



Nephrology Times

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COVID-19 Antibodies and Outcomes in Maintenance Hemodialysis Patients

Individuals at highest risk for adverse outcomes of SARS-CoV-2 infection include the elderly and those with pre-existing health conditions, including chronic kidney disease (CKD). CKD is an established risk factor for mortality and morbidity in the general population. Patients with end-stage kidney disease (ESKD) are at significantly high risk due to the risk for infection-related complications. Patients receiving in-center maintenance hemodialysis have been shown to be at increased risk for contracting COVID-19 compared with patients utilizing in-home dialysis.

Early studies from China, Italy, and England reported a COVID-19 incidence rate of 2% to 3% among outpatient hemodialysis centers, with mortality up to 30%. Those studies identified cases of COVID-19 based on clinical feature and/or positive quantitative, real-time, reverse-transcriptase PCR (RT-PCR) assays of nasopharyngeal swabs, performed primarily on symptomatic patients. PCR tests are prone to false-negative results, and COVID-19 is transmissible by asymptomatic patients, making the true incidence of COVID-19 infection in in-center hemodialysis patients unclear. Serologic SARS-CoV-2 IgG antibody testing in outpatient hemodialysis centers has been limited, but may help provide an improved assessment of SARS-CoV-2 epidemiology.

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Kidney Function after Discharge in Patients with COVID-19 and AKI

Patients hospitalized with COVID-19 commonly develop acute kidney injury (AKI). AKI has been reported in 24% to 57% of COVID-19 hospitalizations and in 68% to 78% of patients with COVID-19 admitted to the intensive care unit (ICU). AKI is more severe in patients with COVID-19 compared with patients without COVID-19, and patients with COVID-19-associated AKI are more likely to require dialysis and less likely to regain kidney function while hospitalized, increasing the risk for incident chronic kidney disease (CKD) or progression of existing CKD.

There are few data available on intermediate- and long-term kidney outcomes following COVID-19-associated AKI. In early studies among survivors of COVID-19 and AKI, 32% of patients had not recovered baseline kidney function at a median of 21 days following hospital discharge.

James Nugent, MD, MPH, and colleagues conducted a retrospective cohort study

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Proteinuria as Prognostic Marker in Hospitalized COVID-19 Patients

The SARS-CoV-2 virus is responsible for COVID-19, a disease that, despite predominant respiratory manifestations, has a broad clinical spectrum, including asymptomatic infection, mild upper airways illness with fever, and severe pneumonia with respiratory failure. Patients may require admission to the intensive care unit (ICU) for acute respiratory distress syndrome or cytokine storm syndrome leading to multiple organ dysfunction. Older patients, as well as those with comorbidities, face risk of mortality.

Early reports of kidney involvement among patients with SARS-CoV-2 infection suggested that acute kidney failure was rare (<5%) in the entire infected population. However, the incidence of renal involvement is much higher (up to 65%) in patients with severe disease admitted to the ICU or with a fatal outcome. Results of a more recent retrospective study of 3993 patients with COVID-19 hospitalized in New York demonstrated that 46% of patients developed acute kidney injury (AKI) and

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Kidney Function after Discharge

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to examine the association between COVID-19 in patients with AKI and the rate of change in estimated glomerular filtration rate (eGFR) over the 6 months following hospital discharge. The researchers sought to test the hypothesis that patients with AKI associated with COVID-19 are at increased risk for decrease in eGFR or worsening CKD after discharge compared with patients with AKI without COVID-19. Results of the study were reported online in *JAMA Network Open* [doi:10.1001/jamanetworkopen.2021.1095].

The study was conducted at five hospitals in Connecticut and Rhode Island from March 10, 2020, to August 31, 2020. Among patients who were tested for COVID-19 and developed AKI, those who survived past discharge, did not require dialysis within 3 days of discharge, and had at least one outpatient creatinine level measurement following discharge were eligible.

The primary outcome of interest, the association between AKI associated with COVID-19 and eGFR slope after discharge, was assessed using mixed-effects models. The secondary outcome was the time to AKI recovery for a subgroup of patients whose kidney function had not returned to baseline level by discharge.

The study population included 182 patients with COVID-19 who developed AKI and 1430 patients with COVID-19 who did not develop AKI. There were 813 women (50.4%), and median age was 69.7 years. Patients with COVID-19-associated AKI were more likely to be Black (73 [40.1%] vs 225 [15.7%]), or Hispanic (40 [22%] vs 126 [8.8%]), and had fewer comorbidities compared with patients with AKI not related to COVID-19. Rates of pre-existing chronic kidney disease and hypertension were similar between the two groups.

A higher proportion of patients with versus without COVID-19-associated AKI were excluded due to death during the index hospitalization (29.6% vs 11.3%). The two groups were similar in the proportions of patients excluded due to the need for dialysis therapy within 3 days of discharge (1.0% vs 0.7%) or lack of an outpatient creatinine measurement following discharge (46.5% vs 47.5%). For 34 patients who were excluded due to the need for dialysis at discharge, two of eight in the COVID-19-associated AKI group and six of 26 with AKI not associated with COVID-19 remained on dialysis 6 months postdischarge; an additional six patients without COVID-19-associated AKI died within 6 months of discharge. Of patients with AKI who had received a SARS-CoV-2 test, patients who were excluded due to lack of an outpatient creatinine measurement had fewer comorbidities compared with included patients. AKI stage, dialysis requirement, ICU admission, and AKI recovery were similar between groups.

Baseline creatinine level and eGFR were

similar between patients with and without COVID-19-related AKI; patients in the COVID-19-related AKI group more commonly had proteinuria on presentation. Patients in the COVID-19-related AKI group were more likely to require dialysis, had longer hospital and ICU stays, and had higher rates of mechanical ventilation and vasopressor use. Prescriptions for angiotensin-converting enzyme inhibitor or angiotensin receptor blocker were similar in the two groups. Follow-up, defined as time from discharge to past outpatient creatinine measurement, was longer among patients with COVID-19-associated AKI. Patients without COVID-19-associated AKI had more outpatient creatinine measurements following discharge.

In the unadjusted mixed-effects model, the mean rate of decline in eGFR was $-11.3 \text{ mL/min/1.73 m}^2$ faster in patients with COVID-19-associated AKI (95% confidence interval [CI], -22.1 to $-0.4 \text{ mL/min/1.73 m}^2$). Following adjustment for baseline demographic characteristics and comorbidities, the difference in eGFR slope persisted (-12.4 ; 85% CI, -23.7 to $-1.2 \text{ mL/min/1.73 m}^2$). In the fully adjusted model, including baseline patient characteristics and comorbidities in addition to peak serum creatinine levels and dialysis requirements, patients in the COVID-19-associated AKI group continued to show an increase in the rate of eGFR decline (-14.0 ; 95% CI, -25.1 to $-2.9 \text{ mL/min/1.73 m}^2$).

By the time of hospital discharge, 82.4% of patients with COVID-19-associated AKI and 79.9% of patients without COVID-19-associated AKI had achieved AKI recovery. In the subset of patients who had not recovered at discharge ($n=319$), those in the COVID-19-associated AKI group had slower recovery after discharge compared with those in the group without COVID-19-associated AKI. There was an independent association between COVID-19-associated AKI and a lower rate of kidney recovery during outpatient follow-up (adjusted hazard ratio, 0.57; 95% CI, 0.35-0.92).

Limitations to the study findings cited by the authors included the need to exclude approximately 45% of patients with AKI in both groups due to lack of an outpatient measurement for creatinine level following hospital discharge.

In conclusion, the researchers said, "In this cohort study of US patients with and without COVID-19 who experienced in-hospital AKI, patients with COVID-19-associated AKI demonstrated faster rates of eGFR decreases after hospital discharge, independent of a patient's baseline comorbidities or AKI severity. Identifying predictors of longitudinal eGFR decrease in patients with COVID-19-associated AKI may help prioritize which patients need closer outpatient follow-up during the pandemic. A better understanding of COVID-19-associated AKI should provide opportunities for clinical trials to improve outcomes and inform the guidelines of post-COVID-19-associated AKI outpatient management." ■

TAKEAWAY POINTS

Researchers conducted a retrospective cohort study to compare the rate of change in estimated glomerular filtration rate (eGFR) between patients with COVID-19 and acute kidney injury (AKI) and patients with AKI without COVID-19.

In the group with COVID-19-associated AKI, eGFR declined by $11.3 \text{ mL/min/1.73 m}^2$ per year faster compared with the group with AKI without COVID-19 in the unadjusted mixed-effects model.

Following adjustment for patient baseline demographic characteristics, comorbidities, and severity of AKI, the findings were similar.

Proteinuria as Prognostic Marker

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19% of patients with AKI required dialysis. A study conducted in China found that 43.9% of patients had proteinuria and 26.7% had hematuria on admission.

Alexandre Karras, MD, PhD, and colleagues conducted a single-center retrospective study designed to examine the prevalence of proteinuria among patients hospitalized with COVID-19 to describe the significance of proteinuria as a prognostic indicator of dialysis initiation, admission to the ICU, and death. Results of the study were reported online in the *Clinical Journal of the American Society of Nephrology* [doi.org/10.2215/CJN.09130620].

Proteinuria was expressed as urine protein-creatinine ratio (UPCR) and albuminuria as urine albumin-creatinine ratio (UACR). Tubular dysfunction was evaluated in a subset of patients by assessment of urine retinol binding protein-concentration, expressed as urine retinol binding protein-creatinine ratio. AKI was defined by the Kidney Disease Improving Global Outcomes (KDIGO) AKI criteria. The KDIGO criteria were applied using only serum creatinine variations.

Of 322 patients admitted to Hôpital Européen Georges Pompidou, Paris, France, by April 15, 2020, 122 were excluded due to lack of data on proteinuria or pre-existing kidney failure requiring long-term dialysis. The remaining 200 patients were included.

Of the 200 patients, 143 were men, median age was 63 years, and 32 patients were >80 years of age. Data on body mass index (BMI) were available for 171 patients; median value was 26.7 kg/m². Thirty-nine percent (n=66) had BMI between 25 and 30 kg/m² and 26% (n=44) had a value above 30 kg/m². Fifty-one percent of the cohort (n=103) reported a history of hypertension, and 25% (n=51) had a history of diabetes mellitus.

Eighteen patients had previously known chronic kidney disease; of those, seven were kidney transplant recipients. Thirty percent

of the cohort (n=60) reported previous use of antihypertensive therapy with angiotensin-converting enzyme inhibitors (ACEi) or angiotensin II receptor blockers (ARBs); 21% (n=42) were receiving diuretics.

At admission, median UPCR was 0.86 g/g. Proteinuria was <0.2 g/g in 24 patients, <0.5 g/g in 72 patients, between 0.5 and 1 g/g in 44 patients, between 1 and 3 g/g in 68 patients, and >3 g/g in 16 patients. Urine specimens were collected within 48 hours of admission; 45 patients had urine tests performed following the diagnosis of AKI made on the basis of serum creatinine elevation.

Only 152 patients had data on baseline UACR (76% of the overall study population). Median UACR was 0.11 g/g. Median UACR-UPCR ratio was 18%. For 8% of the patients, UACR-UPCR was above 50%.

Eighty-five patients had measurement of baseline urine retinol binding protein. All but two had UPCR and UACR measured on the same urine specimen. The urine retinol binding protein-creatinine ratio was below the detection threshold in 32 patients. For the 53 patients with detectable urine retinol binding protein, the median value of urine retinol binding protein-creatinine ratio was 1.35 mg/mmol. Of the 85 patients with available assessment of urine retinol binding protein, those with urine retinol binding protein-creatinine ratio above the detection threshold (≥ 0.03 mg/mmol) had higher levels of baseline proteinuria and slightly higher serum creatinine at admission.

Patients with UPCR ≥ 1 g/g were older, more likely to have hypertension, and more likely to receive ACEi or ARB. There was no difference between the two groups in the sex ratio, prevalence of diabetes, prevalence of CKD, or BMI level. High levels of proteinuria were seen in patients with or without history of diabetes or CKD.

At admission, median serum creatinine level was 0.94 mg/dL. Twenty-nine patients had initial serum creatinine >1.5 mg/dL at admission. Median peak serum creatinine was 1.19 mg/dL; 79 patients had at least one

value >1.5 mg/dL during hospitalization.

Eighty-eight patients were diagnosed with AKI (28 presented stage 1, 24 stage 2, and 36 stage 3). Twenty-seven of those patients required kidney replacement therapy (KRT). During hospitalization, 118 patients were admitted to the ICU for severe pneumonia. At follow-up, 58 patients had died after a median delay of 10 days from admission; 142 were discharged with a median length of stay of 11 days from admission.

Data from long-term follow-up after hospitalization with COVID-19 were available for 135 of the 142 surviving patients. Of the 10 surviving patients with last known serum creatinine >1.5 mg/dL, eight had pre-existing CKD.

There was an association between the presence of a UPCR ≥ 1 g/g and higher peak median serum creatinine (1.79 vs 1.06 mg/dL; $P < .001$). There was also an association between a UPCR ≥ 1 g/g and significant risk of AKI (odds ratio [OR], 3.61; 95% confidence interval [CI], 2.02-6.58; $P < .001$), the need for KRT (OR, 4.87; 95% CI, 2.03-13.00; $P < .001$), the risk of admission to the ICU (OR, 3.55; 95% CI, 1.93-6.71; $P < .001$), and the occurrence of death during hospitalization (OR, 3.56; 95% CI, 1.90-6.84; $P < .001$) in unadjusted analysis. In analysis of only the patients with normal kidney function at admission, UPCR ≥ 1 g/g remained associated with ICU admission, subsequent AKI, need for KRT, and occurrence of death.

Study limitations cited by the authors were inclusion of patients with the most severe forms of COVID-19, missing clinical data, and limited data on urine retinol binding protein.

The researchers said, "In conclusion, this study reveals that COVID-19 is associated with early and frequent tubular proteinuria, which is associated with poor kidney outcome and higher mortality among patients with symptomatic COVID-19. The comprehension of the precise mechanisms underlying this tubular injury requires further investigations." ■

TAKEAWAY POINTS

- Researchers in France conducted a single-center retrospective study to examine the characteristic features of proteinuria in patients hospitalized with COVID-19 and its association with admission to the ICU, initiation of dialysis, and death.
- The cohort included 200 patients with available data. Urine protein-creatinine ratio (UPCR) at admission was ≥ 1 g/g for 84 of those patients.
- UPCR ≥ 1 g/g was associated with initiation of dialysis, admission to the ICU, and death ($P < .001$ for all).

CONFERENCE COVERAGE **KIDNEY WEEK 2020**

Tolvaptan for Treatment of ADPKD in Japan

Results of the TEMPO (Tolvaptan Efficacy and Safety in the Management of ADPKD and Its Outcomes) and REPRIFE (Replicating Evidence of Preserved Renal Function: An Investigation of Tolvaptan Safety and Efficacy in ADPKD) trials demonstrated that tolvaptan slows the decline in estimated glomerular filtration rate (eGFR) in patients with autosomal dominant polycystic kidney disease (ADPKD). However, according to **Yasuhiro Oda, MD**, and colleagues, real-world data on the change in eGFR in patients with ADPKD treated with tolvaptan are lacking. In addition, there are few data comparing the slopes of the change in eGFR prior to and following initiation of tolvaptan.

The researchers conducted a retrospective analysis of patients who initiated tolvaptan between June 2014 and June 2019 at Toranomon Hospital, Tokyo, Japan, and Toranomon Hospital Kajigaya, Kawasaki, Japan. Results of the analysis were reported during a virtual poster session as ASN Kidney Week 2020 in a poster titled *Tolvaptan*

and Renal Function in Autosomal Dominant Polycystic Disease: A Two-Center Experience of 186 Cases.

Approved indication for tolvaptan for ADPKD patients in Japan includes total kidney volume larger than 750 mL and eGFR greater than 15 mL/min/1.73 m². Medical records were used to determine eGFR at 1, 2, 3, 4, and 5 years before and after initiation of treatment with tolvaptan. Patients with missing values were excluded from the analysis.

A total of 186 patients were included in the study. Of those, 43% were men, and average age was 50.2 years. When stratified by chronic kidney disease (CKD) stage, total kidney volume was: stage 1, 1119 mL; stage 2, 1521 mL; stage 3a, 1659 mL; stage 3b, 2106 mL; and stage 4, 2847 mL. Data on eGFR before and after tolvaptan initiation were available for 139 patients; 24 patients had data only before tolvaptan initiation, and 23 had data only after tolvaptan initiation.

The overall eGFR slope after tolvaptan initiation was -3.7 mL/min/1.73 m² per year. When stratified by CKD stage,

the slope was: stage 1, -5.9 mL/min/1.73 m² per year (n=162); stage 2, -4.5 mL/min/1.73 m² per year (n=47); stage 3a, -3.1 mL/min/1.73 m² per year (n=38); stage 3b, -3.5 mL/min/1.73 m² (n=40); and stage 4, 3.3 mL/min/1.73 m² per year (n=33).

The change in eGFR slope following initiation of tolvaptan was -1.2 mL/min/1.73 m² per year in stage 1-3a patients (n=76) and +0.8 mL/min/1.73 m² per year in stage 3b-4 patients (n=63), a statistically significant difference ($P < .003$).

"Real-world data from our institution observed the eGFR slope of -3.7 \pm 2.3 mL/min/1.73 m² after starting taking tolvaptan. The eGFR slope in patients with CKD stage 3b-4 improved on average," the researchers said.

Source: Oda Y, Ikuma D, Mizuno H, et al. Tolvaptan and renal function in autosomal dominant polycystic disease: A two-center experience of 186 cases. Abstract of a poster presented at the American Society of Nephrology virtual Kidney Week 2020 (P01535), October 22, 2020.

COVID-19 Antibodies and Outcomes
continued from page 1

Minesh Khatri, MD, and colleagues conducted an analysis of data from three diverse outpatient dialysis units in the New York City area. Dialysis facilities in the New York City area had significant rates of COVID-19 infection between March and May 2020. The researchers utilized the data to examine asymptomatic transmission in the units, estimate rates of seroconversion, and identify characteristics associated with COVID-19 infection and hospitalization. Results were reported in *Kidney360* [doi.org/10.34067/KID.0006292020].

The three units are in the New York University (NYU) Winthrop Outpatient Dialysis Network, affiliated with NYU Winthrop Hospital. Two of the three units are stand-alone; the third is centered within a subacute rehabilitation facility. Eligible patients with ESKD on in-center hemodialysis were active at one of the three units as of February 1, 2020. Patients receiving peritoneal dialysis or home dialysis were excluded. Follow-up was available through August 25, 2020.

The outcomes of interest were (1) overall prevalence of SARS-CoV-2 seropositivity in the three units; (2) proportion of patients who tested positive for SARS-CoV-2 RT-PCR who developed antibodies; (3) proportion of patients who were asymptomatic who developed antibodies; and (4) severity of COVID-19 (defined as requiring hospitalization). Only hospitalizations for COVID-19 specifically were counted.

There were 386 patients registered at the three units as of February 1, 2020. Of those, 367 met inclusion criteria and had either SARS-CoV-2 PCR (n=156) or IgG antibody (n=343) tests. Of the 367, 104 were COVID-19 positive and 263 were COVID-19 negative. Median age for the overall cohort was 68 years, 44% were female, 45% were White, 34% were Black, and 17% were Hispanic.

Patients in the COVID-19 positive group were significantly younger (65 years vs 69 years) and were more likely to be Black (43% vs 30%) or Hispanic (32% vs 12%) than patients in the COVID-19 negative group. Patients in the COVID-19 positive group were also more likely to have used taxis and ambulettes and less likely to have used personal transportation to

and from the dialysis center than patients in the COVID-19 negative group.

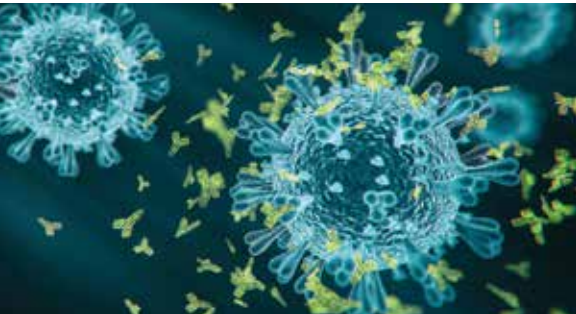
There was significant variation in COVID-19 positivity among the three dialysis units. The highest disease prevalence was in the subacute rehabilitation facility-based unit (Sun Harbor), with 70% of patients affected. There was also a difference in prevalence between the two standalone, community-based dialysis units: 32% of patients at the Mineola center were affected

versus 7% of patients at the Bethpage center. The Mineola unit had a higher percentage of Black (44% vs 6%) and Hispanic patients (22% vs 6%), compared with the Bethpage unit, despite the Bethpage unit having more comorbidities, including older age, vascular disease, and chronic obstructive pulmonary disease (COPD).

Of the 104 patients who tested positive for COVID-19, 35% (n=36) were hospitalized. Fifteen of the 104 patients (14%)

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There was significant variation in COVID-19 positivity among the three dialysis units. The highest disease prevalence was in the subacute rehabilitation facility-based unit, with 70% of patients affected.

died. There were no significant differences between the patients who

were hospitalized and those who were not hospitalized, with the

exception of greater prevalence of COPD. The mortality rate among the hospitalized patients was 33% (12/36).

There was universal seroconversion among the patients who tested positive for COVID-19 by PCR (n=67) and who underwent IgG antibody testing (n=51). Sixteen patients who had a positive PCR test did not have antibody testing. Asymptomatic transmission, defined as patients who had IgG antibodies and either were not given a PCR test (no indication) or were a person under investigation with a negative PCR result, occurred in 32% of patients (28/88).

Limitations to the study cited by the authors included the inability to rule out false positives or false negatives to the serologic testing, not including patients on home dialysis, lack of data on rates of infection among dialysis staff, and the small sample size.

In conclusion, the researchers said, “We found that all patients on dialysis mounted an antibody response to symptomatic infection, and there was a significant rate of asymptomatic spread in dialysis units, as determined on the basis of serologic testing. There were high rates of hospitalization of patients who were symptomatic and subsequent mortality, and there were also substantial racial/ethnic disparities in this population, as well. The durability and efficacy of antibodies needs to be confirmed in larger and longer studies.” ■

TAKEAWAY POINTS

- Researchers in New York conducted a study to examine asymptomatic transmission of COVID-19 infection at three diverse outpatient dialysis units. The study also assessed the patient characteristics associated with COVID-19 infection and hospitalization.
- Of 367 patients, 28% (n=104) had either a positive PCR or IgG test. There was wide variation in COVID-19 positivity among the three centers.
- Among this patient population, rates of asymptomatic infection were high, as were rates of hospitalization and mortality.

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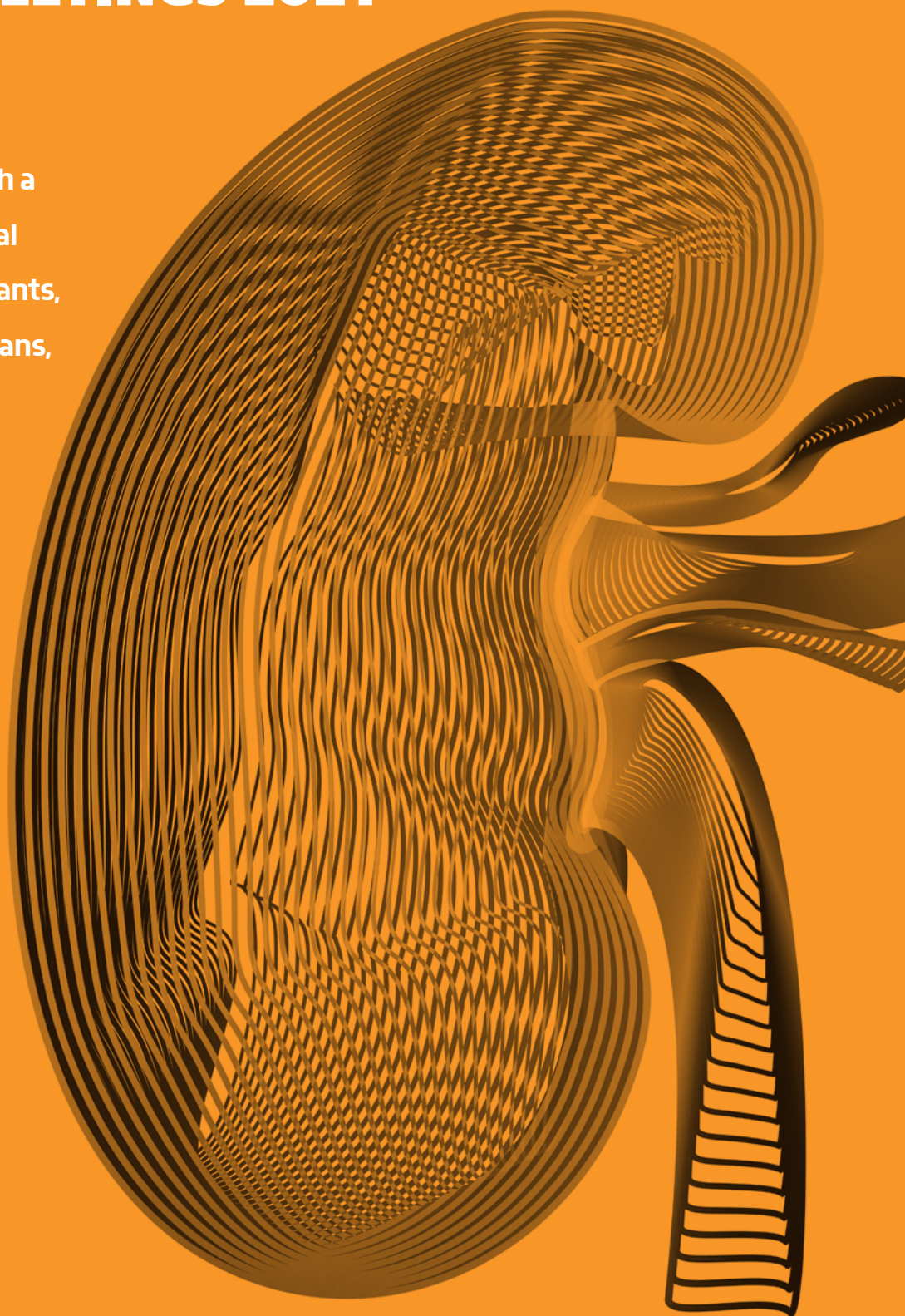
NATIONAL KIDNEY FOUNDATION

SPRING CLINICAL MEETINGS 2021

April 6-10, 2021

Nephrologists, fellows and residents with a special interest in kidney disease, general internists, pharmacists, physician assistants, nurse practitioners, nurses and technicians, social workers, and renal and clinical dietitians all benefitted from the virtual NKF Spring Clinical Meetings in April.

Presenters reported the latest insights into chronic kidney disease care and participants were informed about new and evolving concepts related to kidney disease.



APOL1 High-Risk Genotype and AKI in COVID-19

People of African American ancestry who carry the apolipoprotein L1 (APOL1) genotype who acquire COVID-19 infection are at high risk of acute kidney injury (AKI) and nephrotic-range proteinuria, due to collapsing glomerulopathy. Available data suggest that the majority of cases of AKI in African American patients are associated with acute tubular injury. There are no data on whether the high-risk APOL1 genotype confers an increased risk for AKI related to COVID-19.

Terrance Wickman, MD, and colleagues conducted a study to test the hypothesis that the risk for COVID-19-related AKI is increased in patients with APOL1 high-risk genotype. Results of the study were reported during a virtual poster session at the NKF Spring Clinical Meetings 2021 in a poster titled *Risk of Acute Kidney Injury in COVID-19 Is Increased in African Americans with APOL1 High-Risk Genotype*.

The researchers prospectively identified African American patients who were treated at Ochsner Health System with a nasopharyngeal swab positive PCR for SARS-CoV-2 RNA. Blood samples were retrieved within 72 hours of collection and sent to Arkana Laboratories for genotyping with APOL1 polymorphism.

The outcomes of interest were AKI (Kidney Disease Improving Global Outcomes criteria stage ≥ 2), persistent AKI, defined as no resolution within 72 hours, and AKI requiring renal replacement therapy (RRT) occurring within 21 days of the positive PCR test.

The researchers obtained and assayed specimens from 134 patients. Median age was 59 years, 59% were women, 67% had hypertension, and 29% had preexisting chronic kidney disease (CKD). In incidence of high-risk APOL1 genotype in the overall cohort was similar to known prevalence: 15%.

Among the patients with high-risk APOL1 genotype (2 risk alleles), the odds ratio (OR) for AKI, persistent AKI, and AKI requiring RRT were 4.8 ($P=.005$), 5.3 ($P=.001$), and 3.6 ($P=.03$), respectively. Results of multivariate logistic regression analyses adjusting for age, sex, body mass index, hypertension, and CKD, also demonstrated an increased risk for AKI (OR, 5.6; $P=.009$), persistent AKI (OR, 4.9; $P=.005$), and AKI requiring RRT (OR, 3.3; $P=.05$) for patients in the high-risk APOL1 genotype group.

In summary, the researchers said, "High-risk APOL1 genotype in African Americans is associated with greater risk for AKI stage ≥ 2 , persistent AKI, and AKI requiring RRT in COVID-19. Whether the increased AKI risk is driven by a greater risk for inapparent glomerular insult, a tubular insult, or other factor is not known and warrants further investigation. This observation may have significant public health implications."

Source: Wickman T, Trochez LM, Braga J, Arthur J, Velez JC, Larsen C. Risk of acute kidney injury in COVID-19 is increased in African Americans with APOL1 high-risk genotype. Abstract of a poster presented at the National Kidney Foundation virtual Spring Clinical Meetings (Abstract #25), April 9, 2021.



AKI in COVID-19: Incidence and Outcomes

The pandemic of COVID-19 has had a negative impact on various organ systems and on individuals of all ages. Kidney involvement in patients with COVID-19 typically manifested as acute kidney injury (AKI). However, there are few consensus data on the epidemiology of AKI in COVID-19. **Ronith Chakraborty** and colleagues conducted a systematic literature review to assess the knowledge gap. Results of the review were reported during a virtual poster session at the NKF Spring Clinical Meetings 2021 in a poster titled *A Systematic Review of the Incidence and Outcomes of Acute Kidney Injury in COVID-19*.

The researchers systematically searched Medline and Cochrane Library for literature related to AKI in COVID-19 in patients of all ages. In addition, MEDRxIV was searched for relevant unpublished manuscripts. The literature was independently assessed by two reviewers. Relevant studies assessed the incidence of AKI and the association with mortality, extracting the need for kidney replacement therapy (KRT).

The review included 60 studies, representing 43,871 patients. The pooled incidence of AKI among patients with COVID-19 was 19.45% [95% confidence interval (CI), 14.63% to 24.77%]; the pooled incidence of COVID-19 patients with AKI who required KRT was 39.04% [95% CI, 16.38% to 64.57%]. The pooled proportion of COVID-19 positive patients was significantly lower at 8.83% [95% CI, 5.64% to 12.66%].

The overall mortality of patients with COVID-19 was calculated as 17.71% [95% CI, 11.49% to 24.93%]. Mortality among patients with COVID-19-related AKI was 54.24% [95% CI, 44.70% to 63.63%].

In conclusion, the researchers said, "This review found significantly higher incidence and mortality rates in COVID-19 patients with AKI, especially those requiring KRT. This suggests that kidney involvement during COVID-19 is substantial, requiring additional studies to explore KRT treatments."

Source: Chakraborty R, Mahajan Z, Vasistha P, et al. A systematic review of the incidence and outcomes of acute kidney injury in COVID-19. Abstract of a poster presented at the National Kidney Foundation virtual Spring Clinical Meetings 2021 (Poster #6), April 9, 2021.

Timing of Nephrologist Care in Patients with Newly Diagnosed ADPKD

The most common genetic cause of end-stage kidney disease is autosomal dominant polycystic kidney disease (ADPKD). Favorable outcomes, including improved quality of life and reduction in decline in kidney function, are associated with earlier disease management by nephrologists in the course of kidney disease. **Erin Hulbert, MS**, and colleagues conducted a study to examine timing of nephrology care in a sample of patients with ADPKD.

Results of the study were reported during a virtual poster session at the NKF 2021 Spring Clinical Meetings. The poster was titled *Delay in First Nephrologist Visit among Newly Diagnosed ADPKD Patients*.

The researchers utilized the Optum Research Database to identify commercial and Medicare Advantage with Part D (MAPD) enrollees newly diagnosed with ADPKD. The index date was the first diagnosis of ADPKD from January 2007 to August 2017. Patients were enrolled during 6-month baseline and 2-year follow-up periods. *International Classification of Diseases, Tenth Revision* codes were used to determine chronic kidney disease (CKD) status and estimated glomerular filtration rate laboratory results.

The cohort included 4248 patients newly diagnosed with ADPKD. Of those, 51% were female, 25% were insured via MAPD, and mean age was 52 years. Thirty percent of the cohort had evidence of CKD stage 3-5 at the index date. Forty-eight percent had a visit with a nephrologist in the baseline period (21%) or

on the index date (27%). Twenty-five percent had a nephrologist visit during follow-up.

A total of 1141 patients (27%) did not see a nephrologist within 2 years of the initial diagnosis of ADPKD. Of those, 157 (14%) had known CKD stage 3-5 at index. Patients had mean 8.0 baseline ambulatory visits. Forty-two percent had a baseline diagnosis for hypertension, 10% for cardiovascular complications, 12% for diabetes, 6% for kidney function, and 15% for abdominal pain.

There were no significant differences in comorbidities between patients with and patients without a nephrology visit. At the end of the study period, 31% of patients who did not have a nephrology visit had evidence of progression of CKD.

In conclusion, the researchers said, "These results provide new insight into ADPKD patients with delayed referral to specialist care. Many patients had high healthcare utilization as well as comorbidities with potential to increase risk of CKD progression. Earlier specialist monitoring and intervention may help better manage disease complications and slow disease progression."

Source: Hulbert E, Sanon M, Willey C, Korrer S, Wang S, Seliger S. Delay in first nephrologist visit among newly diagnosed ADPKD patients. Abstract of a poster presented at the National Kidney Foundation virtual Spring Clinical Meetings 2021 (Abstract #308), April 9, 2021.

Conference Coverage

Attitudes among Kidney Transplant Recipients toward COVID-19 Vaccine

Recipients of kidney transplant are at high risk for complications related to COVID-19 infection. **Perry Kerner** and colleagues at SUNY Downstate Health Sciences University, Brooklyn, New York, conducted a telephone survey to assess attitudes toward receiving a COVID-19 vaccine in that patient population to aid in the development of education regarding the vaccine that can be targeted to that specific group. Results of the survey were reported during a virtual poster session at the NKF Spring Clinical Meetings 2021 in a poster titled *Attitudes Towards Receipt of a COVID-19 Vaccine in a Population of Inner-City Kidney Transplant Recipients (KTx)*.

The survey was conducted in a random sample of 33 kidney transplant recipients. The patients were asked about their attitudes toward vaccines in general and whether they would receive a COVID-19 vaccine when available. The Multidimensional Health Locus of Control (MHLC) questionnaire was also administered. Analysis was conducted using the Pearson r model (unless otherwise noted).

Mean age of the sample was 57.9 years and mean time since transplant was 8.1 years. Of the 33 participants, 18 were men, 15 were women, 20 were Black, five were Hispanic, three were White, and three were mixed race or other. Three did not finish high school, 14 completed high school, six finished some college, seven completed college, and two completed graduate school.

When asked "Would you receive a COVID-19 vaccine if one were currently available?," 21 respondents replied "no." Twelve of the 21 patients cited safety as their primary reason for declining, compared with efficacy (two patients) or cost (one patient). There was a correlation between replying no and higher level of education ($r=0.449$, $P=.010$).

There was a correlation between replying yes and higher MHLC subscores of physicians ($r=0.589$, $P<.001$), powerful others ($r=0.652$, $P<.001$), and other people ($r=0.488$, $P=.005$). Replying yes was also correlated with greater trust in information received about vaccines ($r=0.389$, $P=.025$). There were no statistically significant differences with respect to age, sex, or race.

In conclusion, the researchers said, "In our population: (1) The majority of kidney transplant patients would not agree to take a COVID-19 vaccine, citing safety as their main concern. (2) Patients who had completed higher education were less likely to agree to the vaccine. (3) Patients who had an external locus of control, including relying on doctors and other authority figures, and trusting information one receives about vaccines were more likely to agree to the vaccine. (4) Successful implementation of a COVID-19 vaccine program for our inner-city kidney transplant patients should take into account educational background and individual locus of control. (5) Understanding how to increase safety and alleviate patient concerns related to vaccine safety would be valuable next steps in terms of planning a COVID-19 vaccine program for this high-risk population."

Source: Kerner P, Imas A, Udod G, et al. Attitudes towards receipt of a COVID-19 vaccine in a population of inner-city kidney transplant recipients (KTx). Abstract of a poster presented at the National Kidney Foundation virtual Spring Clinical Meetings 2021 (Abstract #216), April 9, 2021.

Incidence of COVID-19-Related AKI Over Time

Patients hospitalized with COVID-19 infection often developed acute kidney injury (AKI). In the initial surge of the pandemic in the United States, estimates of the prevalence of AKI associated with COVID-19 were as high as 40%. **Sergio Dellepiane, MD, PhD**, and colleagues conducted an analysis to estimate the temporal trends of COVID-19-related AKI, both overall and by clinically relevant subgroups.

Results of the analysis were reported during a virtual poster session at the NKF Spring Clinical Meetings 2021. The poster was titled *Changes in Incidence of COVID-19 Associated AKI over 2020*.

The researchers examined trends of AKI, defined by Kidney Disease Improving Global Outcomes creatinine criteria, from March 1, 2020, to November 30, 2020. The temporal trends of AKI were also examined by subgroups: age, sex, race, and preexisting chronic kidney disease (CKD).

The data included information on 6909 patients. Mean age of the cohort was 64 years, 43% were female, 27% were White, and 25% were Black. Hospitalizations peaked in April and declined rapidly in May. Over time, the incidence of AKI showed a significant decrease, from 33.6% in March to 11% in November. The decrease was consistent in the clinically significant subgroups, including age, sex, CKD, and race.

In conclusion, the researchers said, "AKI patients with COVID-19 significantly decreased over the time course of the SARS-CoV-2 pandemic. The reasons for this decrease (change in case-mix, improved therapeutic and triage strategies, novel medications) need to be explored in more detail."

Source: Dellepiane S, Vaid A, Chan L, Coca S, He C, Nadkarni G. Changes in incidence of COVID-19 associated AKI over 2020. Abstract of a poster presented at the National Kidney Foundation virtual Spring Clinical Meetings 2021 (Abstract #9), April 9, 2021.

Pathways of Impaired Natriuresis in PAH

In patients with pulmonary arterial hypertension (PAH), volume overload is a frequent and early complication in the absence of overt kidney dysfunction. Volume overload is associated with progression to right heart failure. There are few data available on the pathophysiology of volume overload and the role of the kidneys in sodium and water retention.

Shweta Bansal, MD, and **Ahmad Altarawneh, MD**, conducted a chart review to identify factors associated with volume overload in patients with PAH. Results of the chart review were reported during a virtual poster session at the NKF Spring Clinical Meetings 2021 in a poster titled *Cardiorenal Syndrome in Pulmonary Arterial Hypertension*.

The researchers reviewed charts of 32 consecutive patients with PAH. Patients on loop diuretic were considered to be volume overloaded. Repeated measures of clinical and laboratory variables recorded at the time of each right heart catheterization (RHC) were included in the analysis. Independent t-test was used for comparisons between patients on diuretics and those not on diuretics for normally distributed variables. The Mann-Whitney U test was used to compare nonparametric variables.

Mean age at last follow-up was 51.2 years, 100% were White, 94% were female, and mean estimated glomerular filtration rate (eGFR) was 93 mL/min/1.73 m². Follow-up was a median of 4 years. Fifty-six percent of the patients were on a diuretic.

Patients in the diuretic group were significantly more edematous (1.24 vs 0.27 score; $P=.005$), had higher body mass index (30.5 vs 25.1 kg/m²; $P=.002$), and covered less distance on the 6-minute walk test (360 vs 420 meters; $P=.012$) compared with patients in the no-diuretic group.

There were no differences in age, sex, blood pressure, New York Heart Association class, or oxygen saturation. On RHC, right arterial pressure was significantly higher (7.9 vs 3.8 mmHg; $P=.006$) and there was a trend toward higher mean pulmonary artery pressure (49 vs 42 mmHg; $P=.08$) in the diuretic group compared with the no-diuretic group. There was no difference in cardiac index or pulmonary vascular resistance.

In the diuretic group, serum alkaline phosphatase was higher than in the no-diuretic group (106.8 vs 76.2 U/L; $P=.02$). There were no differences in other blood work, including brain natriuretic peptide and eGFR. There was no difference in the proportion of patients on PAH-specific therapies.

"High body mass index and right arterial pressure, well-known factors associated with cardiorenal syndrome and volume overload in other edematous disorders, were applicable in our PAH cohort as well as suggestive of the presence of similar pathways of impaired natriuresis despite normal GFR. Further studies are required to confirm these pathways which can guide appropriate early-on therapeutics," the researchers said.

Source: Bansal S, Altarawneh A. Cardiorenal syndrome in pulmonary arterial hypertension. Abstract of a poster presented at the National Kidney Foundation virtual Spring Clinical Meetings 2021 (Abstract #177), April 9, 2021.



ESA Use in Patients with Non-Dialysis Dependent CKD

Patients with non-dialysis dependent chronic kidney disease (NDD-CKD) commonly develop anemia. Since the 1980s, erythropoiesis-stimulating agents (ESAs) have been approved for the treatment of anemia related to CKD; however, use of ESAs in that patient population has been impacted by safety concerns and labeling changes following initial FDA approval.

Christine Ferro and colleagues conducted a retrospective claims analysis to examine ESA use among NDD-CKD patients using real-world data. The researchers also sought to identify predictors of ESA use in NCC-CKD patients with anemia. Results of the analysis were reported during a virtual poster session at the NKF Spring Clinical Meetings in a poster titled *Predictors of ESA Use in the Non-Dialysis Dependent Chronic Kidney Disease Population with Anemia*.

The analysis utilized Centers for Medicare & Medicaid Services 100% Innovator data from 2015-2018. Relevant CKD diagnosis codes were used to identify patients with NDD-CKD. From the total NDD-CKD population, two study populations were identified: ESA users and non-ESA users. Meaningful differences between the two populations were detected using chi-square analysis. Using a stepwise methodology, explanatory variables (comorbidities, markers of disease severity, and encounters with an inpatient or outpatient specialty) were selected for inclusion in a regression model to define factors predictive of ESA use.

The study sample included 1,584,851 patients with NDD-CKD. Of those, 11,335 (0.7%) used ESAs in 2018. Of those patients, 10,760 (94.9%) had an anemia diagnosis at the time of initiation of ESA therapy. Only 125,383 (8.0%) of non-ESA users had a diagnosis of anemia at any time during 2016-2018.

Results of chi-square analysis of ESA users compared with non-ESA users identified associations with variables such as hypertension (78.9% vs 11.9%), heart failure (43.0% vs 7.2%), and outpatient encounters with nephrologists (47.9% vs 3.1%).

"This study of real-world ESA treatment use among NDD-CKD patients with anemia identified predictors of ESA use that may inform those for anemia treatment," the researchers said.

Source: Ferro C, Dieguez G, Pareja K, Szabo E, Michalopoulos E. Predictors of ESA use in the non-dialysis dependent chronic kidney disease population with anemia. Abstract of a poster presented at the National Kidney Foundation virtual Spring Clinical Meetings 2021 (Poster #170), April 9, 2021.

Outcomes in Pediatric COVID-19 with Renal Involvement

There are few data available on the epidemiology of acute kidney injury (AKI), associated risk factors, treatments, and mortality rate among pediatric patients with COVID-19 admitted to the intensive care unit (ICU). AKI is a common and severe complication in children and adolescents with COVID-19, and an understanding of the disease will aid in development of treatment and preventative care strategies to reduce morbidity and mortality in that patient population.

Isabelle Mawby and colleagues conducted a study to examine the incidence of AKI among COVID-19 patients in pediatric ICUs in North American using the Virtual Pediatric Systems (VPS) database. The researchers also sought to assess COVID-19-related risk factors; treatments, including kidney replacement therapy (KRT); and mortality rates. Results of the analysis were reported during a virtual poster session at the NKF Spring Clinical Meetings 2021 in a poster titled *Acute Kidney Injury in COVID-19 Pediatric Patients: Analysis of the Virtual Pediatric Systems Data*.

The retrospective study included patients ≤ 24 years of age with COVID-19 in the VPS COVID-19 database who were admitted to the ICU between January 1, 2020, and June 30, 2020. The poster reported results of analysis of data on 1240 pediatric patients with COVID-19.

Of the 1240 patients, 172 had renal/urinary system involvement. Of those 172, there were 19 confirmed deaths, translating to 45% of all confirmed pediatric COVID-19 deaths associated with renal involvement. Of the 36 patients who required KRT, two died. An additional 264 (24.67%) patients were diagnosed with MIS-C (multisystem inflammatory syndrome in children).

In conclusion, the researchers said, "Although COVID-19 in the pediatric population tends to present more favorably, renal involvement among the pediatric COVID-19 population may be considered a negative prognostic factor with respect to patient outcomes."

Source: Mawby I, Chakraborty R, Pandya A, Mahajan S, Raina R. Acute kidney injury in COVID-19 pediatric patients: Analysis of the virtual pediatric system data. Abstract of a poster presented at the virtual National Kidney Foundation Spring Clinical Meetings 2021 (Poster #16), April 9, 2021.



Outcomes among Kidney Transplant Recipients with COVID-19

The COVID-19 pandemic raised questions and concerns regarding immunosuppression management and outcomes in kidney transplant recipients with COVID-19 infection. **Meredith McAdams, MD**, and colleagues conducted a study of kidney transplant recipients with positive SARS-CoV-2 PCR testing who were seen in outpatient clinics or hospitalized at University and Parkland Hospitals in Dallas, Texas from March 1, 2021, to October 1, 2021.

Results of the study were reported during a virtual poster session at NKF Spring Clinical Meetings. The poster was titled *COVID-19 and Kidney Transplant Recipients: Immunosuppression Management and Outcomes*.

Eligible patients were followed for 90 days. The primary outcome of interest was a composite event of acute kidney injury (AKI), admission to the intensive care unit (ICU), or death. Univariate and multivariate backward selection logistic regression was used to identify risk factors for the primary outcome. Non-parametric methods were used to compare biomarkers based on changes in immunosuppressive drugs.

A total of 59 patients were included in the study. Of those, mean age was 51 years, 35 (59%) were male, 13 (22%) were Black, and 36 (61%) were Hispanic. Half of the cohort (n=29) had a baseline estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m², 88% (n=52) had hypertension, and 56% (n=33) had diabetes. At baseline, 93% (n=55) were on calcineurin inhibitors (CNI) and 83% (n=49) on an antimetabolite. Ten percent (n=6) had been treated for acute rejection in the 12 months prior to baseline.

Initial ferritin level was higher in patients who had CNI dose decrease or discontinued than in patients with CNI unchanged (median, 1271 vs 283 ng/mL; $P = .0002$). Patients who discontinued CNI had significantly higher peak high-sensitivity C-reactive protein (hsCRP) values compared with patients who maintained the same dose (median, 344 vs 41 mg/L; $P = .03$).

There were 31 composite events, 43 hospitalizations, 13 admissions to the ICU, and 12 deaths. Fifty-two patients had creatinine values; of those, 56% (n=29) had AKI, with 35% (n=10) requiring renal replacement therapy. Of the patients with AKI, 46% (n=13) had recovery of AKI at 90 days, defined as serum creatinine within 10% of baseline. In the multivariate model, eGFR < 60 mL/min/1.73 m² and peak hsCRP remained associated with the composite event, with area under the curve = 0.89.

In conclusion, the researchers said, "Over half of kidney transplant patients with COVID-19 had AKI and 73% required hospitalization. Elevated markers of inflammation were associated with changes in CNI regimen. An eGFR < 60 mL/min/1.73 m² and higher peak hsCRP were associated with increased risk of death, ICU admission, or AKI."

Source: McAdams M, Xu P, Abdulrahim N, Hedayati SS. COVID-19 and kidney transplant recipients: Immunosuppression management and outcomes. Abstract of a poster presented at the National Kidney Foundation virtual Spring Clinical Meetings 2021 (Abstract #369), April 9, 2021.

Conference Coverage

Increased Serum Bicarbonate in Patients with CKD and Metabolic Acidosis

Metabolic acidosis at a given point in time is associated with accelerated kidney decline in patients with chronic kidney disease (CKD). **Navdeep Tangri, MD**, and colleagues modeled how changes in serum bicarbonate over time affect the incidence of adverse kidney outcomes.

The analysis utilized data from OPTUM® HER+ Integrated dataset of patients in the United States from 2007–2019 with ≥1 year of prior medical record data, CKD stages 3–5, and metabolic acidosis, defined as index serum bicarbonate 12 to 22 mEq/L. Results of the analysis were reported during a virtual poster session at the NKF Spring Clinical Meetings 2021 in a poster titled *Increasing Serum Bicarbonate Is Associated with Reduced Risk of Adverse Kidney Outcomes in Patients with CKD and Metabolic Acidosis*.

The index date was the date of the first outpatient serum bicarbonate test within 180 days of the first outpatient estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m². The primary predictor of interest was the change in serum bicarbonate, evaluated at each post-index outpatient serum bicarbonate test as a time-dependent continuous variable. Other covariates were age, sex, key comorbidities, and eGFR. The primary outcome of interest was a composite of either a 40% decline in eGFR from index, evidence of dialysis or transplantation, or an outpatient eGFR <10 mL/min/1.73 m² (RRT₄₀), evaluated using adjusted and unadjusted Cox proportional hazard models, and with death as a competing risk.

The analysis included 24,384 patients. Median follow-up was 3.7 years, mean age was 64.9 years, and 48% were men. Mean index serum bicarbonate was 19.2 mEq/L, and mean index eGFR was 36.9 mL/min/1.73 m².

There was an association between a within-patient increase in serum bicarbonate over time and a lower risk of the composite kidney outcome. The unadjusted hazard ratio (HR) per 1-mEq/L increase in serum bicarbonate was 0.911 [95% confidence interval, 0.906–0.916; *P*<.0001]. Following adjustment for baseline eGFR and serum bicarbonate, and the time-dependent effect of eGFR and other covariates, the HR per 1-mEq/L increase in serum bicarbonate was largely unchanged (0.916; 95% CI, 0.911–0.921; *P*<.0001). Following assessment of death as a competing risk, the hazard risk was similar.

In conclusion, the researchers said, “In a real-world population of nearly 25,000 US patients with CKD and metabolic acidosis, a within-patient increase in serum bicarbonate lowered RRT₄₀ risk, suggesting that interventions that increase serum bicarbonate may reduce CKD progression and delay or prevent kidney failure.”

Source: Tangri N, Reaven N, Funk S, Mathur V. Increasing serum bicarbonate is associated with reduced risk of adverse kidney outcomes in patients with CKD and metabolic acidosis. Abstract of a poster presented at the National Kidney Foundation virtual Spring Clinical Meetings 2021 (Abstract #279), April 9, 2021.

Addressing Disparities in Transplant Access among Spanish-Speaking Patients

Compared with non-Hispanic White Americans, Hispanic Americans receive disproportionately fewer organ transplants. In 2018, the Hispanic Transplant Clinic was established at the University of Colorado. **Madhura Pande** and colleagues at the University of Colorado School of Medicine, Aurora, conducted a study to examine the efficacy of the program in reducing this disparity.

The researchers reported results of the analysis during a virtual poster session at the NKF Spring Clinical Meetings. The poster was titled *Reducing Transplant Disparities for Spanish-Speaking Patients*.

The researchers performed a mixed-methods analysis of data from 406 Spanish-speaking patients who were referred for transplant to the University of Colorado Hospital between 2015 and 2019. Outcomes for patients referred between 2015–2017 were compared with outcomes for patients referred between 2018–2019. Semi-structured telephone interviews were conducted with six patients per time period, as well as with nephrology providers in the Denver, Colorado metro area. Interviewees were asked to evaluate communication, transplant education, and overall experience.

In comparisons of averages of the two time periods, there was a percentage increase in the number of patients completing each step of the transplant process during 2018–2019: 74.9% increase in referrals; 87.9% increase in evaluations; 137.5% increase in committee reviews; 38.4% increase in listings; and 11.1% increase in transplants.

In the interviews of patients in the 2018–2019 time period, all patients expressed understanding of the process of kidney transplantation and described the Spanish-speaking providers as thorough. Conversely, patients evaluated prior to 2018 described issues with communications, reporting difficulty understanding their status in the transplant process.

Referral Year	Referred	Evaluated	Reviewed	Waitlisted
2015–2017	158	127	72	53
2018–2019	184	159	114	49

Overall, the nephrologists reported a positive experience with the Hispanic Transplant Clinic. They all indicated it was easier to refer their Spanish-speaking patients and that more patients were undergoing evaluation for kidney transplant.

In conclusion, the researchers said, “The establishment of the Hispanic Transplant Clinic is associated with increased numbers of Hispanic patients per year completing steps of the transplant process. This supports establishing clinics oriented to Spanish-speaking patients as a means of reducing transplant disparities for Hispanic Americans.”

Source: Pande M, Grafals M, Rizzolo K, Kenrick J. Reducing transplant disparities for Spanish-speaking patients. Abstract of a poster presented at the National Kidney Foundation virtual Spring Clinical Meetings 2021 (Abstract #373), April 9, 2021.

Pre-Dialysis Hyperkalemia and Associated Patient Characteristics

The strongest independent predictor of mortality in patients on hemodialysis is pre-dialysis hyperkalemia.^{1,2} To help inform clinical practice, researchers at AstraZeneca (Wilmington, Delaware, United States) conducted a study to update estimates of the prevalence of pre-dialysis hyperkalemia and the patient characteristics associated with higher hyperkalemia prevalence.

Results of the RE-UTILIZE study were reported by **Abiy Agrio, PhD**, at the NKF Spring Clinical Meetings 2021 during a virtual poster session. The poster was titled *The Prevalence of Pre-Dialysis Hyperkalemia and Associated Characteristics among Hemodialysis Patients: The RE-UTILIZE Study*.

RE-UTILIZE was a retrospective, observational analysis that used survey data from DOPPS (Dialysis Outcomes and Practice Patterns) and included data on hemodialysis patients in the United States who underwent in-center hemodialysis three times a week from 2018 to 2020. Included patients in the current analysis had at least one monthly potassium laboratory result within 1 year of enrollment.

The primary study objective was to define the prevalence of hyperkalemia (defined as first pre-dialysis serum potassium level >5.0 mEq/L) anytime over 1 year in all hemodialysis patients. The secondary objective was to identify patient characteristics associated with higher 1-year hyperkalemia prevalence.

The study included 9347 hemodialysis patients. Of those, 58% were men, 83% were ≥51 years of age, 56% first received hemodialysis at the DOPPS facility prior to

2018, and 64% had comorbid diabetes. Within 1-year of enrollment, the prevalence of any pre-dialysis hyperkalemia (serum potassium >5.0 mEq/L), moderate-to-severe hyperkalemia (serum potassium >5.5 mEq/L), and severe hyperkalemia (serum potassium >6.0 mEq/L) was 74%, 43%, and 17%, respectively.

In multivariate regression analysis, there were associations between female sex, Hispanic ethnicity, and younger age and higher rates of annual hyperkalemia prevalence. There were associations between recent (2018–2019) initiation of first dialysis at the facility, Black race, and cancer and lower rates of annual hyperkalemia prevalence.

In conclusion, the researchers said, “The prevalence of pre-dialysis hyperkalemia is relatively high, especially in females, younger patients, and those of Hispanic ethnicity. Therefore, considerations for hyperkalemia management during non-dialysis days will be important to improve patient care and address ethnic and racial disparities.”

Source: Agiro A, Duling I, Eudicone J, et al. The prevalence of pre-dialysis hyperkalemia and associated characteristics among hemodialysis patients: The RE-UTILIZE study [poster]. Presented at: National Kidney Foundation (NKF) SCM21; April 6–10, 2021; Poster 237. Accessed April 9, 2021. <https://casehippo.com/spa/symposium/national-kidney-foundation-2021-spring-clinical-meetings/event/gallery/abstracts?abstractid=1796>

References

- Montford JR, et al. *J Am Soc Nephrol*. 2017;28(11):3155–3185.
- Betts KA, et al. *Curr Med Res Opin*. 2018;34(6):971–978.

Awards and Honors

Healthcare professionals who have made significant contributions to the field of kidney disease were honored at the **National Kidney Foundation 2021 Spring Clinical Meetings.**



James Lash, MD

The *Shaul G. Massry Distinguished Lecture* award was presented to **James Lash, MD**, professor of medicine and chief of the division of nephrology at the University of Illinois at Chicago College of Medicine. Dr. Lash's research focuses on the epidemiology of chronic kidney disease (CKD) and interventional trials in the treatment of kidney disease, with an emphasis on the racial and ethnic minority populations in the United States. He is the UIC principal investigator for the National Institute of Diabetes and Digestive and Kidney Diseases-sponsored Chronic Renal Insufficiency Cohort (CRIC) and Hispanic CRIC Studies. The studies examine risk factors associated with the progression of CKD and cardiovascular disease in patients with CKD.



Mark Perazella, MD

The *Donald W. Seldin Award* was established to recognize excellence in clinical nephrology. The recipient for 2021 is **Mark Perazella, MD**, of Yale University School of Medicine and West Haven VA Medical Center. Dr. Perazella's academic career has focused on his role as a clinician and educator. He was co-chair for the 2019 Spring Clinical Meetings and program chair for the 2020 Spring Clinical Meetings. His clinical areas of interest are drug-induced kidney disease, onco-nephrology, HIV-related kidney disease, and acute tubulointerstitial nephritis.



Jessica Joseph, MBA

Jessica Joseph, MBA, senior vice president of scientific operations at NKF, is the 2021 recipient of the *Garabed Eknoyan Award*. The award honors an individual who has promoted the mission of the NKF in making lives better for people with kidney disease through contributions to innovations such as the Kidney Disease Outcomes Quality Initiative. Ms. Joseph is responsible for the strategic planning, execution, and evaluation of the overall business operations and logistics for NKF's national and local professional education and membership activities.



Paul K. Whelton, MB, MD, MSc

The *David M. Hume Memorial Award* was created in memory of one of NKF's most distinguished members and is the highest honor given by the Foundation to a scientist-clinician in the field of kidney and urologic diseases. The recipient of the 2021 award is **Paul K. Whelton, MB, MD, MSc**, of Tulane University School of Public Health and Tropical Medicine. Dr. Whelton's interests include blood pressure-related cardiovascular/renal disease epidemiology, prevention, clinical trials, and global health.



Kirsten L. Johansen, MD, FASN

The *J. Michael Lazarus Award* recognizes individuals whose research has yielded novel insights related to renal replacement therapy. The 2021 recipient is **Kirsten L. Johansen, MD, FASN**, nephrology division director, Hennepin County medical center co-director, chronic disease research group, professor of medicine, University of Minnesota. Her research focuses on physical function in patients with end-stage kidney disease and ethnic disparities in progression of chronic kidney disease and access to kidney transplantation.



Shivam Joshi, MD

The recipient of the 2021 *Joel D. Kopple Award* for work in the field of renal nutrition is **Shivam Joshi, MD**, a nephrologist, internist, and plant-based physician at NYC Health + Hospitals/Bellevue in New York City. His work focuses on diet and kidney disease. He has published more than a dozen articles in prominent journals, been a featured speaker at numerous meetings and conferences and on multiple podcasts.



Krista L. Lentine, MD, PhD

Krista L. Lentine, MD, PhD, is the recipient of the 2021 *Excellence in Kidney Transplantation Award*. Dr. Lentine is professor of medicine with tenure, medical director of Living Donation, and Mid-America Transplant/Jane A. Beckman Endowed Chair in Transplantation at SSM Saint Louis University Hospital. The award was established to recognize a scientist or clinician whose research has contributed novel insights in or resulted in improved access to kidney transplantation.



Shubha Ahya, MD

Shubha Ahya, MD, professor of medicine at Northwestern University Feinberg School of Medicine and a clinical nephrologist at Northwestern Memorial Hospital and Jesse Brown VA Medical Center, is the recipient of the 2021 *Medical Advisory Board Distinguished Service Award*. The award is given to highlight community service and activities that promote NKF's mission on a local level. Dr. Ahya is the chairperson of the Professional Advisory Board of the National Kidney Foundation of Illinois and she helps plan professional programming including Citywide Grand Rounds and the annual *Controversies in Nephrology*.



Aliza Thompson, MD

The *NKF Public Service Award* honors the work of a kidney health professional who has demonstrated exceptional dedication to public service and has significantly contributed to public policies or government programs aimed at improving outcomes for kidney patients. **Aliza Thompson, MD**, deputy director of the division of cardiology and nephrology at the Center for Drug Evaluation and Research at the US FDA, is the 2021 recipient. Dr. Thompson's work focuses on regulating and reviewing Investigational New Drug applications and marketing applications for drug and biologic products for the treatment of cardiovascular and kidney diseases. She joined the FDA in 2007.



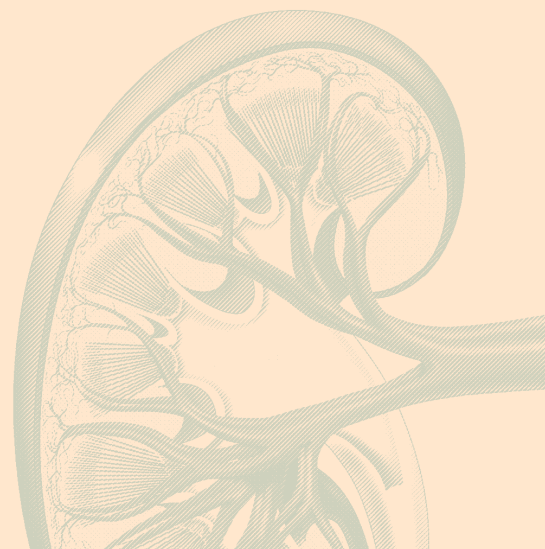
Maria Rosley DeClaro, RN, BSN, CNN

The 2021 *Carol Mattix Award* is presented to **Maria Rosley DeClaro, RN, BSN, CNN**. She has been a Registered Nurse at Fresenius Kidney Care for more than 20 years and has been instrumental in developing nine home therapy programs in the Chicago region. She has recently expanded her skill set to include pediatric dialysis.



Curtis H. Warfield

The *Celeste Castillo Lee Patient Engagement Award* is given to a kidney patient who exemplifies the mission of the NKF. The 2021 recipient is **Curtis H. Warfield**. He is a senior quality analyst for the state of Indiana. He was diagnosed with stage 3 chronic kidney disease in 2012 and initiated peritoneal dialysis in 2014. In January 2016, he received a loving donor kidney transplant from his daughter's college sorority sister. He provides peer counseling with the NKF Peer Program and is a member of NKF's Kidney Advocacy Committee and advocates on Capitol Hill and in Indiana with members of Congress for kidney and organ donor issues.



Adherence Improved with DPP-4 Inhibitors versus Pioglitazone in Type 2 Diabetes

Approximately 9.4% of the population in the United States is affected by diabetes, and an estimated 35% to 40% of patients with type 2 diabetes mellitus are diagnosed with chronic kidney disease (CKD). As kidney function declines, patients experience an increase in the risk of cardiovascular complications, hospitalizations, and mortality. Healthcare costs are substantially higher among patients with both CKD and diabetes compared with patients with diabetes alone.

Adherence and persistence with diabetes medication both play a key role in glycemic control in patients with diabetes. However, according to Deval Gor, MPharm, and colleagues, there are few data available on comparisons of various diabetic medications in patients with renal impairment.

The researchers conducted a retrospective cohort study designed to compare adherence and persistence in patients with type 2 diabetes mellitus and nondialysis CKD treated with dipeptidyl peptidase-4 (DPP-4) inhibitors versus pioglitazone. Results of the study were reported in the *Journal of Managed Care & Specialty Pharmacy* [2020;26(1):67-75].

The study utilized Truven MarketScan administrative claims databases from 2009 to 2015. The proportion of days covered (PDC) following an initial dispensing was used to measure 1-year adherence for patients with diabetes and nondialysis CKD who initiated therapy with either a DPP-4 inhibitor or pioglitazone; PDC ≥ 0.80 was defined as adherent. The days between the index date and the last day with an index medication on hand were used to calculate persistence, based on the end of the last day's supply or the end of follow-up (365 days), whichever occurred first. Confounder-adjusted differences between the study groups were estimated using multivariate logistic regression and Cox proportional hazards models for adherence and persistence.

Following application of inclusion and exclusion criteria, the study cohort included 9019 patients with type 2 diabetes and CKD; of those, 7002 initiated therapy with

a DPP-4 inhibitor and 2017 initiated therapy with pioglitazone. The two groups were generally similar in baseline characteristics; patients in the DPP-4 inhibitor group were slightly older, more likely to be female, and had higher cardiovascular comorbidities.

Among patients in the DPP-4 inhibitor group, mean PDC was higher than among those in the pioglitazone group (mean, 0.77 vs 0.72). The DPP-4 inhibitor group also had higher proportion of patients with PDC ≥ 0.80 (59.5% vs 52.4%). The odds of being adherent were higher among patients initiating therapy with DPP-4 inhibitors compared with patients in the pioglitazone group (adjusted odds ratio [aOR], 1.41; 95% confidence interval [CI], 1.25-1.59).

In a stratified analysis by cost sharing at each level, patients in the DPP-4 inhibitor group were more likely to be considered adherent compared with patients in the pioglitazone group ($P < .01$). When the analysis was restricted to 2013-2014 when generic pioglitazone was available and cost sharing as a covariate was removed from the regression model, there was a smaller, nonstatistically significant difference in adherence (aOR, 1.18; 95% CI, 0.92-1.51).

In measures of persistence, a higher proportion of patients in the DPP-4 inhibitor group persisted for 1 year compared with the pioglitazone group (56.7% vs 46.3%; $P < .01$). The overall adjusted hazard ratio for persistence was 0.74 (95% CI, 0.69-0.79), which favored DPP-4 inhibitors compared with pioglitazone.

Results of multivariate adjusted analysis demonstrated that from 2011-2012, DPP-4 inhibitors were associated with lower odds of switching (2010 aOR, 0.60; 95% CI, 0.44-0.82; 2011-2012 aOR, 0.31; 95% CI, 0.23-0.40) and discontinuation (2010 aOR, 0.72; 95% CI, 0.58-0.89; 2011-2012 aOR 0.46; 95% CI, 0.37-0.56) compared with pioglitazone. In 2013-2014, DPP-4 inhibitors had lower odds of switching and discontinuation; the differences were not statistically significant.

There were several limitations to the study, including assessing medication adherence based on pharmacy claims data

that may not correlate accurately with how patients actually took the medication, and the lack of socioeconomic or clinical variables such as race, income, education, hemoglobin A1c, duration of diabetes, and glomerular filtration rate, with potential for confounding. In addition, a claims-based diagnosis of CKD had relatively lower sensitivity, limiting the generalizability of the findings beyond this selective population. Also, the study was not able to determine the reasons for nonadherence or the long-term effect of adherence on clinical outcomes. Finally, the study population was comprised of primarily commercially insured patients; results may differ in patients with Medicare, Medicaid, or no insurance.

In conclusion, the researchers said, "Patients with type 2 diabetes mellitus and nondialysis CKD who initiated DPP-4 inhibitors adhered more to their medications compared with those initiating pioglitazone. The difference between adherence decreased following introduction of low-cost generic pioglitazone, suggesting that cost sharing may be an important factor in determining adherence to these medications. This finding can help providers make an informed decision when selecting therapy for patients with renal impairment.

"The duration of therapy changed substantially among the pioglitazone initiators, which coincided with the timeline of the FDA warnings and its generic approval. This shift in the results, and the attitudes towards the changing status of pioglitazone warrants further investigation. Nonetheless, pharmacotherapy-related decisions should be based on multiple factors that include patient characteristics, contraindications to therapy, and intended outcomes, in addition to the formulary status or cost of diabetes medications." ■

TAKEAWAY POINTS

- Management of patients with type 2 diabetes mellitus and renal impairment carries specific challenges; only selected antidiabetic medications can be prescribed in patients with chronic kidney disease.
- In a retrospective cohort study comparing medication adherence and persistence among patients with type 2 diabetes and chronic kidney disease treated with dipeptidyl peptidase-4 (DPP-4) inhibitors or pioglitazone, adherence was better among those initiating therapy with DPP-4 inhibitors.
- Persistence with pioglitazone decreased in 2011-2012 following safety warnings; following approval of generic pioglitazone in 2013-2014, the differences in persistence between DPP-4 inhibitors and pioglitazone did not reach statistical significance.

Blood Pressure Control with Alpha-Blockers in Patients with CKD

There is a high prevalence of chronic kidney disease (CKD) among older patients; more than 20% of individuals ≥ 65 years of age are affected by CKD and have high rates of morbidity, mortality, and use of healthcare resources. Hypertension is nearly ubiquitous among patients with CKD; hypertension prevalence is $>80\%$. Cardiac outcomes are improved with adequate blood pressure control in patients with CKD, who, on average, require two to four blood pressure lowering medications to achieve recommended targets.

Alpha-blockers (ABs) reduce blood pressure through competitive inhibition of postsynaptic α_1 -adrenoceptors of vascular smooth muscle, resulting in vasodilation of veins and arterioles and a decrease in peripheral vascular resistance. Due to concerns about safety, ABs are considered add-on therapy for resistant or refractory hypertension. However, they are commonly prescribed due to their effectiveness.

There are few data available on the association between AB use and kidney, cardiac, and safety outcomes in patients with CKD. **Gregory L. Hundemer, MD, MPH**, and colleagues conducted a population-based retrospective cohort study to examine whether the association of AB use and kidney disease progression, cardiac events, all-cause mortality, and safety-related events (hypotension, syncope, falls, and fractures) varied by CKD stage compared with non-AB blood pressure lowering medications. Results of the study were reported in the *American Journal of Kidney Diseases* [2021;77(2):178-189].

The study exposure was new use of an AB versus new use of a non-AB blood pressure

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lowering medication. The primary outcomes of interest were $\geq 30\%$ decline in estimated glomerular filtration rate (eGFR); kidney replacement therapy (initiation of dialysis or kidney transplantation); a composite of acute myocardial infarction, coronary revascularization, congestive heart failure, or atrial fibrillation; safety events; and mortality.

The study utilized data on older adults (≥ 66 years of age) treated for hypertension from 2007 to 2015 in Ontario, Canada. Demographics and vital status data were obtained from the Ontario Registered Persons Database; medication data were obtained from the Ontario Drug Benefit Claims database.

A total of 381,120 eligible Ontario residents were diagnosed with hypertension during the study period. Of those, 4% ($n=16,511$) were prescribed an AB. A total of 16,088 of those patients were matched 1:1 to patients prescribed non-AB blood pressure lowering medications. Prematching, compared with the non-AB group the AB group had a higher proportion of men, lower eGFR, higher prevalence of diabetes and use of glucose-lowering medications, and higher statin use. Following matching, the two groups were similar in those characteristics.

Mean patient age was 76 years and mean eGFR was 62 mL/min/1.73 m². Following matching, there was no detectable difference between the two groups with the exception of a minor imbalance in the rates of nephrology care. The most commonly prescribed AB was terazosin (66%), followed by doxazosin (30%) and prazosin (4%). The most commonly

prescribed non-AB blood pressure lowering medications at index date were angiotensin receptor blockers (28%), beta blockers (23%), and calcium channel blockers (18%).

Overall, there was an association between AB use and a higher risk for $\geq 30\%$ greater decline, compared with non-AB use (121 vs 107 events/1000 person-years; hazard ratio [HR], 1.14; 95% confidence interval [CI], 1.08-1.21). There was also an association between AB use and higher risk for dialysis or kidney transplantation compared with non-AB use (15.2 vs 11.4 events/1000 person years; HR, 1.28; 95% CI, 1.13-1.44). A small number of kidney replacement therapy events occurred in patients with eGFR ≥ 60 mL/min/1.73 m² (AB group, 45 events; non-AB group, 47 events) compared with patients with eGFR < 60 mL/min/1.73 m² (AB group, 597 events; non-AB group, 428 events).

For the total population, there was an association between AB use and lower risk for cardiac events compared with non-AB use (207 vs 224 events/1000 person-years; HR, 0.92; 95% CI, 0.89-0.95). There was also an association between AB use and lower all-cause mortality risk compared with non-AB use (60.7 vs 67.6 events/1000 person-years; HR, 0.89; 95% CI, 0.84-0.94).

Among patients with eGFR < 30 mL/min/1.73 m², there was an association between AB use and a 29% reduction in mortality risk (138 vs 195 events/1000 person-years; HR, 0.71; 95% CI, 0.64-0.80). Among patients with eGFR 30 to 59 mL/min/1.73 m², AB use was associated with a

15% reduction in mortality risk (73.0 vs 85.7 events/1000 person-years; HR, 0.85; 95% CI, 0.78-0.93). The difference in risk between AB and non-AB users was nonsignificant among patients with eGFR ≥ 60 mL/min/1.73 m².

For the total population, the only safety-related event that was found to have an increased association with AB use compared with non-AB use was syncope (19.5 vs 15.9 events/1000 person-years; HR, 1.23; 95% CI, 1.11-1.37). The only safety-related outcome in which effect modification between eGFR and AB use was present was hypotension (P for interaction $\leq .001$), with AB use generally associating with higher risk for hypotension among those with higher eGFR and lower risk for hypotension among those with lower eGFR.

The researchers cited some limitations to the study including the observational design, the lack of data on blood pressure measurements, and missing data on frailty, medication intolerances, side effects, and allergies.

The researchers said, "In conclusion, AB use in older patients with CKD is associated with more rapid decline in kidney function but lower risks for cardiac events and all-cause mortality. These disparate results demonstrate the need for clinical trials to assess the safety and efficacy of AB use in CKD. We suggest that close monitoring of eGFR in patients using ABs is warranted and caution should be exercised when initiating a patient with CKD on AB therapy. Future prospective studies are needed to further understand the mechanisms by which AB therapy contributes to adverse kidney outcomes." ■

TAKEAWAY POINTS

- Associations between use of alpha-blockers (ABs) to control resistant or refractory hypertension in patients with chronic kidney disease are largely unknown.
- Results of a population-based retrospective cohort study found an association between use of ABs and a higher risk for adverse kidney outcomes, including kidney disease progression.
- There was an association between AB use and lower risk of cardiac events across all categories of estimated glomerular filtration rate.

Social Determinants among Patients with CKD and Diabetes

Chronic kidney disease (CKD) affects 15% of adults in the United States and is the 9th leading cause of death. Results of studies conducted over the past 20 years have revealed an uneven burden of CKD and identified disparities in the incidence and outcomes of CKD, with minorities being at highest risk. Social determinants are increasingly being shown as explanations for those disparities.

The World Health Organization defines social determinants as "conditions in which people are born, grow, work, live, and age." Social determinants have been categorized into four groups of interacting factors: (1) socioeconomic circumstances; (2) psychosocial factors; (3) neighborhood environment; and (4) political, economic, and cultural factors (e.g., food insecurity, housing instability, social support, and violence in one's community).

Recent studies have shown associations between socioeconomic status (poverty) and CKD risk factors, CKD progression, incident end-stage kidney disease, and mortality. There are few data available on the cumulative effects of social determinants of health factors on health outcomes in individuals with CKD with or without diabetes. **Mukoso N. Ozieh, MD**, and colleagues conducted a study to define the cumulative and individual association between social determinants of health and mortality in that patient population. Results of the study were reported in *BMC Nephrology* [doi.org/10.1186/s12882-021-02277-2].

The researchers utilized data from National Health and Nutrition Examination Surveys (2005-2014) for 1376 adults ≥ 20 years of age (representing 7,579,967 US adults) with CKD and diabetes. The outcome of interest

was all-cause mortality.

Diabetes was defined as self-reported diabetes, or a hemoglobin A1c (HbA1c) $\geq 6.5\%$ per 2016 American Diabetes Association guidelines. CKD was defined based on estimated glomerular filtration rate (eGFR) categories (G1-G5) and albuminuria/urine albumin-to-creatinine ratio categories (A1-A3) according to the Kidney Disease Improving Global Outcomes Clinical Practice Guidelines for the Evaluation and Management of Chronic Kidney Disease.

Social determinants of health measures included family income to poverty ratio level, household food insecurity, and depression. Demographic variables included sex, age, race-ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, and other minority), education level, and insurance coverage (dichotomized as yes vs no). Lifestyle variables included physi-

cal activity (no physical activity vs moderate to vigorous physical activity), smoking status (never smoker vs former or current smoker), and drinking status (none drinker vs moderate or above moderate drinker), Glycemic control measures using HbA1c level was included as a continuous variable based on every 1% increase in HbA1c level. Comorbidities were defined as the presence or absence of cancer, hypertension, heart disease, and stroke.

Mean age of the sample was 63.5 years, 30.6% reported poverty, 16.1% reported food insecurity, 32.6% reported depression, and 53.4% reported the presence of any adverse social determinants. The majority of the sample was non-Hispanic White (63.2%) and had insurance coverage (89.5%).

Prior to adjustment, the association between a cumulative social determinants of health score and mortality was not statistically significant (hazard ratio [HR], 1.11; 95% confidence interval [CI], 0.97-1.28). Following adjustment for demographics, the adjusted HR reached statistical significance (1.41; 95% CI, 1.18-1.67). The association remained significant following the addition of lifestyle variables, glycemic control and comorbidities (HR, 1.41; 95% CI, 1.18-1.68) for every 1 score increase in the cumulative social determinant scale. In the fully adjusted model examining the association between the dichotomous social determinants and mortality, results were similar, indicating a significant association between the presence of any adverse social determinants of health factor and mortality (HR, 1.41; 95% CI, 1.08-1.84).

In analyses incorporating all three social determinants of health measures as individual factors (family income to poverty ratio level, household food insecurity, and depression), prior to adjustment, when the three variables were entered into the same model, only depression had a statistically significant association with mortality (depression, HR, 1.33; 95% CI, 1.04-1.71). Following adjustment for demographics, lifestyle variables, glycemic control and comorbidities, depression (HR, 1.41; 95% CI, 1.10-1.82) maintained statistical significance. There was an independent association between depression and mortality. There was no independent association between either food insecurity (HR, 1.41; 95% CI,

0.95-2.07; $P=.09$) or poverty (HR, 1.40; 95% CI, 1.00-1.97) and mortality.

Limitations to the study cited by the authors included the cross-sectional design that precluded an analysis of causality, the lack of control for medication use, and the inability to completely rule out the possibility of residual confounding.

The researchers said, "In conclusion, in a national sample of adults with CKD and

diabetes, we found that every unit increase in cumulative social determinant of health score was associated with increased mortality. We also found that particular social determinant of health factors, such as depression, are independently associated with mortality in this population. These findings suggest that interventions are needed to address social determinant factors in individuals with CKD and diabetes. ■

Print-only Content

Early Discontinuation of Corticosteroids: Long-Term Outcomes

Recipients of kidney transplantation are required to maintain immunosuppressive drug treatment to prevent allograft rejection. There are three drugs in the most common immunosuppressive drug regimen: a calcineurin inhibitor (cyclosporine or tacrolimus), mycophenolic acid or azathioprine, and corticosteroids (e.g., prednisone).

Due to adverse effects of corticosteroids, inclusion in immunosuppressive protocols is undesirable; however, cessation is associated with a higher risk of short-term rejection. Long-term outcomes of patients withdrawn from corticosteroids are unclear. **E. Steve Woodle, MD**, and colleagues conducted a study designed to compare long-term kidney transplant outcomes of patients randomized to continue or withdraw corticosteroids. Results of the prospective, multicenter, randomized, double-blind, placebo-controlled trial were reported online in *JAMA Surgery* [doi:10.1001/jamasurg.2020.6929].

Patients were randomized to receive tacrolimus and mycophenolate mofetil with or without corticosteroids 7 days following transplant. The outcomes of interest were kidney allograft failure from any cause, including death, and allograft failure censored for patient death, defined by the requirement for long-term dialysis or repeat transplant.

Of 385 patients, 191 were randomized to withdraw from corticosteroids (mean age, 46.5 years) and 194 were randomized to continue corticosteroids (mean age, 46.3 years). Of the 191 in the corticosteroid withdraw group, all 191 patients were identified for long-term follow-up in the Organ Procurement and Transplant Network (OPTN) registry; in the continued corticosteroid group, all 194 were identified for long-term follow-up in the OPTN registry.

During the 5-year trial follow-up period, 25 patients in the withdraw group and 31 in the continuation group were lost to follow-up or withdrew consent. A total of 24 patients died (11 in the withdrawal group and 13 in the continuation group) and there were 18 cases of allograft loss censored for death (11 in the withdrawal group and 7 in the

continuation group) reported in the trial.

The median follow-up time was 15.8 years after transplant. Outcomes in the trial participants beyond 5 years after transplant were ascertained in the OPTN registry until June 2018.

In the intention-to-treat analysis, there were no differences between the corticosteroid withdrawal group and the corticosteroid continuation group in time to allograft failure from any cause including death and time to allograft failure censored for death. The unadjusted hazard ratio (HR) of allograft loss from any cause in patients in the withdrawal group was 0.84 (95% confidence interval [CI], 0.64-1.12; $P=.23$) compared with patients in the continuation group. The HR for allograft loss censored by death was 0.77 (95% CI, 0.52-1.16; $P=.21$). Results of multivariable analysis were similar.

Actual allograft half-lives were defined as time from transplant until allograft failure from any cause including death. In the corticosteroid continuation group, actual allograft half-lives were 14.7 years compared with 17.5 years in the group that discontinued corticosteroids. Results of the per protocol analysis were similar.

There were no significant differences between the two groups in time to death at any time after transplant and time to death censored at time of allograft failure.

In subgroup analysis of time to allograft failure from any cause including death, better outcomes were seen in living donor recipients, non-Black recipients, patients without rejection, and patients without diabetes. There were no significant differences between the group that continued corticosteroids and the group that discontinued corticosteroids in those subgroups. In subgroup analyses of time to allograft failure censored for death, results were similar.

The trial findings were validated comparing characteristics of the transplant recipients in the OPTN registry in the original trial with contemporary registry patients grouped by whether they were or were not treated with maintenance corticosteroids. With the exception of receiving more nondepleting induction, the contemporary

registry patients were similar to trial participants. During the median follow-up of 15.8 years, the outcomes of trial participants treated with or without corticosteroids were similar to those of registry patients.

In multivariable analyses that combined trial patients and OPTN registry patients, the HR for graft loss from any cause including death was 0.86 (95% CI, 0.70-1.08) in patients in the corticosteroid withdrawal group compared with patients treated with corticosteroids. The HR for allograft loss censored by death was 1.06 (95% CI, 0.79-1.40).

Outcomes among trial participants were similar to those of OPTN registry patients (allograft failure from any cause: HR, 0.90; 95% CI, 0.73-1.10; $P=.31$; allograft failure censored by death: HR, 1.01; 95% CI, 0.75-1.34; $P=.97$). The interaction terms for corticosteroid use by trial participants were nonsignificant (allograft failure from any cause: HR, 0.99; 95% CI, 0.70-1.41; $P>.99$; allograft failure censored by death: HR, 0.76; 95% CI, 0.46-1.25; $P=.28$). Those results suggest there was no significant variation between trial participants and registry patients in the association of corticosteroid use with either outcome.

Limitations to the study cited by the authors included the inability to determine long-term differences in nonfatal outcomes such as cardiovascular disease, diabetes, infections, and metabolic bone disease between patients treated with maintenance corticosteroids and those treated without maintenance corticosteroids.

“In summary, corticosteroid withdrawal is not associated with an increased risk of long-term allograft failure from any cause including death or allograft failure censored for death in low- to moderate-immune risk kidney transplant recipients treated with induction immunosuppression tacrolimus and mycophenolic mofetil,” the researchers said. ■

TAKEAWAY POINTS

- Researchers reported results of a study examining long-term outcomes of early discontinuation of corticosteroids in kidney transplant recipients.
- Outcomes of interest were kidney allograft failure from any cause including death and allograft failure censored for patient death.
- There were no significant differences in either outcome between patients who discontinued corticosteroids and those who continued maintenance corticosteroid use.

Outcomes among Kidney Transplant Recipients Hospitalized with COVID-19

Among patients with COVID-19, reported mortality rates vary from 1% to 7.2%, reaching as high as 49% among patients with critical illness. Patients with known comorbidities, including old age, diabetes, hypertension, chronic kidney disease, morbid obesity, coronary heart disease, and chronic lung disease, are at increased risk for severe illness.

There are few data available on the infectious course of COVID-19 in solid organ transplant recipients. It is unclear whether complications associated with COVID-19 are increased in the presence of immunosuppression in that patient population. Early reports suggest that the frequency of cytokine storms, a significant cause of mortality, may be reduced in patients taking immunosuppressive drugs.

Ozgur Akin Oto, MD, and colleagues in Turkey, conducted a multicenter, retrospective study to define the clinical manifestations, course of disease, and outcomes among a large cohort of adult kidney transplant recipients with COVID-19. The study also was designed to assess the predictions of worse clinical outcomes among kidney transplant patients hospitalized with COVID-19. Results of the study were reported in *BMC Nephrology* [doi.org/10.1186/s12882-021-02299-w].

The primary outcomes of interest were in-hospital mortality and the need for admission to the intensive care unit (ICU). Secondary outcome was a composite of in-hospital mortality and/or ICU admission. Data were collected from 34 centers in Turkey from April 17, 2020, to June 1, 2020. The researchers reviewed data on demographic characteristics, clinical findings, laboratory parameters (hemogram, C-reactive protein, aspartate transaminase, alanine aminotransferase, lactate dehydrogenase, and ferritin) at admission and follow-up, and treatment strategies.

The diagnosis of COVID-19 was based on clinical symptoms, polymerase chain reaction (PCR) test for SARS-CoV-2 from the nasopharyngeal swab, and/or radiological findings. Patients whose first swab PCR test was negative, but with a positive repeated test, were considered to be confirmed cases. Patients whose clinical and radiological findings were consistent with COVID-19, but swab PCR tests were negative or not available, were also considered probable COVID-19 patients and were included in the study.

The final study cohort included 109 patients; of those, 63 were male and mean age was 48.4 years. The most common comorbidity was hypertension, affecting 76.4% of patients, followed by diabetes (23.4%), ischemic heart disease (17.5%), cancer (5.7%), and chronic obstructive pulmonary disease (4.8%). Previous or current smoking history was reported in 21.1% of patients. Median time between transplantation and diagnosis of COVID-19 was 5.0 years.

Twenty-two patients (20.2%) were admitted to the intensive care unit, and 19 (17.4%) required invasive mechanical ventilation.

Median length of stay was 9 days. A total of 46 patients (42.2%) developed acute kidney injury (AKI) and four patients (3.7%) required renal replacement therapy. Twenty-two patients (20.2%) were admitted to the ICU, and 19 (17.4%) required invasive mechanical ventilation (IMV). In non-survivors, the development of AKI, the need for IMV, and the need for RRT were significantly higher than in survivors: 71.4% vs 37.9%; $P=.018$; 68.4% vs 31.6%; $P=.025$; and 21.4% vs 1.1%; $P<.001$, respectively. Fourteen patients (12.8%) died and 23 (21.2%) reached the secondary outcome.

Ischemic heart disease (38.5% vs 15.3%; $P=.033$) and heart failure (14.3% vs 2.2%; $P=.028$) were higher in patients who died compared with patients who survived and those who reached the secondary outcome (31.8% vs 13.6%, $P=.046$; and 13.0% vs 1.2%; $P=.009$, respectively). Patients who died had longer length of stay: 14 days versus 8 days; $P=.038$.

There were no significant differences between the patients reaching the primary and secondary outcomes in terms of age, sex, transplantation duration, primary kidney disease, comorbidities (with the exception of those mentioned above), smoking history, maintenance immunosuppression, or use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers.

Patients who were admitted to the ICU were significantly older (≥ 60 years of age) (38.1% vs 14.9%; $P=.016$). In results of univariate analysis, there were associations between the presence of ischemic heart

disease and initial serum creatinine levels and mortality. In multivariate analysis, both parameters were predictive of mortality.

Nearly all of the patients were treated with hydroxychloroquine (99.1%), the majority of patients (67%) received macrolide, oseltamivir (56.2%), glucocorticoids (58.4%), and favipiravir (49.0%). A smaller subset of patients received tocilizumab (10.1%) or anakinra (3%) and lopinavir/ritonavir (10.6%). There was significant difference

in mortality among tocilizumab (41.7% vs 5.7%; $P<.001$), glucocorticoids (85.7% vs 54%; $P=.026$), and favipiravir (91.7% vs 42.3%; $P=.002$) treatments of COVID-19.

Results of univariate analysis revealed that associations between older age (>60 years), initial serum creatinine level, ferritin, albumin level, and lymphocyte count and admission to the ICU. In multivariate analysis, the association between older age and initial serum creatinine and ICU admission remained.

In univariate analysis, older age (>60 years), baseline lymphocyte counts, and initial serum creatinine and albumin levels were predictive of the secondary outcomes. Following multivariate adjustment, older age and initial lymphocyte count remained predictive of the secondary outcome.

Limitations to the study findings cited by the authors included the retrospective design that may not have reflected the causal relationship between mortality and some of the parameters; changes in treatment algorithm during the study period that made it difficult to evaluate results; problems related to patient selection that made it difficult to evaluate treatment results; and the inclusion of PCR negative patients as the clinical diagnosis of COVID-19.

In conclusion, the researchers said, "COVID-19 in kidney transplant recipients has a high mortality rate, especially in patients with ischemic heart disease or poor graft function. Low lymphocyte counts at admission and age >60 years increased the risk for their combined end point of death or ICU admission." ■

TAKEAWAY POINTS

Researchers in Turkey reported results of a retrospective study designed to define the characteristics, clinical presentation, and outcomes of a multicenter adult cohort of kidney transplant recipients hospitalized with COVID-19.

The cohort included 109 patients; 46 developed acute kidney injury and four required renal replacement therapy. 22 were admitted to the intensive care unit (ICU) and 19 required invasive mechanical ventilation.

Fourteen of the patients died. In multivariate analysis, the presence of ischemic heart disease and initial serum creatinine levels were independent risk factors for mortality; age >60 years and initial serum creatinine levels were independent risk factors for ICU admission.

WORLDWIDE DIALYSIS USE AND PRACTICE PATTERNS: INTERNATIONAL SURVEY STUDIES

The International Society of Nephrology convened stakeholders in 182 countries, including clinicians, policy makers, and consumer representatives, from July to September 2018, for the 2019 edition of the Global Kidney Health Atlas survey. The survey examined the incidence, prevalence, availability, accessibility, affordability, and quality of hemodialysis and peritoneal dialysis care for patients with kidney failure around the world.

Hemodialysis

Kidney replacement therapy (KRT) is essential in the treatment of patients with kidney failure. However, many patients in low- and lower-middle-income countries do not have access to KRT. A previous study reported that at least 2.28 million patients with kidney failure do not have access to KRT, and that number is projected to increase in parallel with growth in population and aging worldwide.

The primary mode of KRT is hemodialysis, accounting for 90% of all dialysis globally. Hemodialysis is technically more challenging than peritoneal dialysis and is commonly more expensive. The first Global Kidney Health Atlas (GKHA) provided data on the number of countries with capacity to deliver hemodialysis to patients with kidney failure.

Htay Htay, MBBS, and colleagues conducted a cross-sectional survey based on data from the 2019 edition of the GKHA survey, designed to examine global access and treatment characteristics of kidney failure care. The survey was conducted by the International Society of Nephrology (ISN). Results of the current analysis were reported in the *American Journal of Kidney Diseases* [2021;77(3):326-335].

The survey was conducted via an online questionnaire. All countries with kidney societies were invited to participate. Key stakeholders identified by project leaders were sent invitations to participate in the survey. The survey was available in English, French, and Spanish and was conducted from July to September 2018.

Availability of hemodialysis was defined as generally available if available in $\geq 50\%$ of centers, hospitals, or clinics as a treatment option for patients with kidney failure in a country. Accessibility was defined as the proportion of patients with kidney failure able to access dialysis at the onset of kidney failure in a country. The current study examined the global use of maintenance hemodialysis, global hemodialysis center density, accessibility, within-country variation in dialysis access, affordability (defined as the proportion of treatment paid for directly by the patient), vascular access type on initiation of hemodialysis, and availability of services for kidney failure care.

A total of 182 countries were contacted. Of those, 160 responded, including 58 of 66 high-income countries, 41 of 48 upper-middle-income countries, 38 of 42 lower-middle-income countries, and 23 of 26 low-income countries. By ISN region, data were collected from 42 countries in Africa, 19 countries in Eastern and Central Europe, 18 countries in Latin America, 11 countries in the Middle East, 10 countries in the Newly Independent States and Russia, 10 countries in North America and the Caribbean, seven countries in North and East Asia, 15 countries in Oceania and South East Asia, seven countries in South Asia, and 21 countries in Western Europe.

In all, 317 participants responded to the survey: 260 nephrologists, 22 non-nephrologist physicians, 7 other health professionals, 17 administrators/policy makers/civil servants, and 11 others.

The GKHA survey included a single-item question asking if maintenance hemodialysis, both adult and pediatric, was available in their country. Of the 156 countries that responded to the GKHA questionnaire, all 156 reported that maintenance hemodialysis service was available.

Data for maintenance hemodialysis use were available from 126 countries. The median global use of hemodialysis was 298.4 per million population (pmp). There was wide variation across countries, ranging from 0.3 pmp in the Democratic Republic of Congo to 2148 pmp in Japan. In low-income countries, use of maintenance hemodialysis was very low: 5.8 pmp in Ethiopia, 2.8 pmp in Zimbabwe, and 0.5 pmp in Tanzania. Twenty-six countries provided data for hemodialysis use among patients with incident kidney failure. Of those 26 countries, median use was 108.8 pmp. No similar data were available for low-middle-income countries and low-income countries.

A total of 154 countries responded to a question regarding how many centers in the country provided maintenance hemodialysis. The median number of centers was 4.5 pmp. Density of hemodialysis centers was extremely low in low-income countries. In response to survey items regarding the availability of hemodialysis, 129 of the 154 countries indicated that hemodialysis service was available in most hospitals or centers. Most low-income countries reported less than half the hospitals in the country providing hemodialysis services.

The frequency of center-based hemodialysis services was reported as adequate (3-4 hours three times a week) in 118 of the 154 countries responding (77%). The proportion ranged from 95% (53/56) in high-income countries to 27% (6/22) in low-income countries. Home-based hemodialysis services were available in most centers in 13% (20/154) of countries; 32% (49/154) indicated that home-based services were available in less than half the centers. There were no home-based hemodialysis services available in 55% (85/154) of countries responding.

In general, patients in high-income countries paid less or were not required to provide copayment for hemodialysis services. People in low-income countries such as Ethiopia, Sierra Leone, and Chad had to pay 100% of hemodialysis costs out of pocket.

Of the 159 countries providing data on vascular access creation, 38% (n=61) reported that catheter insertion costs for hemodialysis were fully paid by the government. Sixty-four countries reported that costs for arteriovenous fistulas or grafts were fully covered. There was wide variation in health care systems' coverage for vascular ac-

TAKEAWAY POINTS

- A recent study utilized data from an international survey to examine the availability, accessibility, affordability, and quality of hemodialysis dialysis worldwide.
- The survey revealed wide variations in use and practice patterns of hemodialysis around the world.
- The lowest use, availability, accessibility, and affordability of hemodialysis was evident in low- and lower-middle-income countries.

cess creation by country income level.

Hemodialysis quality was assessed based on the proportion of centers routinely monitoring patient-reported outcomes, blood pressure, small-solute clearance, hemoglobin level, bone mineral markers, technique and patient survival, and vascular access. Overall, 22 of the 144 countries contributing data on hemodialysis quality did not monitor patient-reported outcomes. Forty-six countries reported that >75% of hemodialysis centers in the country monitored patient-reported outcomes.

Eighty-six percent of the 144 countries monitored blood pressure in >75% of hemodialysis centers; 8% reported no monitoring of blood pressure. Sixty-one percent of countries monitored small-solute clearance in >75% of hemodialysis centers. Monitoring of small-solute clearance in almost all hemodialysis centers varied from 87% of high-income countries to 28% of low-income countries.

Hemoglobin levels were monitored in 88% of countries in >75% of hemodialysis centers, a proportion that varied from 98% of high-income countries to 71% of low-income countries. Six percent of countries did not monitor hemoglobin levels in any centers. Most countries (60%) reported monitoring of bone mineral markers in >75% of hemodialysis centers. The proportion varied from 85% of high-income countries to 17% of low-income countries. Eight percent of countries did not monitor bone mineral markers. Technique and patient survival were monitored in >75% of hemodialysis centers in 51% and 60% of countries, respectively. Those markers were not monitored in 12% and 8% of countries, respectively.

Data on vascular access for hemodialysis were provided by 152 countries. Only 13% of countries reported having most patients with kidney failure initiating dialysis using functioning vascular access. Forty-six percent of countries reported having most patients with kidney failure initiation dialysis using a temporary catheter.

Limitations to the study included the fact that it was a cross-sectional study based on an online survey relying on respondents' knowledge, raising the possibility of response bias.

"In summary, this global survey of maintenance hemodialysis care revealed considerable within- and between-country variations in hemodialysis use, availability, accessibility, affordability, quality monitoring, and reporting. These disparities were more marked in low-income countries and low-middle-income countries, particularly in Africa and South Asia. The findings from this study carry significant implications for policymakers and advocacy groups with respect to delivering equitable, cost-effective, high-quality hemodialysis to patients around the globe in the future," the researchers said.

Peritoneal Dialysis

Worldwide, the number of individuals with kidney failure is increasing, creating a population of patients at risk for death without kidney replacement therapy (KRT). An estimated five to 10 million people die each year due to a lack of access to dialysis for treatment for kidney failure or acute kidney injury.

There are wide disparities in the provision of KRT, either dialysis or kidney transplantation, globally. Patients in low-income countries typically face the most barriers to access to KRT. Residents of remote communities with limited access to facilities providing nephrology care must also deal with significant barriers to treatment access.

Peritoneal dialysis may provide an attractive KRT modality relative to hemodialysis. Peritoneal dialysis is home-based and relatively simple and easy to master, eliminating the need for proximity to a dialysis unit. In many parts of the world, peritoneal dialysis is also the most cost-effective form of KRT.

Approximately 11% of patients worldwide with kidney failure are treated with peritoneal dialysis. Researchers, led by **Yeoungjee Cho, MBBS, PhD**, conducted an analysis of data from a cross-sectional survey examining peritoneal dialysis use and practice patterns across the globe. Results were reported in the *American Journal of Kidney Diseases* [2021;77(3):315-325].

The survey was part of the second iteration of the Global Kidney Health Atlas (GKHA), commissioned by the International Society of Nephrology (ISN). The outcomes of interest were peritoneal dialysis use, affordability, delivery, and reporting of quality outcome measures. The survey was distributed to stakeholders including clinicians, policy makers, and patient representatives in 182 countries between July and September 2018.

The survey defined accessibility as peritoneal dialysis being a treatment option in a country; accessibility as proportion of incident patients with kidney failure receiving peritoneal dialysis; affordability as copayment requirements and the funding model for peritoneal dialysis. Survey questions also addressed any intracountry variations in practice patterns. Proportions of units reporting peritoneal dialysis quality outcomes (patient-reported outcomes measures, blood pressure, small-solute clearance, hemoglobin/hematocrit levels, bone mineral marker levels, technique survival, and mortality) were also assessed.

During the second iteration of GKHA, data for the PD domain were provided by responses from 313 participants. Of the participants, 82% (n=257) were nephrologists, 7% (n=22) were non-nephrologist physicians, 2% (n=6) were other health professionals, 5% (n=17) were administrators/policy makers/civil servants, and 4% (n=11) were other professions. The 313 responders represented 156 of the 182 surveyed countries.

Data on peritoneal dialysis use were available from 110 countries. Median use of peritoneal dialysis within those countries was 38.1 per million population (pmp), ranging from 0.1 pmp in Egypt to 531 pmp in Hong Kong. Use of peritoneal dialysis was highest in high-income countries (53 pmp), followed by upper-middle-income countries (26.5 pmp), low-middle-income countries (5.8 pmp) and low-income countries (0.9 pmp). Data on use of peritoneal dialysis use among incident patients with kidney failure were available from only 24 countries. Overall, median peritoneal dialysis use was 20.8 pmp, ranging from 2.4 pmp in Romania to 140.6 pmp in Thailand.

Peritoneal dialysis was available in 81% of participating countries (n=126), especially in Eastern and Central Europe and the Middle East. The modality was more readily available in high-income countries than in low-income countries. Countries where peritoneal dialysis was not available were low-income countries in Africa, Oceania, and South East Asia. In countries with peritoneal dialysis availability, the median density was 1.3 pmp, ranging from 0.01 pmp in Pakistan to 26.5 pmp in New Caledonia. In countries where peritoneal dialysis was available, it was not the initial mode of treatment in 11 countries; seven of those were in Africa and most were low-income or low-middle-income countries.

Of the 126 countries with peritoneal dialysis availability, 121 provided data on the proportion of incident dialysis patients receiving that modality. For most of those countries, only 1% to 10% of incident dialysis patients received peritoneal dialysis; those rates were consistent across ISN regions and World Bank income groups. In 69% of countries, peritoneal dialysis was the initial modality for ≤10% of patients with newly diagnosed kidney failure.

The costs of peritoneal dialysis catheter insertion were fully covered by the governments of 64 countries, with no out-of-pocket expenses for patients. In 47 countries, patients partially covered costs in the context of a mix of public and private funding systems and incomplete public funding coverage. Patients in Africa and in low-income countries were most likely to pay for all costs related to catheter insertion.

Patients receiving peritoneal dialysis, particularly those in high-income countries and upper-middle-income countries, were commonly expected to cover 1% to 25% of costs related to maintenance treatment. Patients receiving peritoneal dialysis in low-middle-income countries and in Eastern and Central Europe were most likely to bear a high cost burden, with requirements to cover 100% of treatment costs.

A total of 121 countries submitted data about peritoneal dialysis quality. In 72% of responding countries, average exchange volumes were adequate (defined as 3-4 exchanges per day or the equivalent for automated peritoneal dialysis). Respondents from 53 countries indicated that most peritoneal dialysis programs did not collect and report patient-reported outcomes measures (defined as ≤50% of peritoneal dialysis centers). Patient-reported outcomes were more frequently reported (defined as >50% of peritoneal dialysis centers) by centers in high-income countries than in low-income countries.

The authors cited some limitations to the study, including low responses from policy makers, a limited ability to provide more in-depth explanations underpinning outcomes from each country due to the lack of granular data, and the lack of objective data gathered.

In conclusion, the authors said, "This study has shown evidence of large inter- and intraregional variability in availability, accessibility, affordability, and quality of peritoneal dialysis for patients requiring KRT around the world. In general, patients from low-income countries and low-middle-income countries were found to be most disadvantaged with respect to peritoneal dialysis access, which incurred a higher cost burden when it was available. The delivery of peritoneal dialysis treatment and reporting of peritoneal dialysis-related quality measures were found to be similarly heterogeneous. The findings from this study carry significant implications for policy makers and advocacy groups with respect to delivering equitable cost-effective peritoneal dialysis to patients around the globe in the future." ■

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Conference Coverage

May 2-5, 2021

2021 ANNA NATIONAL SYMPOSIUM

The American Nephrology Nurses Association (ANNA) celebrated more than 50 years of education, advocacy, networking, and science for nephrology nurse members at its virtual 2021 National Symposium. From its beginning in 1969, ANNA has grown to 8500 members, representing healthcare professionals working in areas that include conservative management, hemodialysis, peritoneal dialysis, continuous renal replacement therapy, transplantation, industry, and government and regulatory agencies.

Due to COVID-19, ANNA's 2021 National Symposium was held virtually, May 2-5. As always, the symposium provided an opportunity for ANNA members to learn, collaborate, and network with fellow nephrology professionals from across the country and the world. Expert speakers and colleague nurses presented innovations and knowledge in all areas of quality patient care in the nephrology setting.

Mobile Health App to Track Self-Care Post-Transplant

To prevent graft rejection and death, recipients of kidney transplants must maintain life-long self-care responsibilities. The emergence of consumer-based mobile health applications (mHealth apps) has presented an opportunity for kidney transplant recipients to manage their post-transplant requirements, set goals, and monitor self-care practices in real time. At present, there are few data available on kidney transplant patients' experiences with mHealth apps as a self-care tool.

Tara O'Brien, PhD, RN, CNE, conducted a qualitative study to examine perceptions among kidney transplant recipients regarding the use of consumer-based mHealth apps for tracking self-health. Results of the study were reported during a virtual poster session at the 2021 ANNA National Symposium in a poster titled *Kidney Transplant Recipients Perceptions of Consumer-Based Mobile Health Applications for Self-Health Tracking*.

The study cohort was comprised of a purposive sample of adult kidney transplant recipients recruited from a Midwest transplant program. Researchers used a semi-structured interview guide to conduct face-to-face interviews designed to gather perspectives for using consumer-based mHealth apps for self-health tracking. The interviews were audio recorded, transcribed verbatim, and coded using NVivo 12.0 qualitative software.

The researchers conducted interviews with 20 kidney transplant recipients. Mean age of the majority of the participants was 54 years and annual income was \$66,000 or higher. Qualitative analysis of the interviews revealed five themes relating to self-health tracking: medication, nutrition, fluid intake, laboratory values, and physical activity.

The most popular mHealth app used by the study participants tracked physical activity and nutrition (n=13; 65%). All 20 participants indicated a desire for access to an app that had been specifically designed for self-care following kidney transplantation.

In summary, the authors said, "Our study is the first study to explore kidney recipients' perceptions of using consumer-based mHealth apps as a tool for self-health tracking. Overall, the participants in this study reported a positive experience when using consumer-based mHealth apps for self-care post-transplant. Consumer-based mHealth apps have the potential to be a cost-effective strategy for providing tailored education and real-time self-tracking which might ultimately improve survival rates for kidney recipients."

Source: O'Brien T. Kidney transplant recipients perceptions of consumer-based mobile health applications for self-health tracking. Abstract of a poster presented at the virtual 2021 American Nephrology Nurses Association National Symposium, May 2-5, 2021.

One Center's Experience with Dialysis in Patients with COVID-19

In the United States, COVID-19 emerged in early 2020. Patients with comorbidities, including end-stage kidney disease (ESKD), were particularly vulnerable to the virus and there was no information on treating patients with ESKD who developed COVID-19.

During a virtual poster session at the 2021 ANNA National Symposium, **Leslie Senyitko, MSN, RN, CNN, NE-BC**, described a performance improvement initiative at MedStar Georgetown, Springfield, Virginia. The poster was titled *COVID-19 in the Inpatient Dialysis Setting*.

The target population was hemodialysis patients hospitalized with COVID-19 at the large medical center, as well as hemodialysis personnel. Daily shift huddles were held to reinforce standard dialysis infection prevention practices. Supply chain issues were addressed to ensure adequate personal protective equipment (PPE), and education regarding the correct use of PPE was updated frequently to comply with recommendations from the Centers for Disease Control and Prevention.

Dialysis machines were dedicated for use on the patients with COVID-19 infection and were stored in a location separate from machines used for non-COVID patients. Machines were disinfected per standard protocol between each use and with bleach at the end of each day. A Surfadise disinfection was performed each night on the equipment. Coordination with the bed placement team enabled patients to be placed in negative air flow rooms to allow visibility and monitoring from outside the room.

Patients were assessed daily by a nephrologist and dialysis needs and treatment orders were adjusted as needed to limit exposure. A surge staffing plan was developed and implemented. Treatments were performed later in the day and, when possible, a dedicated staff provided support. Heparin protocols were adjusted to preserve the dialysis circuit.

Bedside treatment volume doubled from 4 to 6 to 15 to 16 per day; most were performed in COVID-19 isolation. Over a 3-month surge of COVID-19 infections, 300 treatments were performed on patients with COVID-19 infection. As of the writing of the poster, no dialysis personnel had tested positive for COVID-19, and there was no nosocomial transmission among dialysis patients.

"While there is much still to be learned about COVID-19, an increase in knowledge and experience in caring for this population has reduced anxiety and established a COVID-19 workflow in our department," the author said.

Source: Senyitko L. COVID-19 in the inpatient setting. Abstract of a poster presented at the virtual 2021 American Nephrology Nurses Association National Symposium, May 2-5, 2021.



Chart Review of Patients Opting for Conservative Care for CKD

Treatment options for patients with late stage chronic kidney disease (CKD) have traditionally focused on prolonging life with dialysis-based therapies. Over the past 20 years, there has been interest in the option of conservative care, excluding dialysis therapies, to delay disease progression and minimize complication. Decisions regarding conservative care are commonly made early in the trajectory of CKD. There are few data available on the actual treatment provided for patients who opt for conservative care when they reach end-stage kidney disease (ESKD).

Candice Halinski, MBA, MHCDS, MSN, NP-C, conducted a chart review of male and female patients participating in a care management program for patients with late stage CKD (stages 4 and 5). Results of the review were reported during a virtual poster session at the 2021 ANNA National Symposium in a poster titled *Decisions Surrounding Conservative Care Are Not Absolute*.

The program is located in the northeast region of the United States. All patients included in the chart review opted for conservative care, defined as active medical management without dialysis, as a treatment option for late-stage CKD and ESKD. The review included 71 patients who participated in the program from April 9, 2014, to the present. The chart review aimed to identify patients' final treatment pathways.

Of the 71 patients who confirmed the decision to forego dialysis, nine initiated hemodialysis and one has documented the desire to pursue treatment if necessary (14% conversion rate). Of the patients who opted to initiate hemodialysis, all were >75 years of age: 67% were 75 to 85 years of age and 33% were 86 to 95 years of age, 60% were female, 50% were White, 30% were Black, and 20% were other or multi-racial. Eighty-nine percent initiated treatment in the in-patient setting.

In summary, Ms. Halinski said, "Active medical management without dialysis or conservative care has become widely recognized by professional organizations and societies as a valid treatment pathway, yet no formalized approaches exist to support such treatment. The choice to forego renal replacement therapies is complex. When decisions surrounding the reversal of conservative management are made, the nephrology team should consider how conversations surrounding treatment options, goals, and quality of life can serve to honor a patient's wishes. This is especially important in cases that are acute in origin.

"Formalized treatment pathways, organizational communication campaigns, and education programs surrounding medical management in late stage chronic kidney disease may serve to empower the patient and support the provider in facilitating the decision to forego renal replacement therapies. Further research should focus on the psychosocial dynamics that surround medical treatment decisions and the supportive structure required to uphold medical management without dialysis."

Source: Halinski C. Decisions surrounding conservative care are not absolute. Abstract of a poster presented at the virtual 2021 American Nephrology Nurses Association National Symposium, May 2-5, 2021.

Conference Coverage

Pooled Data on Studies of Difelikefalin for CKD-Associated Pruritus

Patients undergoing hemodialysis commonly develop chronic kidney disease-associated pruritus (CKD-aP), creating a negative impact on quality of life. Difelikefalin is a selective kappa opioid receptor agonist in development for the treatment of CKD-aP. In a phase 3 study in the United States, difelikefalin significantly reduced itch intensity based on the Worst Itching Intensity Numerical Rating Scale (WI-NRS) and was generally well tolerated in a cohort of patients with moderate-to-severe CKD-aP on hemodialysis in the United States (KALM-1). Results of global phase 3 studies (KALM-2) were similar.

Molly Cahill, MSN, RN, ANP-C, CNN, and colleagues reported itch-related quality of life outcomes in a pooled analysis of results of KALM-1 and KALM-2 during a virtual poster session at the 2021 ANNA National Symposium. The poster was titled *Improvements in Itch-Related Quality of Life with Difelikefalin for Moderate-to-Severe Chronic Kidney Disease-Associated Pruritus: Pooled Analysis of KALM-1 and KALM-2 Phase 3 Studies in Hemodialysis Patients*.

Patients were randomized to intravenous difelikefalin 0.5 mcg/kg or placebo three times per week for 12 weeks. Multi-dimensional itch-related questionnaires (5-D Itch and Skindex-10 scales) were used to assess quality of life. The pooled data were analyzed based on mixed model for repeated measures.

The pooled studies included 851 patients; 426 were in the difelikefalin group and 425 in the placebo group. Mean baseline WI-NRS scores were 7.2 (1.4; difelikefalin) and 7.2 (1.5; placebo), confirming moderate-to-severe itch. In both studies, the primary endpoint of ≥ 3 -point reduction in WI-NRS score at 12 weeks was met. Estimates for the pooled population were 51.1% with difelikefalin versus 35.2% with placebo ($P < .001$). Compared with placebo, difelikefalin showed overall greater and clinically meaningful improvements in 5-D Itch and Skindex-10 total scores. Improvements in most of the domains on the two tests were greater with difelikefalin than with placebo.

In conclusion, the authors said, "Difelikefalin administered for 12 weeks to patients with moderate-to-severe CKD-aP undergoing hemodialysis resulted in significant relief of their itching accompanied by meaningful improvements in itch-related quality of life."

Source: Cahill M, Fishbane S, Wooldridge T, Wen W, Munera C, Menzaghi F. Improvements in itch-related quality of life with difelikefalin for moderate-to-severe chronic kidney disease-associated pruritus: Pooled results of KALM-1 and KALM-2 phase 3 studies in hemodialysis patients. Abstract of a poster presented at the virtual 2021 American Nephrology Nurses Association National Symposium, May 2-5, 2021.



Intervention to Achieve Blood Pressure Targets in Patients with CKD

Patients at risk for progression of chronic kidney disease (CKD) need to adhere to a low sodium diet and strict blood pressure control. Minority patients often lack complete information on maintaining a diet low in sodium and access to healthy food. **Anitha Philip, APRN, FNP-C**, of Rush University, Chicago, Illinois, and colleagues conducted a study to examine the effect of an educational intervention to increase patient knowledge of a low sodium diet and achieve target blood pressure control, defined as $< 140/90$ mmHg, in a cohort of patients with CKD. The intervention was called Eat Well and Protect Your Kidneys.

Results of the intervention were reported during a virtual poster session at the 2021 ANNA National Symposium. The poster was titled *The Effect of Educational Intervention (Eat Well and Protect Your Kidneys) to Improve Blood Pressure Control among Minority Patients with Chronic Kidney Disease*.

The study to evaluate the intervention used a one-group pretest/post-test design. Patients were recruited from a renal clinic serving large minority communities. The intervention class curriculum included two main areas: understanding of CKD and preserving kidney function through adherence to a low sodium diet.

The two-item Food Insecurity Questionnaire was used to assess all patients for food insecurity. Patient knowledge of CKD was assessed with the 10-item Chronic Kidney Disease Knowledge Questionnaire. Blood pressure was calculated pre-intervention using two pre-intervention readings (3 months prior to baseline and the day of the intervention).

Eighteen patients participated in the intervention. Sixty-seven percent were African American and 27% were Hispanic. Sixteen of the 18 patients had a history of hypertension and screened positive for food insecurity. Following the intervention, paired t-tests revealed a statistically significant increase in knowledge ($P < .00$). Differences between pre- and post-intervention blood pressure readings were not statistically significant.

In conclusion, the authors said, "The educational intervention was effective in improving patient knowledge. However, it is essential to address food insecurity issues to improve adherence to a low sodium diet and achieve target blood pressure among minority CKD patients."

Source: Philip A, Mayahara M, Hart P. The effect of educational intervention (Eat Well and Protect Your Kidneys) to improve blood pressure control among minority patients with chronic kidney disease. Abstract of a poster presented at the virtual 2021 American Nephrology Nurses Association National Symposium, May 2-5, 2021.

Intradialytic Hypotension across Crit-Line Profiles

In hospitalized patients with heart failure, achieving estimated dry weight (EDW) without causing intradialytic hypotension (IDH) is challenging. One goal of dialysis treatment is to increase ultrafiltration (UF) without causing IDH.

Patients' fluid status can be assessed using Crit-Line profiles: profile A indicates the patient's plasma refill is greater than or the same as the UF rate of $\leq 3\%$, and the UF rate can be increased without causing IDH; profile B is ideal, with a change of $\geq 3\%$ to $\leq 6.5\%$; and profile C $\geq 6.5\%$ indicates a rapid decrease in plasma volume. Patients in profile C are more likely to have symptomatic IDH.

During a virtual poster session at the 2021 ANNA National Symposium, **Jacqueline Chandler, BA, RN, CNN**, and colleagues at the Good Samaritan Regional Medical Center, Springfield, Oregon, reported results of a retrospective data analysis of the prevalence of IDH across Crit-Line profiles. The poster was titled *Prevalence of Intradialytic Hypotension (IDH) across Crit-Line Profiles in the Acute Setting: A Retrospective Data Analysis*.

The analysis included data on 87 hospitalized patients with end-stage kidney disease with three consecutive hemodialysis treatments. Eligible patients had data on ending profile, total fluid removed, the occurrence of IDH, and achievement of EDW. The outcomes were calculated overall and compared across patients with and without heart failure.

In the first dialysis treatments, IDH occurred in 33% of patients with heart failure and 24% of those without heart failure. In the last dialysis treatment, the percentages of patients who developed IDH in the heart failure and non-heart failure groups were 41% and 24%, respectively. Of the patients with heart failure, 54% ended with profile A in the first treatment and 50% ended with profile A in the last treatment. The majority of patients with IDH ended in profile A: 56% during the first dialysis and 51.7% during the last dialysis. At the end of the hospital admission, 60% of patients with heart failure and 46% of those without heart failure achieved EDW.

In conclusion, the authors said, "Monitoring the profile throughout the patient treatment via Crit-Line can help nurses safely increase UF goals to achieve EDW at each treatment while avoiding complications of IDH. Although 60% of heart failure patients and 46% of non-heart failure [patients] achieved EDW, the majority of the patients were in profile A indicating the need for more aggressive UF."

Source: Chandler J, Khanna S, Mansur A. Prevalence of intradialytic hypotension (IDH) across Crit-Line profiles in the acute setting: A retrospective data analysis. Abstract of a poster presented at the virtual 2021 American Nephrology Nurses Association National Symposium, May 2-5, 2021.

Quality Improvement Project in Patients with Sickle Cell Disease

Various indications for sickle cell disease call for red blood cell exchange. Standard practice to determine the efficacy of the procedure without increasing blood viscosity following exchange is hemoglobin electrophoresis (HgbS) in conjunction with obtaining hematocrit (HCT) levels via complete blood count. Current policy at the New York Presbyterian Hospital-Columbia University Medical Center, New York, New York, requires obtaining pre-HgbS and complete blood counts, but does not require the same laboratory measurements to be drawn following red blood cell exchange.

In a virtual poster presentation at the 2021 ANNA National Symposium, **Kyle Daniel Gault, BSN, RN, CNN, CDN, QIA (ASCP)**, described a Quality Improvement Project aimed at determining whether obtaining HgbS and hct levels following red blood cell exchange provides accurate measurement of predicted levels and aids clinicians in assessing the efficacy of the exchange in correlation with improvement of symptoms. The poster was titled *Obtaining Hemoglobin S and Hematocrit Levels Post Red Blood Cell Exchange: Target and Actual Result*.

The project involved seven patients with sickle cell disease, ≥ 30 years of age, both men and women, who required chronic red blood cell exchange every 4 to 6 weeks in the outpatient apheresis unit as part of their treatment maintenance.

Over a period of 5 months, 35 red blood cell exchange procedures were performed on the included patients. Mean post HgbS levels and complete blood counts were drawn following every red blood cell exchange, and were tracked throughout the study period. All levels were within the targeted HgbS levels at $<30\%$, in compliance with the current treatment guidelines.

In summary, the author said, "The project gave way to change our current policy and apply it to our practice. By having actual data on hand, apheresis nurses can optimize the use of red blood cell exchange and patients can return for their next appointment as directed by their referring hematologist (usually between 4 and 6 weeks). The numerical data obtained post red blood cell exchange aid clinicians in assessing the effectivity of exchange in correlation with symptom improvement experienced by the patient (Mandal et al, 2014). The practice change will also be implemented to our inpatient sickle cell population requiring acute red blood cell exchange."

Source: Gault KD. Obtaining hemoglobin S and hematocrit levels post red blood cell exchange: Target and actual result. Abstract of a poster presented at the virtual 2021 American Nephrology Nurses Association National Symposium, May 2-5, 2021.

Mean post HgbS levels and complete blood counts were drawn following every red blood cell exchange and were tracked throughout the study period. All levels were within the targeted HgbS levels at $<30\%$.



Preventing Line Infections: Hemodialysis Nurses and ICU Nurses Work Together

During a virtual poster session at the 2021 ANNA National Symposium, **Nicole Ingram, BSN, RN, CNN, CNIV**, and **Susan McKenna, MSN, RN, CNIII**, of the acute hemodialysis unit at VCU Medical Center, Richmond, Virginia, reported on a collaboration between specialized acute care hemodialysis nurses and intensive care unit (ICU) nurses in treating patients receiving continuous renal replacement therapy (CRRT). The collaboration was created to decrease central line infections, improve patient safety, and empower peer nurses through real-time audits and education. The poster was titled *Infection Prevention through Collaboration in Hemodialysis Line Care*.

CRRT delivered in the ICU setting requires expertise of both ICU and hemodialysis nurses. To prevent central line-associated bloodstream infections (CLABSIs), air emboli, and bleeding, current evidence-based practice calls for the use of hemodialysis-specific connectors and caps when de-accessing lines. Results of a learning needs assessment revealed that understanding and application of such connectors and caps by ICU nurses performing CRRT was inconsistent, creating potential safety risks.

Hemodialysis nurses collaborated with ICU nurses to develop an education plan to address correct hemodialysis line care in adults receiving CRRT in the ICU. Multiple shared governance committees and key stakeholders were given information on hemodialysis line care, safety concerns, and education on specialty connectors and caps. The education effort was reinforced by placing toolkits on all CRRT machines. Following

implementation of the initiative, weekly audits with just-in-time education have been ongoing to support the practice change.

Results of the initiative were measured by calculating CRRT-related CLABSI rates per 1000 CRRT patients across adult ICUs. In July 2018, prior to implementation of the initiative, rates were a concerning high of 4.27, paralleling the initial observation of inconsistent, unsafe practice. The intervention began with planning, followed by implementation that included education, construction of the toolkits, and weekly audits with just-in-time education.

Following implementation of the initiative, CLABSI rates fell to 0 in February/March 2019, bumped to 3.26 in April 2019, returned to 0 in May 2019. Over the following year, rates of CRRT-related CLABSIs remained at minimal levels, indicating successful integration into practice.

"The partnership between adult ICUs and hemodialysis nurses resulted in improved outcomes in patients receiving CRRT. Dissemination extended beyond the adult ICUs to create positive change at the organizational level through a reduction in overall hemodialysis-related CLABSI rates," the authors said.

Source: Ingram N, McKenna S. Infection prevention through collaboration in hemodialysis line care. Abstract of a poster presented at the virtual 2021 American Nephrology Nurses Association National Symposium, May 2-5, 2021.

Conference Coverage

Vitamin D Supplementation and Cardiovascular Outcomes in CKD

The prevalence of cardiovascular disease is higher among patients with chronic kidney disease (CKD) than in the general population. Patients with CKD commonly have vitamin D deficiency, an imbalance that has recently been linked to cardiovascular disease, due to an increased risk of inflammation and dysfunction of the vascular endothelium.

Awareness among primary care providers of the association between vitamin D deficiency and cardiovascular disease in patients with CKD can help prevent adverse cardiovascular outcomes. **Alix M. Duarte Gomez, MSN, RN,** and **Fay Callejo Gbolo, MPH, MSN, RN,** of Columbia University School of Nursing, New York, New York, conducted a review of the current evidence on the impact of vitamin D supplementation in adults with non-dialysis dependent CKD. Results of the review were reported during a virtual poster session at the 2021 ANNA National Symposium in a poster titled *Evaluating the Impact of Vitamin D Supplementation in Cardiovascular Outcomes in Patients with Chronic Kidney Disease Not Requiring Dialysis*.

The researchers searched PubMed, CINAHL, and EMBASE using the search terms “chronic kidney disease AND vitamin D AND cardiovascular disease.” Population-based studies published between 2015 and 2020 that used flow mediated dilation (FMD) and/or pulse wave velocity (PWV) as proxies for cardiovascular function in non-dialysis dependent adults with CKD were eligible for review, as were eligible studies from the reference lists of those articles. Non-human and pediatric studies were excluded, as were studies that included patients on dialysis.

A total of nine articles met inclusion criteria. The review revealed conflicting evidence regarding the impact of vitamin D supplementation on adults with non-dialysis dependent CKD. Most of the studies found an association between vitamin D supplementation and improved FMD/PWV measurements, demonstrating improved vascular elasticity and cardiovascular health. However, those results may have been due partially to some studies including patients diagnosed with cardiovascular disease taking medications such as antihypertensives.

“Therefore, more well-designed studies, with longer follow-ups, are required to better determine the effects of vitamin D supplementation on cardiovascular health in non-dialysis CKD patients to best determine the true added benefit with vitamin D supplementation, as well as its cost-effectiveness,” the authors said.

Source: Duarte Gomez AM, Gbolo FC. Evaluating the impact of vitamin D supplementation in cardiovascular outcomes in patients with chronic kidney disease not requiring dialysis. Abstract of a poster presented at the virtual 2021 American Nephrology Nurses Association National Symposium, May 2-5, 2021.



ILLUMINATE-B Study Results: Lumasiran in Young Children with PH1

Primary hyperoxaluria type 1 (PH1) is a rare genetic disorder that is characterized by hepatic oxalate overproduction, recurrent kidney stones, nephrocalcinosis, progressive kidney failure, and multiorgan damage from systemic oxalosis. ILLUMINATE-B is an open-label, phase 3 study of lumasiran in young children with PH1. Lumasiran is a subcutaneous investigational RNAi therapeutic that reduces hepatic oxalate production by targeting glycolate oxidase.

Debbie Barrera, BNS, presented results of the ILLUMINATE-B study during a virtual poster session at the 2021 ANNA National Symposium. The poster was titled *ILLUMINATE-B, a Phase 3 Open-Label Study to Evaluate Lumasiran, an RNAi Therapeutic, in Young Children with Primary Hyperoxaluria Type 1 (PH1)*.

Study inclusion criteria were age ≤ 6 years, diagnosis of PH1, estimated glomerular filtration rate >45 mL/min/1.73 m² in participants ≥ 12 months of age or normal serum creatinine in participants <12 months of age. Lumasiran dosing was monthly for 3 months, then monthly or quarterly. The primary end point of interest was percentage change in urinary oxalate excretion from baseline to month 6. A total of

18 patients were enrolled. Median age was 4.3 years (range, 0.3 to 6 years), baseline mean urinary oxalate:creatinine was 0.63 mmol/mmol, which was equivalent to 5.8 times the upper limits of normal.

There were no serious adverse events related to lumasiran, and no deaths, severe adverse events, or treatment discontinuation during the study period. The most common adverse events related to lumasiran were mild, transient injection site reactions in three of the 18 patients.

Efficacy and safety results in ILLUMINATE-B were consistent with those seen in ILLUMINATE-A, a phase 3 trial of lumasiran in older children and adults.

Source: Barrera D, Deschenes G, Cochat P, et al. ILLUMINATE-B, a phase 3 open-label study to evaluate lumasiran, an RNAi therapeutic, in young children with primary hyperoxaluria type 1 (PH1). Abstract of a poster presented at the virtual 2021 American Nephrology Nurses Association National Symposium, May 2-5, 2021.

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AOPO Proposes Changes to CMS Rules Affecting Organ Donation

The US Department of Health and Human Services has moved to accept additional comments on Centers for Medicare & Medicaid Services (CMS) rules that affect organ donation and transplantation. In a recent press release, the Association of Organ Procurement Organizations (AOPO) praised that move. The AOPO is the national voice of 57 federally designated Organ Procurement Organizations.

The AOPO responded to the request for comments with recommendations that will align the organ donation and transplantation system to achieve 50,000 organ transplants annually by 2026, a goal that will save more lives than the proposed rule would have done.

Joe Ferreira, president of AOPO, said, “Real patient lives hang in the balance so any policy changes must be carefully considered. Unfortunately, rules put forth at the end of the last administration oversimplify an incredibly complex system based on misguided data. We support reform and the necessary accountability for performance that enables more alignment, and we welcome opportunities to collaborate with CMS and other stakeholders toward our shared goal of saving more lives.”

Under the new regulations, CMS puts forth a forced competition model designed to be run by community-based nonprofits that in the past have depended on collaboration for mutual success. OPOs competing for donation service areas will hinder information and best practice sharing critical to driving system improvement, according to the press release.

Steve Miller, CEO of AOPO, said, “AOPO supports the overall goal of improving performance in order to save more lives. However, the new tiered competition model proposed under the rule has the potential to disrupt the collaborative efforts that have led to year-over-year increases in organ donation over the last 10 years. Given the independent nature of the organ donation and transplantation system, we propose a collaborative effort which will save substantially more lives.”

The press release continued: “Meaningful progress will require a coordinated, system-wide effort to boost collaboration, improve and align performance metrics, and deploy targeted interventions to address the current system’s most acute failures. This includes utilizing the thousands of organs per year being recovered by OPOs from complex and older donors but declined for transplantation by transplant programs and addressing racial equity gaps in organ donation and transplantation.”

Positive Study Results of KidneyIntelX™ Reported

Study findings reported in the April issue of *Diabetologia*, the official journal of the European Association for the Study of Diabetes, suggested that KidneyIntelX™ more accurately predicted decline in progressive kidney function and kidney failure compared with the current standard of care. The findings were highlighted in a press release from RenalytixAI, developer of artificial intelligence-enabled in vitro diagnostic solutions for kidney disease, including KidneyIntelX. The multi-center study was conducted in a diverse cohort of 1146 patients with type 2 diabetes with early stages (stages 1, 2, and 3) of kidney disease.

KidneyIntelX was seen to be highly effective at both ends of the risk spectrum, and more accurately identified and segmented patients into three risk categories (low, intermediate, and high) compared with clinical models that included the current standard of care, the Kidney Disease Improving Global Outcomes (KDIGO) risk stratification algorithm. When guideline-recommended urine albumin to creatinine ratio testing was performed, the positive predictive value for progressive decline in kidney function was 69% for those scored as high risk by KidneyIntelX compared with the 40% identified as highest risk by KDIGO stratification, representing a 72% improvement versus standard of care. In addition, only 7% of patients scored as low risk by KidneyIntelX experienced progression.

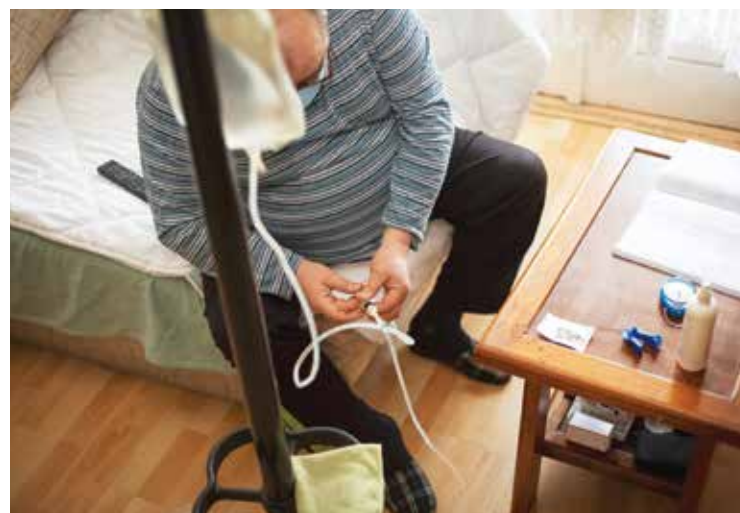
Michael J. Donovan, MD, PhD, chief medical officer at RenalytixAI, said, “Given these additional clinical study findings, we are confident that KidneyIntelX will be adopted as standard of care in assessing the risk of progressive kidney decline in individuals with early-stage diabetic kidney disease. These results published in *Diabetologia* further validate our rigorous scientific and clinical approach, which is focused on early detection and aggressive clinical intervention for those found to be at the highest risk.”

Collaboration Empowers Patients to Choose Home Hemodialysis

Fresenius Medical Care and DaVita Kidney Care are collaborating in an effort to provide home dialysis technology, including NxStage home hemodialysis machines, dialysis supplies, and a connected health platform to DaVita patients across the United States. The agreement, announced in a press release, highlights the companies’ shared goal of empowering patients to choose home dialysis as a treatment

modality. NxStage is the first and only truly portable hemodialysis system approved by the US FDA for home use.

DaVita group vice president for DaVita home modalities, **Keith Hartman**, said, “For patients choosing home dialysis, it can mean more freedom and also active participation in their care, which is why we’re always looking for new solutions that ease the burden on our patients. We’re expanding our use of NxStage home hemodialysis machines that have invaluable remote capabilities and connectivity for our patients. By transmitting treatment information, we hope to help identify irregularities and prevent avoidable complications, thus supporting patients’ desire to stay on their treatment of choice longer.”



Joe Turk, president of home and critical care therapies for Fresenius Medical Care North America, added, “We are excited to expand our longstanding collaboration with DaVita to help more patients benefit from the portability, dependability, and flexibility of our NxStage home machines, which are designed to be easy to use. Our home hemodialysis technology is bringing home dialysis to more patients than ever before, aligning both with evidence supporting dialysis at home as well as the recently confirmed Medicare programs to accelerate home adoption.”

The agreement also allows patients to access Nx2me Connected Health, a platform that simplifies collection and sharing of treatment information with the dialysis clinic and care teams. The platform accesses treatment data, including weight, blood pressure, and temperature via Bluetooth directly from the home hemodialysis machine, as well as answers to questions entered by the patient.

Martin Schreiber, MD, chief medical officer for DaVita home modalities, said, “Home hemodialysis can be a fantastic clinical option for many patients while also better aligning with their lifestyles. We’re committed to bringing innovation solutions that build on our prior advancements and can help further transform our patients’ experience while treating at home.”

FDA Grants Priority Review for NDA for KORSUVA™

In a late spring press release, Cara Therapeutics and Vifor Pharma announced that the US FDA has accepted and granted Priority Review for the New Drug Application (NDA) for KORSUVA™ (difelikefalin) solution for injection for the treatment of moderate-to-severe pruritis in hemodialysis patients. The PDUFA target action date for KORSUVA is August 23, 2021. The FDA does not plan to hold an advisory committee meeting to discuss the application.

Priority Review is granted to applications for potential therapies that, if approved, would be significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions compared with standard applications. Results of two pivotal phase 3 trials—KALM-1, conducted in the United States, and the global KALM-2—as well as supportive data from an additional 32 studies were submitted to support the NDA.

Derek Chalmers, PhD, DSc, president and CEO of Cara Therapeutics, said, “The FDA acceptance for filing and granting of Priority Review for the KORSUVA NDA marks a significant milestone for Cara and for the substantial number of hemodialysis patients with chronic intractable pruritus. The FDA’s agreement to expedite the timeline through Priority Review designation aligns with our understanding of the therapeutic potential of KORSUVA to fundamentally change the treatment paradigm for this serious unmet need. We look forward to working with the FDA through the review process and, along with our commercial partner, Vifor Pharma, remain focused on preparing for the US launch of KORSUVA injection, if approved.”

Stefan Schulze, CEO of Vifor Pharma Group, added, “We are delighted that the FDA accepted and granted Priority Review for this breakthrough therapy. Pruritis in hemodialysis patients is a debilitating condition with a significant impact on quality of life and increased risk for hospitalization and mortality. It impacts up to 40% of dialysis patients around the world. If KORSUVA is approved, we will be able to offer a medicine that is in line with our aim to deliver innovative therapies to patients with high unmet medical needs. We are highly committed to bringing this important new treatment to patients in the US as soon as possible following FDA approval, together with our partner Cara Therapeutics.”

FOTIVDA® Approved for Patients with RCC

The FDA has granted approval for FOTIVDA® (tivozanib) for the treatment of adults with relapsed or refractory advanced renal

cell carcinoma (RCC) who have received two or more prior therapies, according to a press release from AVEO Oncology. FOTIVDA is an oral, next generation vascular endothelial growth factor tyrosine kinase inhibitor.

The approval is based on TIVO-03, a pivotal phase 3 study that compared FOTIVDA to sorafenib in relapsed or refractory advanced RCC following two or more prior systemic therapies. Data from three additional trials and safety data from more than 1000 clinical trial participants also supported the application.

Brian Rini, MD, chief of clinical trials at Vanderbilt Ingram Cancer Center and principal investigator for the TIVO-03 trial, said, “The approval of FOTIVDA provides a new tool for treating patients with kidney cancer who have relapsed or become refractory to two or more prior systemic therapies. With advances in RCC treatment, patients are living longer, increasing the need for proven, well tolerated treatment options in the relapsed or refractory setting. The TIVO-3 study is the first positive phase 3 study in RCC patients who received two or more prior systemic therapies, and also the first phase 3 RCC study to include a predefined population of patients who have received prior immunotherapy, the current standard of care in earlier-line treatment. With this approval, I believe FOTIVDA represents an attractive intervention, and expect it to play a meaningful role in the evolving RCC treatment landscape.”

Michael Bailey, president and CEO of AVEO, said, “We believe in FOTIVDA’s potential to provide a differentiated treatment option for the growing number of individuals in the US with relapsed or refractory RCC...With this approval, AVEO begins its journey as a commercial-stage company, a noteworthy accomplishment in our industry. On behalf of the entire AVEO team, I would like to thank all the patients, their families, and caregivers whose tireless efforts made this day possible.”

AKF Applauds Introduction of Medigap Expansion Act

Reps. Cindy Axne (D-IA) and Jaime Herrera Beutler (R-WA) have introduced the Jack Reynolds Memorial Medigap Expansion Act. The bill would expand Medigap coverage for patients with end-stage kidney disease under age 65, who are currently unable to purchase Medigap coverage in 20 states.

The American Kidney Fund (AKF) applauds the bill’s introduction. In a press release, **LaVarne A. Burton**, president and CEO of AKF, said, “Where you live

shouldn’t determine whether your Medicare coverage is affordable—every state should make Medigap available to Medicare’s ESKD beneficiaries under 65. AKF is deeply grateful to Reps. Axne and Herrera Beutler for introducing this critical legislation. It has the power to make a real difference in the lives of people we represent.”

Having Medigap coverage is also important to patients who want to be added to the kidney transplant waiting list. Demonstrating the ability to pay Medicare’s out-of-pocket expenses is often a requirement to be accepted to the waiting list. “Without a Medigap plan, ESKD patients can be denied the lifesaving procedure of a kidney transplant—the best treatment option for people with kidney failure,” Ms. Burton added.

“This legislation would ensure that all ESKD patients, regardless of their age and where they live, will be able to purchase Medigap coverage. Introduction of this bill is just the first step. AKF is asking other members of Congress to co-sponsor this important legislation so that we can make 2021 the year Medigap becomes available to everyone with kidney failure,” Ms. Burton said.

CONFIRM: Terlipressin in Patients with HRS-1

Results from the phase 3 CONFIRM study assessing the efficacy and safety of terlipressin in adults with hepatorenal syndrome type 1 (HRS-1) have been published online in the *New England Journal of Medicine* according to a recent press release from Mallinckrodt, a global biopharmaceutical company.

HRS-1 is an acute and life-threatening syndrome involving acute kidney failure in patients with cirrhosis, and has a median survival time of approximately 2 weeks and more than 80% mortality within 3 months if left untreated. Terlipressin is an investigational product and its safety and effectiveness have not yet been established by the US FDA or Health Canada.

The phase 3 CONFIRM trial met its primary end point of verified HRS reversal, defined as improvement in renal function, avoidance of dialysis, and short-term survival. The primary objective of the CONFIRM trial was to examine the efficacy and safety of terlipressin, in combination with albumin, versus placebo in adults in the United States and Canada. The trial met three of four prespecified secondary end points: HRS reversal, HRS reversal without renal replacement therapy (RRT) by day 30, and HRS reversal in the systemic inflammatory response syndrome subgroup. The

fourth prespecified secondary end point of verified HRS reversal without HRS recurrence by day 30 was 50% greater in the terlipressin group but did not reach statistical significance.

Florence Wang, MBBS, MD, FRACP, FRCPC, hepatologist at Toronto General Hospital and professor of medicine at the University of Toronto and lead author of the study, said, “The durability of HRS reversal with terlipressin in CONFIRM persisted to day 30 without the need for RRT. This is a clinically significant observation, as RRT poses many challenges for patients with advanced cirrhosis. Results from CONFIRM provide critical information on a potential treatment option for HRS-1 and these data indicate that, if approved, terlipressin has the potential to reverse the course of HRS-1 in the appropriate patients and help the healthcare community better manage this critically ill and undeserved patient population.”

Long-Term Data on Treatment for Fabry Disease

Results of a real-world observational study and a clinical trial on long-term treatment with Fabrazyme® (agalsidase beta) for people living with Fabry disease are now included in the FDA-approved label. Fabrazyme received accelerated FDA approval in 2003 and is the first approved treatment for adults and pediatric patients ≥2 years of age with confirmed Fabry disease.

According to a press release from Sanofi Genzyme, the long-term data demonstrated that fewer patients treated with Fabrazyme experienced a clinically significant event such as renal, cardiac, cerebrovascular, or death, compared with patients in the placebo group (28% vs 42%). The data confirm the safety and efficacy of Fabrazyme as an enzyme replacement therapy for patients with Fabry disease.

Fabry disease is a genetic disease that results in the

progressive accumulation of the globotriaosylceramide lipid throughout the body, associated with a decline in kidney function, pain, fatigue, and other symptoms affecting the nervous and cardiovascular systems. Fabry disease can also cause damage to organs, leading to kidney failure, heart disease, and stroke.

Robert J. Desnick, MD, dean for genetics

and genomic medicine at the Ichan School of Medicine at Mount Sinai and lead investigator, said, “Fabry disease is an X-linked genetic disorder affecting approximately 10,000 women and men worldwide. These findings are a remarkable contribution to the ongoing understanding of this rare disease and the long-term impact of Fabry on renal function and clinically significant events.” ■

Print-only Content

COVID-19

AKI and ACI in Patients with COVID-19

European Review for Medical and Pharmacological Sciences. 2021;25(4):2114-2122

W.-Z. Li and colleagues reported results of a study in China designed to determine the incidence and risk factors for acute cardiac injury (ACI) and acute kidney injury (AKI), and the effect of those complications on severity and mortality in patients with COVID-19.

The retrospective study included 1249 patients with COVID-19. Multivariable logistic regression models were used to determine the association of ACI or AKI with COVID-19 severity and mortality.

Median age of the cohort was 36 years and 61.9% were male. Fifty-three patients (4.2%) developed ACI and 91 (7.3%) developed AKI. Higher odds of developing ACI were seen among patients >60 years of age, and those with heart disease, decreased lymphocyte, and increased C-reactive protein, procalcitonin, and erythrocyte sedimentation rate on hospital admission, as well as use of lopinavir/ritonavir.

The odds of developing AKI were higher among patients >60 years of age, and in men and those with obesity, hypertension, chronic kidney disease, decreased lymphocyte, and increased C-reactive protein, procalcitonin, and erythrocyte sedimentation rate on hospital admission.

Increased high-sensitive cardiac troponin (>300 ng/L), N-terminal pro-brain natriuretic peptide (>2500 pg/mL), and decreased estimated glomerular filtration rate (<60 mL/min/1.73 m²) were associated with higher adjusted mortality.

In conclusion, the researchers said, “ACI and AKI were not common in COVID-19 patients in Shanghai, China. However, patients with ACI/AKI had higher severity rate and mortality rate when compared with those without ACI/AKI.”

Changes in COVID-19-Related AKI Severity and Outcomes Over Time

Kidney International Reports. doi.org/10.1016/j.ekir.2021.01.036

Patients with COVID-19 frequently develop acute kidney injury (AKI); however, data on the risks and outcomes associated with AKI in that patient population are incomplete. It is also unknown whether kidney outcomes have evolved during the course of the pandemic.

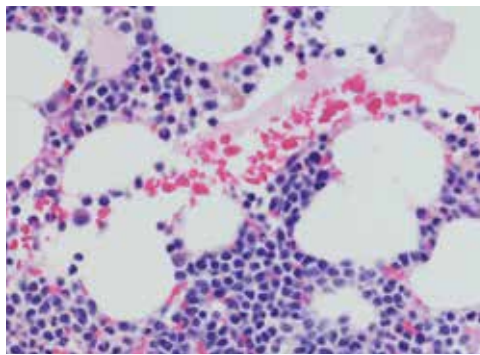
David M. Charytan, MD, and colleagues at the New York University Grossman School of Medicine, New York, New York, conducted an analysis of electronic health records of patients with COVID-19 with and without AKI who were admitted to three New York hospitals between March 2, 2020, and August 25, 2020.

Outcomes of interest were AKI overall and according to admission week, AKI stage, the need for renal replacement therapy (RRT), mortality, and recovery of kidney function. Associations between patient characteristics and outcomes were examined using logistic regression.

During the study period, there were 4732 admissions with COVID-19. Of those, 29.3% (n=1386) had AKI. In the group with AKI, 51.7% (n=717) had stage 1 disease, 9.5% (n=132) had stage 2 disease, 38.7% (n=537) had stage 3 disease, and 17.1% (n=237) required initiation of RRT.

In March, 32.5% (536/1648) of patients developed AKI, compared with 17.2% (n=15/87) in August ($P<.001$ for trend). Initiation of RRT was required in 6.9% of admissions in March and 0% of admissions in August. Mortality among patients with AKI was higher than among patients without AKI (51.5% vs 8.6%), and was 71.9% among patients requiring RRT. Most patients with AKI who survived to discharge (77%) recovered to within 0.3 mg/dL of baseline creatinine. Of the patients who survived to discharge, 62% discontinued RRT.

In conclusion, the researchers said, “AKI impacts a high proportion of admitted patients with COVID-19 and is associated with high mortality, particularly when RRT is required. AKI incidence appears to be decreasing over time and kidney function frequently recovers in those who survive.”



CHRONIC KIDNEY DISEASE

Outcomes in Elderly Patients with Multiple Myeloma and CKD

Clinical Lymphoma Myeloma Leukemia. doi:10.116/j.clml.2021.01.015

Chronic kidney disease (CKD) is a common comorbidity of patients with multiple myeloma and is associated with a poor prognosis. Shuling Li, MD, and colleagues conducted a study to examine clinical outcomes associated with CKD in a cohort of elderly patients with multiple myeloma initiating chemotherapy in the United States.

The study cohort included Medicare beneficiaries ≥66 years of age diagnosed with multiple myeloma who initiated first-line therapy from 2008 to 2014. Diagnosis codes were used to identify patients with CKD. Patients were followed for death, time to next treatment, and myeloma-defining events (anemia, hypercalcemia, skeletal-related events, progression to/of CKD) until September 30, 2015. The Kaplan-Meier method was used to estimate overall survival, time to next treatment, and cumulative incidence of myeloma-defining events; Cox proportional hazards were used to assess the risk of CKD-associated outcomes, adjusting for demographics and comorbid conditions.

A total of 22,484 patients were included in the analysis. Of those, 39% (n=8704) had CKD at initiation of first-line therapy. Compared with patients without CKD, those with CKD had shorter median overall survival (2.1 vs 3.6 years) and median time to next treatment (10.0 vs 12.4, 9.7 vs 11.2, 8.3 vs 9.2, and 6.9 vs 8.3 months at first- to fourth-line therapy).

For patients with CKD stages 1 to 5, progression was higher than the probability of developing CKD for patients without CKD: 3-year cumulative incidence, 47% vs 27%. The adjusted hazard ratios for CKD versus non-CKD were: all-cause mortality, 1.23 (95% confidence interval [CI], 1.18-1.28); anemia, 1.34 (95% CI, 1.24-1.45); hypercalcemia, 1.23 (95% CI, 1.09-1.38); skeletal-related events, 0.85 (95% CI, 0.90-0.91); and time to next treatment, 1.03 (95% CI, 0.96-1.10) at third-line therapy to 1.15 (95% CI, 1.04-1.27) at fourth-line therapy.

In conclusion, the researchers said, “Data from the study suggest that CKD-associated clinical burden is substantial in elderly patients with multiple myeloma.”

DIABETES

Secondary Analysis of Data from the CREDENCE Trial

Clinical Journal of the American Society of Nephrology. 2021;16(3):384-395

The renal protective effects of renin-angiotensin system inhibitors are greater in individuals with higher levels of albuminuria at treatment initiation. It is not known whether that is the case with sodium-glucose cotransporter 2 (SGLT2) inhibitors, particularly in patients with very high urine albumin-to-creatinine ratio (UACR, ≥3000 mg/g).

Meg Jardine, MBBS, PhD, and colleagues conducted a secondary analysis of data from the CREDENCE (Canagliflozin and Renal Endpoints in Diabetes with Established Nephrology Clinical Evaluation) randomized controlled trial to examine the association between baseline UACR and the effects of canagliflozin on efficacy and safety outcomes.

Eligible patients had type 2 diabetes, an estimated glomerular filtration rate (eGFR) 30 to <90 mL/min/1.73 m², and UACR of >300 to 5000 mg/g (n=4401). The researchers used Cox proportional hazards regression to examine the relative and absolute effects of canagliflozin on kidney, cardiovascular, and safety outcomes based on a baseline UACR of ≤1000 mg/g (n=2348), ≥1000 to ≤3000 mg/g (n=1547), and ≥3000 mg/g (n=506). Additional outcomes of interest were the effects of canagliflozin on UACR itself, eGFR slope, and intermediate outcomes of glycated hemoglobin, body weight, and systolic blood pressure.

Overall, there was an association between higher UACR and higher rates of kidney and cardiovascular events. Canagliflozin reduced efficacy outcomes for all UACR levels, with no evidence that relative benefits varied between levels. Canagliflozin reduced the primary composite outcome by 24% (hazard ratio [HR], 0.76; 95% confidence interval [CI], 0.56-1.04) in the lowest UACR subgroup, 28% (HR, 0.72; 95% CI, 0.56-0.93) in the UACR subgroup >1000 to <3000 mg/g, and 37% (HR, 0.63; 95% CI, 0.47-0.84) in the highest subgroup. Absolute risk reductions for kidney outcomes were greater in participants with higher baseline albuminuria. The rates of kidney-related adverse events were lower with canagliflozin, with a greater relative reduction in higher UACR categories.

“Canagliflozin safely reduces kidney and cardiovascular events in people with type 2 diabetes and severely increased albuminuria. In this population, the relative kidney benefits were consistent over a range of albuminuria levels, with greatest absolute kidney benefit in those with an UACR ≥3000 mg/g,” the researchers said.



Biochemical Parameters of Diabetic Ketoacidosis with Varying Levels of Renal Function

The Journal of Clinical Endocrinology & Metabolism. doi.org/10.1210.1210.climem/dgab126

There are few data available related to differences in biochemical parameters of diabetic ketoacidosis (DKA) in patients with end-stage kidney disease (ESKD). **Rodolfo J. Galindo, MD**, and colleagues conducted an observational study to examine the relationship between degree of metabolic acidosis and β -hydroxybutyrate in patients with ESKD (defined as estimated glomerular filtration rate <15 mL/min/1.73 m²), moderate renal failure (eGFR 15 to 60 mL/min/1.73 m²), or preserved renal function (eGFR >60 mL/min/1.73 m²).

The study cohort included adults, 18 to 80 years of age, with DKA who were admitted to Emory University Hospitals between January 1, 2006, and December 31, 2016. Bicarbonate and pH levels were similar among the three groups at admission (13.9 vs 13.4 vs 13.8 mmol/L and 7.2 vs 7.2 vs 7.2, respectively). Patients with ESKD had lower mean β -hydroxybutyrate, but higher admission glucose (852 vs 714 vs 518 mg/dL), anion gap (23.4 vs 23 vs 19.5 mmol/L), and osmolality (306 vs 303 vs 293 mOsm/kg) compared with patients with moderate renal failure or preserved renal function.

The sensitivity of β -hydroxybutyrate >3 mmol/L for diagnosing DKA by bicarbonate level <15 and <18 mmol/L was 86.9% and 72% in ESKD, 89.3% and 83.7% in moderate renal failure, and 96.2% and 88.3% in preserved renal function. In patients with ESKD, the corresponding β -hydroxybutyrate with bicarbonate levels <10 , 10 to 15, and <18 mmol/L were 5.5, 3.9, and 3.0 mmol/L, respectively.

In conclusion, the researchers said, “Significant metabolic differences were found among DKA patients with different levels of renal function. In patients with ESKD, a β -hydroxybutyrate level >3 mmol/L may assist with confirmation of DKA diagnosis.”

TRANSPLANTATION

Risk of Mortality in Transplant Recipients who Develop Cancer

Nephrology Dialysis Transplantation. 2020;35(10):1802-1810

It is well established that transplantation is a risk factor for malignancy. However, according to **Susan L. Murray, MB BCh**, and colleagues, there are few data on the outcomes of cancer in transplant recipients compared with non-transplant recipients. The researchers conducted a study to examine survival in kidney transplant recipients who develop cancer and compared outcomes among cancer patients in the general population.

Data from the National Cancer Registry Ireland were linked with the National Kid-

ney Transplant Database. The study period was January 1, 1994, through December 31, 2014. Transplant recipients were considered at risk from the time of the cancer diagnosis.

During the study period there were 907 renal transplant recipients and 426,679 patients in the general population diagnosed with cancer. Of patients with non-melanoma skin cancer, the hazard ratio (HR) for 10-year all-cause mortality and cancer-specific mortality was significantly higher among transplant recipients than in the general population (HR, 3.06; 95% confidence interval [CI], 2.66-3.52; and HR, 3.91; 95% CI, 2.57-5.96, respectively). Among patients with non-Hodgkin lymphoma and prostate cancer, the risk of all-cause mortality, but not cancer-specific mortality, was higher among transplant recipients than in the general population (HR, 2.89; 95% CI, 1.96-4.25 and HR, 4.32; 95% CI, 2.39-7.82, respectively). There were no significant increases in risk of death in transplant recipients who developed colorectal, lung, breast, and renal cell cancer.

In conclusion, the researchers said, “Cancer-attributable mortality is higher in kidney transplant recipients with non-melanoma skin cancer compared with non-transplant patients. The American Joint Committee on Cancer staging should reflect the increased hazard of death in these immunosuppressed patients.”

Variation in Probability of Deceased Donor Kidney Transplant

Journal of the American Society of Nephrology. 2020; 31(12):2900-2911

Despite the Kidney Allocation System (KAS) introduced in 2014, geographic disparities in access to deceased donor kidney transplantation in the United States remain. According to **Kristen L. King** and colleagues, the effect of transplant center practices on the probability of transplanta-

tion for wait-listed patients is unclear.

The researchers conducted a registry study designed to compare the probability of transplantation across centers nationally and within donation service areas (DSAs). The study included all incident adult kidney transplant candidates wait-listed in 2011 (pre-KAS) and 2015 (post-KAS). The pre-KAS cohort included 32,745 individuals and the post-KAS cohort included 34,728 individuals. For each center, using competing risk regression, the researchers calculated the probability of deceased donor kidney transplantation within 3 years of wait listing, with living donor transplantation, death, and removal from the wait list as competing events. Associations between center-level and DSA-level characteristics and the adjusted probability of transplant were examined.

Patients received deceased donor kidney transplants within 3 years of wait listing more frequently post-KAS than pre-KAS (22% vs 19%). Nationally, the probability of transplant varied 16-fold between centers, ranging from 4.0% to 64.2% in the post-KAS era. Within DSAs, there was a median 2.3-fold variation between centers, with up to 10-fold and 57.4 percentage point differences. The probability of transplantation was correlated in the post-KAS cohort with the willingness of the center to accept hard-to-place kidney ($r=.055$; $P<.001$) and local organ supply ($r=.044$; $P<.001$).

“Large differences in the adjusted probability of deceased donor kidney transplantation persist under KAS, even between centers working with the same local organ supply. Probability of transplantation is significantly associated with organ offer acceptance patterns at transplant centers, underscoring the need for greater understanding of how centers make decisions about organs offered to wait-listed patients and how they relate to disparities in access to transplantation,” the researchers said. ■





Sarah Tolson

Taking a Closer look at the Insurance Verification Process

Recently I was on a call with an individual who is working on starting up a practice that focuses on servicing patients who are residents of skilled nursing facilities (SNFs), nursing homes, and assisted living facilities (ALFs). We discussed one of the biggest hurdles of providing care to patients in this setting—obtaining complete and accurate insurance coverage information for the patients. In a SNF, this can be especially challenging because when a patient runs out of covered days for SNF stays, the secondary insurance becomes primary for the patient's stay at the SNF. In this scenario, all other services the patient receives would likely be covered under their primary insurance. This coverage scenario is most commonly encountered in a very specific setting. However, in every setting where patients receive medical care, complete and accurate insurance verification is a critical piece of the revenue puzzle.

In addition to the setting of care playing a role in complicating a patient's insurance verification, the insurance market a practice operates in also plays a role. States like Texas, California and New York have incredibly complex markets that contain not only many regional insurance carriers but also many independent physician associations, further complicating insurance verification and the revenue cycle.

COMPONENTS OF A GOOD INSURANCE VERIFICATION PROCESS

In most care settings and insurance markets, a solid insurance verification process will go a long way toward increasing collections and reducing bad debt. To build a solid insurance verification process, it's helpful to know which payers have special requirements such as authorizations or referrals from the patient's primary care physician. Identifying the payers that have special coverage requirements and which payers simply require a patient has active coverage will save a significant amount of time during the verification process.

Performing a detailed insurance verification can take anywhere from a few minutes to an hour or more, depending on insurance company hold times. For payers that have special coverage requirements, the company I work for typically performs the eligibility verification over the phone so we can be sure to obtain all the detail we need that is specific not only to the patient's plan but also the provider's network participation status. This level of detail is often dif-

ficult to obtain from an automated, online eligibility verification.

The timing of an insurance verification is also important to this process.

In the event that a patient's insurance requires an authorization or referral,

it's helpful to perform the insurance verification far enough in advance of the patient's scheduled appointment in order to obtain the referral or authorization.

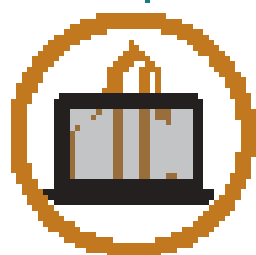
Another item to consider is that some insurance markets allow patients to change Medicaid-managed care plans on a monthly basis. If a patient schedules an appointment with your office on the second of the month and you verified their insurance coverage on the 25th of the previous month, it might be a good idea to do an online verification to make sure the patient is still covered with the same plan you verified eligibility with initially.

Maintaining well-organized records of insurance verifications and copies of patient insurance cards when they are available can be incredibly helpful. On occasion, my company has encountered scenarios where a patient's coverage is terminated retroactively, and the insurance verification documents play a role in filing timely appeals to the replacement payer.

Performing appropriately detailed insurance verifications when utilizing efficient time frames as they relate to a patient's appointment and insurance company requirements and keeping well-organized records are the building blocks of a solid insurance verification process. It is equally important to identify the individuals in the office who are responsible for performing the verifications and the checks and balances that will be maintained to ensure the verifications are performed for each patient. Additionally, each staff member in the practice whose role is impacted by a patient's insurance coverage—front desk, appointment schedulers, billing staff, and credentialing staff—should be familiar with the entire process so they can obtain the information regarding a patient's insurance coverage they need to perform their role. ■

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