplantation Network Act is a sign of just how seriously lawmakers are taking the issue and a clear victory for patients. We've long said the transplantation system is in critical need of reform. This is the next step to finally beginning a much-needed modernization of how we secure, transport, and transplant lifesaving donated organs.

This initiative will strengthen accountability, transparency, equity, and performance in the organ donation and transplantation system. The new law will allow the Health Resources and Services Administration (HRSA) to enable competition and strengthen accountability to reduce waste and improve patients' access to the gold-standard therapy for kidney failure: transplantation. It will allow for innovation and new ways of thinking about improving the nation's transplant system which has remained virtually unchanged for 40 years. It will allow new bidders with expertise in one, but not all, of the many important functions of the OPTN to bid, bringing fresh ideas and expertise. It will allow the nation to invest in the transplant system more appropriately, including modernizing the dated IT system it relies on currently. Finally, it will ensure accountability and good governance by having separate boards for the OPTN and any OPTN contractor(s).

NKF applauds both the Senate and House for their leadership and unanimous support on this issue. We'd especially like to thank Senators Ron Wyden, Chuck Grassley, Ben Cardin, Todd Young, and Bill Cassidy for introducing this legislation and moving it forward. We would also like to thank Representatives Larry Bucshon and Robin Kelly for sponsoring the, already passed, companion bill in the House. We look forward to President Biden signing this into law as soon as possible. We'd also like to thank all of the volunteers and patients for their continued advocacy for improving our organ donation system.

COVID-19

Kidney Disease Following COVID-19 Infection and Vaccination

QJM: An International Journal of Medicine. doi.org/10.1093/qjmed/hcad159

Patients with COVID-19 infection may develop acute kidney injury (AKI), a complication that has been linked to high mortality rates. **Gaosi Xu, PhD, MD,** and colleagues at the Second Affiliated Hospital of Nanchang University, China, performed a review of data from 20 clinical studies on post-COVID-19-related AKI and 97 cases of AKI associated with COVID-19 vaccination.

The most common finding in the kidneys of patients with AKI related to COVID-19 was acute tubular injury. Of patients hospitalized for COVID-19, 34.0% developed AKI; 59.0% were stage 1, 19.1% were stage 2, and 21.9% were stage 3 AKI.

Incidences of kidney disease and other adverse effects following vaccination for COVID-19 are rare. However, there have been case reports suggesting that COVID-19 vaccination may be associated with a risk of subsequent kidney disease. Among patients with postvaccination AKI, the most common pathologic findings are crescentic glomerulonephritis (29.9%), acute tubular injury (23.7%), and IgA nephropathy (18.6%). Crescentic glomerulonephritis seems to be more prevalent in patients with newly diagnosed renal involvement.

In summary, the authors said, "In general, cases of new-onset and recurrent nephropathy with AKI after COVID-19 vaccination have a positive prognosis. In this article, we also explore the underlying pathophysiological mechanisms of AKI associated with COVID-19 infection and its vaccination by describing key renal morphological and clinical features and prognostic findings."

Remdesivir and Tacrolimus Exposure in Transplant Recipients With COVID-19

Kidney International Reports. 2023;8(7):1315-1322

Remdesivir has been shown to have benefits against COVID-19. However, according to **Ehsan Habeeb, PharmD,** and colleagues, there are few data on drug-drug interactions. The researchers conducted a retrospective study to examine the effect of remdesivir on calcineurin inhibitor levels.

The study cohort included adult solid organ transplant recipients who were hospitalized for COVID-19 and received remdesivir while on a calcineurin inhibitor. Exclusion criteria included patients on other medications known to interact with calcineurin inhibitors. The percentage of change in calcineurin inhibitor levels following initiation of remdesivir therapy was the primary end point of interest. Time until calcineurin inhibitor levels reached a maximum increase in trough levels, the incidence of acute kidney injury, and the time until calcineurin inhibitor levels normalized were secondary end points.

Eighty-six patients were screened. Of those, 61 were included in the study; 56 were on tacrolimus and five were on cyclosporin. Most of the cohort (44.3%) were kidney transplant recipients, and baseline demographics were similar among the patients with various transplanted organs.

The median increase in tacrolimus levels following initiation of remdesivir therapy was 84.8%; only three patients had no significant change in calcineurin inhibitor levels. Lung and kidney transplant recipients had more pronounced increase in tacrolimus levels compared with heart recipients (96.5% vs 93.9% vs 64.6%, respectively). Median time to maximum increase in tacrolimus trough levels was 3 days. It took 10 days after the remdesivir course for levels to return to baseline.

"This retrospective analysis demonstrates that calcineurin inhibitor levels were significantly elevated after starting remdesivir. However, future studies are warranted to evaluate this interaction further," the authors said.

ADPKD

PKD1 Hypomorphic Alleles and Modification of ADPKD Severity

Genes. doi.org/10.3390/genes14061230

The most common genetic cause of kidney failure in adults is autosomal dominant polycystic kidney disease (ADPKD). Diagnosis of ADPKD in utero or in infancy is rare; the genetic mechanism underlying such severe presentation is related to reduced gene dosage.

According to **Enrico Ambrosini, MD,** and colleagues in Italy, early onset ADPKD has been shown to be related to biallelic PKD1 variants, with one main pathogenic variant and a modifier hypomorphic variant showing an in trans configuration. The researchers presented case reports on two unrelated individuals with early onset cystic kidney disease and unaffected parents. A combination of next-generation sequencing of cystic genes, including *PKHD1, HNF1B,* and *PKD1* facilitated the identification of biallelic PKD1 variants.

To estimate a minimal allele frequency of 1/130 for this category of variants taken as a group, the researchers performed a medical literature review to identify likely *PKD1* hypomorphic variants reported to date.

"This figure could help to orient genetic counseling, although the interpretation and the real clinical impact of rare *PKD1* missense variants, especially if previously unreported, remain challenging," the authors said.

Assessing Thirst Intensity Among Patients With ADPKD

Clinical and Experimental Nephrology. doi.org/10.1007/s10157-023-02373-7

Among patients with autosomal dominant polycystic kidney disease (ADPKD), increased fluid intake and treatment with tolvaptan can decelerate the growth rate of cysts. Researchers, led by **Sibel Gokcay Gocay Bek, MD,** conducted a prospective study to assess thirst sensation among patients with ADPKD, as well as parameters affecting the intensity of thirst.

The study cohort included 41 patients with ADPKD being treated with tolvaptan and 40 patients with ADPKD not being treated with tolvaptan who were evaluated for thirst distress sensation and intensity. The Thirst Distress Scale-HF (12 questions)

continued on page 28

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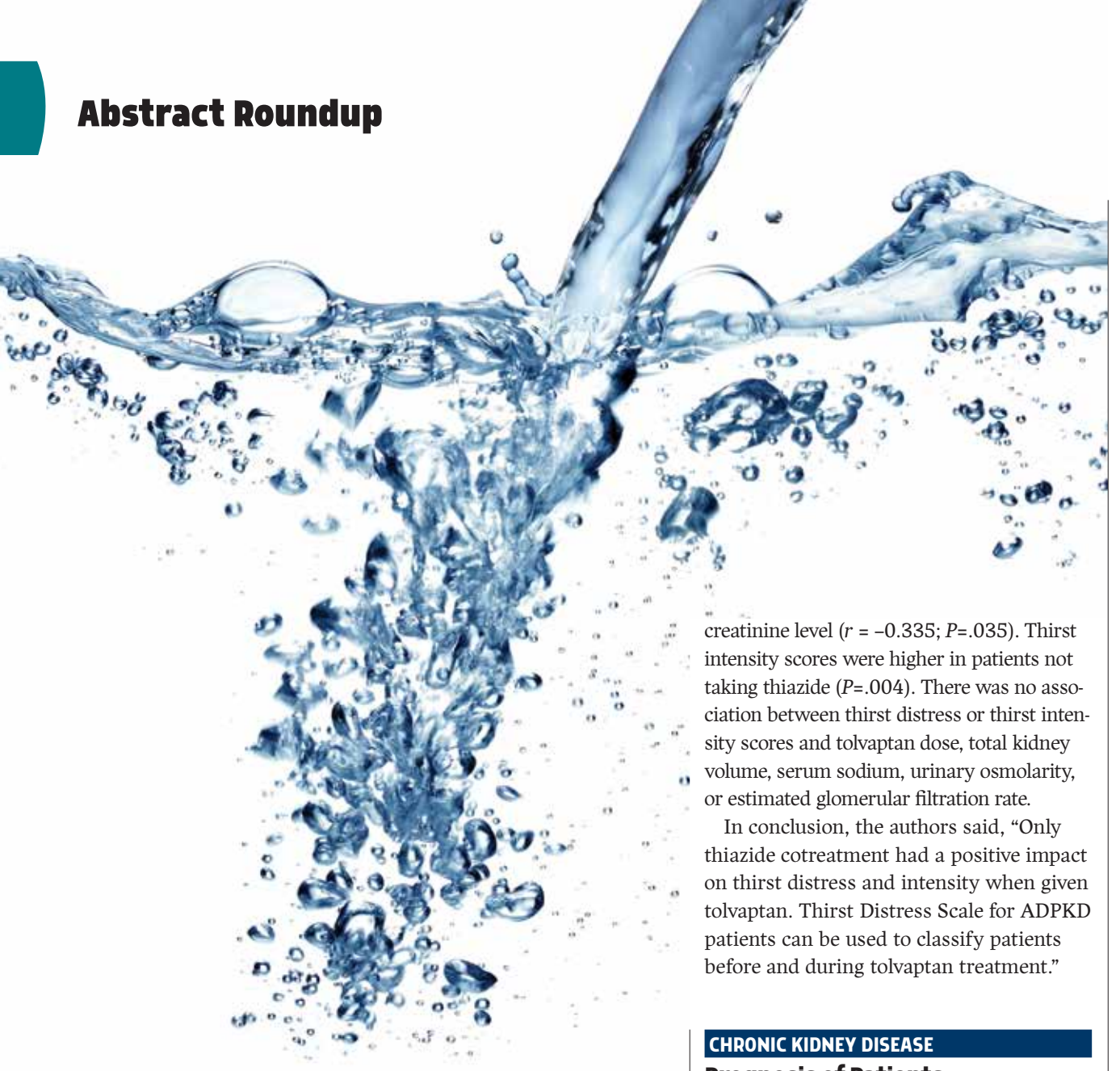

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was used to evaluate the feeling of thirst and the discomfort caused by excessive fluid intake. A 100 mm visual scale was used to evaluate thirst intensity.

Of the overall cohort, 35.8% (n=29) were male and 64.2% (n=52) were female. Mean age of the tolvaptan group was 39.17 years, and mean age of the non-tolvaptan group was 41.95 years.

Following 1 year of tolvaptan treatment, there was a negative correlation between the thirst distress score and an increase in creatinine level (r = –0.335; P=.035). Thirst intensity scores were higher in patients not taking thiazide (P=.004). There was no association between thirst distress or thirst intensity scores and tolvaptan dose, total kidney volume, serum sodium, urinary osmolarity, or estimated glomerular filtration rate.

In conclusion, the authors said, "Only thiazide cotreatment had a positive impact on thirst distress and intensity when given tolvaptan. Thirst Distress Scale for ADPKD patients can be used to classify patients before and during tolvaptan treatment."

CHRONIC KIDNEY DISEASE

Prognosis of Patients With CVC and CKD

PeerJ. doi:10.7717/peerj.15569.eCollection 2023

Researchers, led by **Ju Wang, MD,** reported results of a single-center, retrospective analysis designed to examine the effect of cardiac valve calcification (CVC) on the prognosis of individuals with chronic kidney disease (CKD). The analysis included data on 343 patients with CKD. The cohort was divided into two groups based on the presence or absence of CVC. Patients were followed until death, loss to follow-up, or the end point of the study (December 2021).

Among the 343 patients with CKD, the overall incidence of CVC was 29.7%: 21 cases of mitral valve calcification, 63 cases of aortic valve calcification, and 18 cases of mitral valve combined with aortic valve calcification. Among those with CKD stage 1-2 the incidence of CVC was 0.3%; among patients with CKD stage 3-4, the CVC incidence was 5.2%; and among those with CKD stage 5, the incidence was 24.2% (P<.05).

There were associations between advanced age, higher serum albumin, higher cystatin C, and lower uric acid levels and higher risk of CVC. After 6 years of follow-up, 22.4% of the cohort (n=77) had died. Causes of death were cardiovascular and cerebrovascular diseases (46.7%, n=36), infection (37.3%, n=29), gastrointestinal bleeding (11.7%, n=9), and other (3.9%, n=3). Results of a Kaplan Meier survival analysis suggested that the overall survival rate was lower in patients with CVC compared with that in patients without CVC.

"The incidence of CVC, mainly aortic calcification, is high in patients with CKD," the researchers said. "Advanced age, higher serum albumin, and higher cystatin C levels were associated with a higher risk of CVC. Hyperuricemia was associated with a lower risk of CVC. The overall survival rate of patients with CVC was lower than that of patients without CVC."

DIABETIC KIDNEY DISEASE

Potential Biomarkers of Disease Progression in DKD

Science China Life Sciences. doi.org/10.1007/s11427-022-2348-0

Patients with type 2 diabetes mellitus commonly develop diabetic kidney disease (DKD), a major microvascular complication of diabetes. Management of patients in the early diagnostic period and monitoring disease progression are key in treatment of patients with DKD.

CONFERENCE COVERAGE KIDNEY WEEK 2022

Patiromer Use Reduced Potassium in Veterans With Hyperkalemia

Among patients with end-stage kidney disease (ESKD) on dialysis, hyperkalemia is a common, potentially life-threatening metabolic disorder, presenting a challenge for clinicians caring for those patients. Patiromer, a non-absorbed sodium-free potassium-binding polymer, has been approved for the treatment of hyperkalemia.

Csaba P. Kovesdy, MD, FASN, and colleagues conducted a historical cohort study designed to describe utilization of patiromer and associated changes in serum potassium in a cohort of US veterans with ESKD and hyperkalemia on dialysis. Results were reported during a poster session at the American Society of Nephrology Kidney Week 2022 in a poster titled *Treatment Response and Dosing of Patiromer in Veterans With Dialysis-Dependent ESKD and Hyperkalemia.*

The researchers utilized data from the National VA Corporate Data Warehouse from January 1, 2016, to February 28, 2021, to assess patiromer utilization and changes in serum potassium. Eligible patients were ≥18 years of age with at least two *International Classification of Diseases* codes for ESKD, on dialysis, receiving patiromer, and had a serum potassium ≥5.1 mEq/L recorded within 91 days of the date of the first patiromer dispensing (index date).

Serum potassium was measured at baseline, and at 1, 3, and 6 months from the index date. Paired t-test was used to assess the change in serum potassium from baseline to each time point.

A total of 1267 veterans with ESKD using patiromer were identified. Of those, 458 met inclusion criteria and had a serum potassium measurement available during the 3 months prior to the index date. At baseline, mean age was 66 years, 97% were male, 45% were Black, and mean serum potassium was 5.91 mEq/L. Comorbidities included diabetes (72%), heart failure (50%), and coronary artery disease (45%).

In 87% of the cases, patiromer was dosed daily, with an average daily dose of 8.4 g. During the follow-up period, 11% (n=52) had a patiromer dose increase and 5% (n=24) had a patiromer dose decrease. Following initiation of patiromer, there were significant reductions in mean serum potassium concentrations from baseline within 1 month (-1.02 mEq/L; n=307), 3 months (-1.04 mEq/L; n=351), and 6 months (-1.05 mEq/L; n=351).

In conclusion, the researchers said, "Among US veterans with ESKD and hyperkalemia on dialysis, patiromer use was associated with clinically relevant reductions in serum potassium concentrations at all study timepoints."

Source: Kovesdy CP, Tangri N, Pinnell D, Woods SD, Boutin S, Sauer BC. Treatment response and dosing of patiromer in veterans with dialysis-dependent ESKD and hyperkalemia. SA-P0307. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2022; November 5, 2022; Orlando, Florida.

Researchers in China, led by **Shichun Du, MD,** reported results of a study designed to examine the molecular characteristics of urinary proteins and urinary exosome proteins in type 2 diabetes mellitus. They conducted large-scale urinary proteomics (n=144) and urinary exosome proteomics (n=44) analyses on patients with type 2 diabetes mellitus with albuminuria in varying degrees.

The analyses revealed potential urinary biomarkers in patients with DKD, including SERPINA1 and transferrin. The biomarkers were validated as markers for diagnosis and monitoring of DKD.

"The results of our study comprehensively elucidated the changes in the urinary proteome and revealed several potential biomarkers reflecting the progression of DKD, which provide a reference for DKD biomarker screening," the authors said.

DIALYSIS

Plasma Refill Rate and Intradialytic Hypotension

Kidney 360. doi:10.34067/KID.0000000000000082

For patients receiving maintenance hemodialysis, attaining the optimal balance between achieving adequate volume removal while preserving organ perfusion is a challenge. According to **Christina H. Wang, MD,** and colleagues, "current strategies to guide ultrafiltration are inadequate."

Using hematocrit and ultrafiltration data from a retrospective cohort of patients receiving maintenance hemodialysis at 17 dialysis centers from January 2017 to October 2019, the researchers developed an approach to calculate the plasma refill rate (PRR) throughout hemodialysis. Using logistic regression, the researchers sought to identify an association between PRR and traditional risk factors for hemodynamic instability. Using Cox proportional hazard regression, they sought to identify an association between low starting PRR and intradialytic hypotension (IDH). Finally, using marginal structural modeling, they sought to identify an association between time-varying PRR throughout hemodialysis and hypotension.

The analysis included data on 180,319 hemodialysis sessions among 2554 patients. PRR had high within-patient and between-patient variability. There were associations between female sex and hypoalbuminemia and low PRR at multiple time points during the first hour of hemodialysis. Low starting PRR had a higher hazard of IDH, while high starting PRR was protective (hazard ratio [HR], 1.26; 95% CI, 1.18-1.35 vs HR, 0.79; 95% CI, 0.73-0.85, respectively).

When accounting for time-varying PRR and time-varying confounders, however, compared with a moderate PRR, a consistently low PRR was associated with an increased risk of hypotension (odds ratio [OR], 1.09; 95% CI, 1.02-1.16), and a consistently high PRR had a stronger association with hypotension within the next 15 minutes (OR, 1.38; 95% CI, 1.30-1.45).

continued on page 30

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continued from page 29

In conclusion, the authors said, "We present a straightforward technique to quantify plasma refill that could easily integrate with devices that monitor hematocrit during hemodialysis. Our study highlights how examining patterns of plasma refill may enhance our understanding of circulatory changes during hemodialysis, an important step to understand how current technology might be used to improve hemodynamic instability."

TRANSPLANTATION

Long-term Outcomes Among Kidney Transplant Recipients With MGUS

Nephrology Dialysis Transplantation.
doi.org/10.1093/ndt/gfad144

Elderly patients are increasingly being given access to kidney transplantation, resulting in an increase in the prevalence of monoclonal gammopathies of unknown significance (MGUS) in kidney transplantation. According to **Marie-Sophie Meuleman, MD,** and colleagues, there are few data available on the effects of MGUS on long-term outcomes.

The researchers conducted a study of 3059 patients who underwent kidney transplant at two kidney transplantation centers in France. Of the 3059 patients, 70 kidney transplant recipients had MGUS present at transplantation (KTMG) and 114 kidney transplant recipients developed MGUS after kidney transplant (DNMG). Outcomes of KTMG were compared with those of matched controls.

With the exception of older age in the KTMG group compared with the DNMG group (62 vs 57 years; *P*=.03), the groups were similar in baseline characteristics. Transient MGUS occurred more frequently in patients in the DNMG group (45% vs 24%; *P*=.007).

In comparison with matched controls without MGUS, patients in the KTMG group had higher frequency and earlier posttransplant solid cancers (15% vs 5%; *P*=.04), and a trend for more bacterial infections (63% vs 48%; *P*=.08). There were no differences in patient and graft survival, rejection episodes, or hematological complications. Overall survival was shorter among the patients in the KTMG group with an abnormal kappa/lambda ratio and/or severe hypogammaglobulinemia at the time of kidney transplant.

In conclusion, the authors said, "MGUS detection at the time of kidney transplant is neither associated with a higher occurrence of graft rejection, nor adversely affects graft or overall survival. MGUS should not contraindicate kidney transplantation. However, MGUS at the time of kidney transplantation may be associated with higher risk of early neoplastic and infectious complications and warrants prolonged surveillance.

"Measurement of serum free light chain should be performed before transplant to refine the risk evaluation of KTMG patients and propose personalized follow-up and immunosuppression." ■

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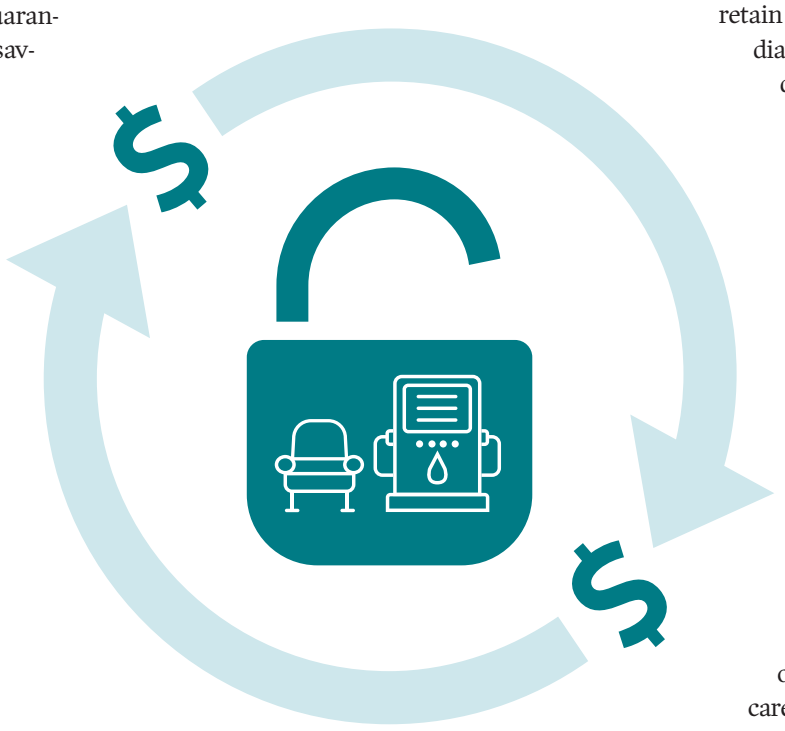
Sarah Tolson

Improved Reimbursement in Dialysis Facilities: A Call for Action to Ensure Access to Care

The readers of this column are all too familiar with the physical and emotional challenges faced by patients with end-stage renal disease (ESRD). For these patients, dialysis facilities serve as a lifeline, not only providing life-sustaining treatment, but often assisting patients with rides to and from treatment, assisting with insurance issues, and ensuring access to adequate nutrition. Unfortunately, despite the critical nature of this care, many dialysis facilities face significant financial challenges, primarily due to reimbursement not keeping pace with the significant cost increases that arose during the pandemic. Advocacy for improved reimbursement is not just a matter of ensuring the financial viability of these facilities, but also a vital step toward guaranteeing continued and enhanced access to lifesaving care for ESRD patients.

In the complex web of health care funding, dialysis centers, particularly those serving a large Medicare population, often operate on thin margins. The reimbursement rates set by the Centers for Medicare & Medicaid Services (CMS) and other insurers frequently do not cover the actual costs of providing high-quality dialysis treatments. Recently, CMS announced their proposed changes to the base rate for 2024, and unfortunately the proposal does little to close the gap between cost of treatment and reimbursement. The discrepancies between the costs of care and reimbursement can hinder these facilities' abilities to maintain and upgrade equipment, hire skilled staff, and expand services to meet growing patient needs.



Advocacy for improved reimbursement is crucial to ensuring continued access to care. Without adequate funding, some dialysis facilities might be forced to close their doors, leaving ESRD patients with limited options. In rural and underserved areas, where dialysis centers might already be few and far between, even a single facility's closure can have devastating consequences. There are several rural facilities that I have worked with that have many patients who have no other feasible options for dialysis. The next nearest facility is hours away and the patients are not candidates for home dialysis.

With the prevalence of ESRD expected to rise due to factors like an aging population and increasing rates of diabetes and hypertension, it is crucial that dialysis facilities are prepared to meet this growing demand. Adequate reimbursement can provide these centers with the funds necessary to expand and meet the needs of a medically fragile population. In busy metropolitan areas there are facilities that are at capacity, as are the neighboring facilities. Patients not on their census have no options other than the local emergency department for obtaining treatment.

Dialysis care requires skilled professionals, including nephrologists, specialized nurses, technicians, and social workers. Competitive salaries and benefits, made possible by improved reimbursement rates, ensure that dialysis facilities are able to hire and retain care teams that will not only provide quality dialysis care, but also work to address social determinants of health that prevent many people from accessing home dialysis.

Advocating for adequate reimbursement for dialysis treatments is likely the only way to bring about satisfactory change. There are several ways stakeholders can advocate for and help to bring about change, such as initiating public awareness campaigns, collaborating with patient advocacy groups, engaging with policymakers and lawmakers on a local and national level individually or with the help of an association, highlighting the financial implications, and staying updated.

Ensuring optimal care for ESRD patients is not just a moral imperative but a societal one. As we navigate the intricacies of health care funding and policy, it is crucial to remember that at the heart of these debates are real individuals whose lives depend on the decisions made. Advocacy for improved reimbursement for dialysis facilities is more than a financial discussion; it is about safeguarding a vulnerable population's right to health and life. The time to act is now. ■

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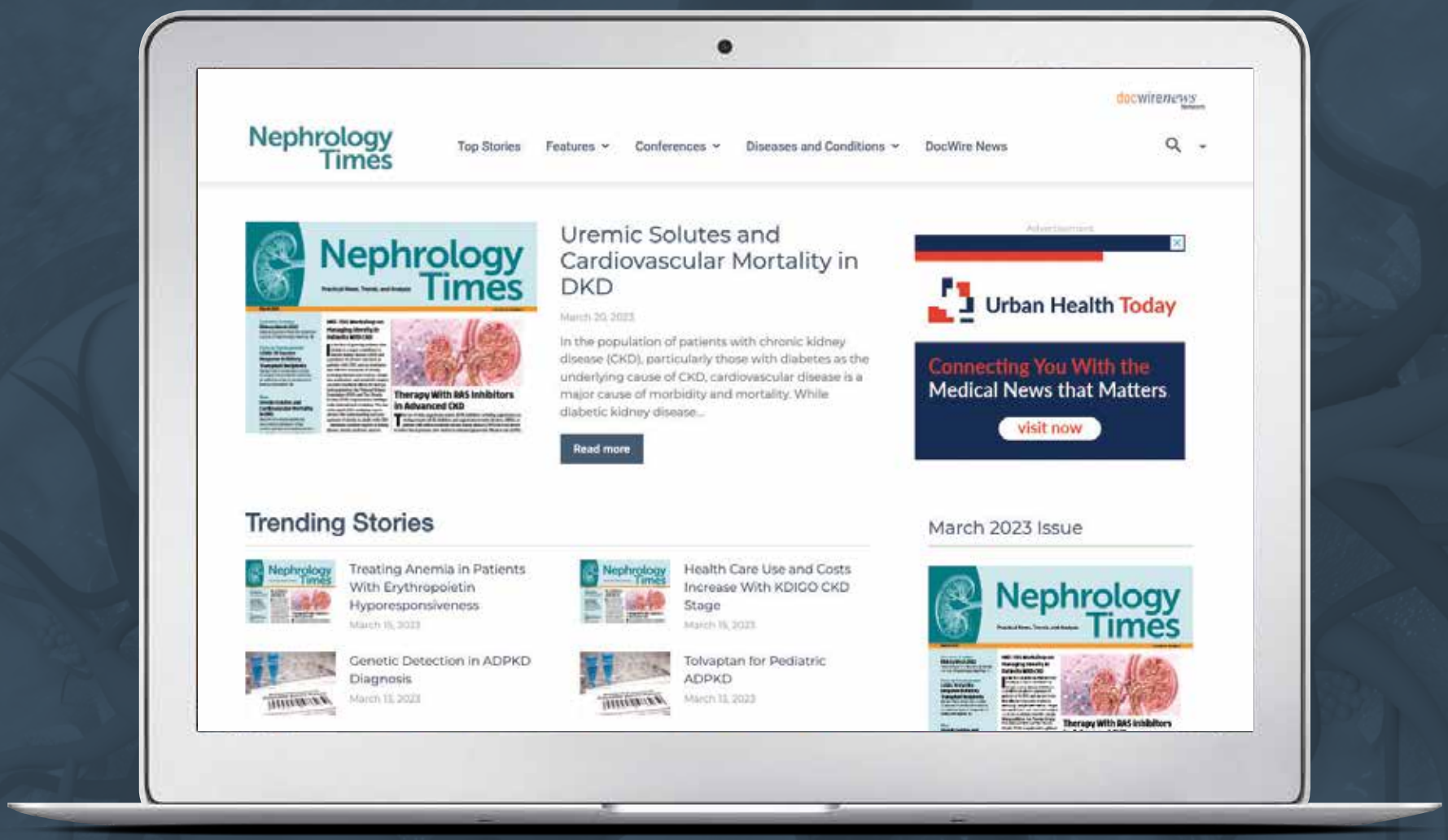

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