Nephrology Times

Practical News, Trends, and Analysis

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Effects of Ozone on ESRD Risk, Mortality in CKD

Air pollution has been recognized as a global health burden, but epidemiologic studies on the effects of long-term exposure to ozone (O_3) have been inconclusive. Moreover, studies on the effects of O_3 on renal outcomes and mortality in chronic kidney disease (CKD) are lacking. To address the absence of data, **Ejin Kim** and other researchers examined the effects of ozone on the risk of end-stage renal disease (ESRD) and mortality in a two-pollutant model adjusted for socioeconomic status. The results appeared in *BMC Nephrology* [doi:10.1186/s12882-024-03500-6].

Study data came from 61,073 patients with CKD who visited one of three hospitals in Seoul, South Korea, between January 2001 and December 2016. Enrolled patients met the definition of CKD as outlined in the 2012 Kidney Disease Improving Global Outcomes Clinical Practice Guideline for the Evaluation and Management of CKD report and had functional and/or structural damage to the kidneys lasting more than 3 months. To examine ozone's effects on individuals, the researchers included data from nationwide and district disease surveillance.

The cohort included 56,470 participants aged 58.37 ± 17.37 years with an estimated glomerular filtration rate (eGFR) of 61.07 ± 29.92 mL/min/1.73m^2; 29,961 of the participants were male (48.82%). In addition, 23.06% of patients were diagnosed

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ETC Payment Model Unfavorable to Facilities Serving Patients at Higher Social Risk

The Centers for Medicare & Medicaid Services (CMS) implemented the End-Stage Renal Disease Treatment Choices (ETC) payment model in 2021. This pay-for-performance model randomly assigned approximately 30% of US dialysis facilities and nephrologists to receive financial bonuses or penalties based on their patients' use of home dialysis, placement on a kidney transplant waitlist, or receipt of a transplant.

Although up to 85% of patients with kidney failure may be medically eligible for

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Long-term Outcomes for COVID-19-Associated Acute Kidney Injury

One-fifth of patients hospitalized for COVID-19 experience acute kidney injury (AKI). COVID-19 has been associated with more severe AKI, higher incident chronic kidney disease (CKD), and higher mortality than AKI related to other respiratory viral illnesses. Patients whose AKI is related to COVID-19 also experience a greater decline in kidney function in the 6 months after hospital discharge than those whose AKI relates to another illness. However, data on the longer-term effects of COVID-19–associated AKI (COVID-AKI) are limited.

To that end, **Abinet M. Aklilu, MD, MPH,** and fellow researchers conducted a retrospective, longitudinal, multicenter, cohort study to assess the long-term kidney outcomes of patients who had COVID-AKI. Their results appeared in *JAMA Internal Medicine* [2024;184(4):414-423].

The researchers used data from a large hospital system's electronic health records focusing on adult hospitalized patients (age ≥18 years) with AKI and COVID-19 or other illnesses. The study included patients who were hospitalized during the COVID-19 pandemic (March 2020-June 2022), were screened for SARS-CoV-2,

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Update on IgA Nephropathy Treatment: Several Newer Therapies on the Horizon

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IgA nephropathy (IgAN) is at the forefront of newer treatments for glomerular disease. Therapeutic strategies like sparsentan and targeted-release budesonide are already approved, while therapies targeting complement and B-cell survival factors are being actively investigated.

In two recent articles, one a review in the *Journal of the American Society of Nephrology (JASN)*[1] and the other a review in the *Clinical Journal of the American Society of Nephrology (CJASN)*,[2] the treatment of IgAN is the focus. In the *JASN* article by El Karoui et al, both current and evolving treatment strategies are discussed. In the *CJASN* article by Cheung et al, strategies targeting B-cell survival factors—a proliferation-inducing ligand (APRIL) and B-cell activating factor (BAFF)—are reviewed.

The El Karoui review in *JASN* points out that because IgAN involves several hits (summarized in the TABLE), targeting one factor is likely to be of limited value. It also emphasizes the importance of selecting patients at high risk by trying to predict which patients are likely to progress and identifying patients with active as opposed to chronic disease.

TABLE | **Multi-Hit Pathogenesis of IgA Nephropathy**

Hit 1: Nephritogenic immune complexes with anti-galactose-deficient IgA1 (Gd-IgA1)-IgG, IgA, and/or IgM, because of circulating self-antigen Gd-IgA1
Hit 2: Glomerular inflammation and fibrosis from deposition circulating IgA-containing immune complexes in the glomerular mesangium
Hit 3: Heightened glomerular inflammation because of activation of complement–the alternative and lectin pathways
Hit 4: Progressive glomerular injury mediated by glomerular hemodynamics (glomerular hypertension)

El Karoui et al review four therapeutic approaches that should be considered in the management of IgAN: renin-angiotensin-aldosterone blockade, sodium-glucose cotransporter-2 (SGLT2) inhibition therapy, endothelin receptor antagonism, and broad-acting immunosuppression (corticosteroids and/or mycophenolate mofetil).

Among current therapies, the "new kid on the block" is sparsentan, a selective endothelin type A receptor and angiotensin II subtype 1 receptor antagonist. It has generated tremendous excitement because it significantly reduces proteinuria, which led to its conditional accelerated approval from the US Food and Drug Administration (FDA). However, the excitement has become somewhat muted due to its modest effects on stabilizing kidney function. This latter issue may slow down or impact its full approval from the FDA.

Budesonide, a corticosteroid, is likely to become a first-line steroid therapy for IgAN. Like sparsentan, budesonide has received accelerated approval from the FDA. Budesonide appears to work by delayed release in the gastrointestinal tract so that it targets the cells in Peyer's patch in the distal ileum and proximal colon that produce IgA and Gd-IgA1. The delayed release is a result of packaging budesonide in a pH-sensitive starch capsule. The other advantage of budesonide is that, although it is a corticosteroid, only a fraction is absorbed systemically. The results of the Effect of Nefecon in Patients With Primary IgA Nephropathy at Risk of Developing End-stage Renal Disease (NEFIGAN) trial and the phase 3 Efficacy and Safety of Nefecon in Patients With Primary IgA Nephropathy (NefIgArd) study of high-risk patients with IgAN were very promising in terms of both proteinuria reduction and stabilization of kidney function.

Therefore, in addition to supportive therapies (eg, renin-angiotensin inhibition and SGLT2 inhibition), both sparsentan and targeted-release budesonide should be considered, especially for high-risk IgAN patients.

Several emerging therapies are either in phase 2 or phase 3 trials, including agents that target complement and those homing in on B-cell factors APRIL and BAFF.

Anticomplement agents under development include avacopan, an oral C5a receptor inhibitor; iptacopan, which impacts the alternative pathway; and narsoplimab, which targets the lectin pathway. Anti-APRIL agents include sibeprenlimab (VIS649) and the anti-APRIL/BAFF targeting therapy zigakibart (BION-1301) and atacicept. These novel compounds are promising because they reduce proteinuria and appear to slow kidney disease progression.

In summary, IgAN is on the cusp of a transformational change in its treatment. In addition to sparsentan and targeted-release budesonide, specific treatments that inhibit complement pathways and B-cell survival are on the horizon. ■

REFERENCES

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2. Cheung CK, Rajasekaran A, Barratt J, Rizk DV. An update on the current state of management and clinical trials for IgA nephropathy. *J Clin Med*. 2021;10(11):2493. doi:10.3390/jcm10112493

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Conference Coverage

NKF SPRING CLINICAL MEETINGS 2024: LONG BEACH, CALIFORNIA

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


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ETC Payment Model

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TAKEAWAY POINTS

- Facilities that disproportionately serve populations with high social risk have a lower use of home dialysis and kidney transplant. Therefore, these sites may fare worse in the ETC payment model implemented in 2021.
- An observational study of 2191 dialysis facilities examined how facilities that serve patients with high social risk performed in the first year of the ETC model compared with those serving populations with lower social risk.
- In its first year, the study found that the ETC model disproportionately penalized dialysis facilities serving patients with higher social risk. These facilities had lower performance scores and were more likely to be financially penalized, mostly due to their lower use of home dialysis.

home dialysis, only 13.3% of incident patients in the United States initiated treatment with home dialysis in 2020. Dialysis rates are lower among Black patients with kidney failure, who are 24% less likely to start peritoneal dialysis than White patients.

Racial, ethnic, and socioeconomic disparities also hinder transplant rates. Dialysis facilities disproportionately serving patients who are non-Hispanic Black, Hispanic, uninsured, on Medicaid, or living in highly disadvantaged neighborhoods have lower home dialysis and transplant rates. This disparity raises concerns that the ETC model may disproportionately penalize such sites.

To determine the impact of the ETC model on dialysis facilities serving populations with higher social risk, **Kalli G. Koukounas, MPH,** and colleagues conducted an observational study to assess how they fared compared with facilities serving populations with lower social risk. The results were published in *JAMA* [2024;331(2):124-131].

The study analyzed CMS-published data on 2021 ETC model performance and payment adjustments, stratified by a facility-level composite social risk score developed using historical data from incident patients. The study sample included 2191 dialysis facilities participating in the ETC model from January 1 to December 31, 2021.

The researchers identified which facilities were in the highest quintile of the proportion of incident patients who were non-Hispanic Black, Hispanic, living in a highly disadvantaged neighborhood, or uninsured or covered by Medicaid at the start of dialysis. Researchers then assigned each facility a composite social risk score representing those in the highest quintile of having zero, one, or at least two of those characteristics. Next, they examined 1-year proportions of achieved home dialysis, achieved and improved transplant, performance payment adjustments, and modality performance scores across facilities with a social risk score of one, two, or more compared with those with a social risk score of zero. They also compared facilities in the highest-risk quintile with those in other quintiles for each category.

Using data from 125,984 incident patients (median age, 65 years [IQR, 54-74]; 41.8% female; 28.6% Black; 11.7% Hispanic), the researchers determined that 1071 dialysis facilities (48.9%) had no social risk factors, while 49 (22.4%) had two or more. In the first year of the ETC model, dialysis facilities with two or more had lower mean performance scores (3.4 vs 3.6; P=.002) and lower use of home dialysis (14.1% vs 16.0%; P<.001) compared with sites with no social risk factors. Facilities with two or more social risk factors were more likely to incur financial penalties (18.5% vs 11.5%; P< .001), more frequently received the highest payment cut of 5% (2.4% vs 0.7%; P=.003), and were less likely to achieve the highest bonus of 4% (0% vs 2.7%; P<.001). Compared with all other facilities, those in the highest quintile of treating uninsured patients or those covered by Medicaid experienced more financial penalties (17.4% vs 12.9%; P=.01), as did sites with the highest quintile of patients who were Black (18.5% vs 12.6%; P=.001).

The authors identified four study limitations: (1) Using historical data on incident patients to characterize facilities' 2021 social risk could lead to misclassification. (2) CMS uses the proportion of prevalent traditional Medicare patients with dual coverage or who are eligible for a low-income subsidy to identify facilities eligible for the health equity scoring adjustment. However, the study used the proportion of patients who were uninsured or covered by Medicaid at initiation. (3) The researchers were unable to assess facility-level variations in home dialysis, transplant wait-listing, or transplant rates. (4) The small number of evaluated nonprofit facilities, which received much higher financial penalties given their lower rates of home dialysis, precludes deeper analyses.

In summary, the authors wrote, "These findings, coupled with the escalation of penalties to as much as 10% in future years, support monitoring the ETC model's continued impact on dialysis facilities that disproportionately serve patients with social risk factors, as well as its influence on outcomes and disparities in care among patients treated in these sites." ■

Long-term Outcomes for AKI

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TAKEAWAY POINTS

- A rapid decline in kidney function is known to occur in the first few months after COVID-19–associated acute kidney injury (COVID-AKI). However, the longer-term effects were unclear.
- In a multicenter, cohort study, researchers found that patients with COVID-AKI had a 33% lower risk of major adverse kidney events, a 22% lower risk of worsened kidney function, and a 69% lower risk of mortality compared with patients with AKI due to other illnesses.
- The results show that patients hospitalized with COVID-AKI have a significantly lower risk of long-term kidney function decline and all-cause mortality than patients with AKI related to other illnesses.

had AKI, and survived to discharge, or had been hospitalized during the 5 years before the pandemic (October 2016-January 2020), had a positive influenza A or B test result, had AKI, and survived until hospital discharge. The researchers followed patients for a maximum of 2 years after discharge and performed data analyses from December 2022 to November 2023.

The primary outcome was major adverse kidney events (MAKE)—a combination of mortality and worsened kidney function (estimated glomerular filtration rate [eGFR] decline by 25% from discharge eGFR or kidney failure requiring dialysis). The team performed multivariable time-to-event analyses to compare MAKE between individuals with COVID-AKI and those who had AKI associated with other illnesses hospitalized during the same period. For further comparison, this outcome was evaluated for a historic cohort of patients with influenza-associated AKI (flu-AKI).

The study cohort comprised 9624 hospitalized patients (mean [SD] age, 69.0 [15.7] years; 4955 [51.5%] females and 4669 [48.5%] males; 1576 [16.4%] Black, 1007 [10.5%] Hispanic, and 7098 [73.8%] White individuals). There were 987 patients with COVID-AKI, 276 with flu-AKI, and 8361 with AKI associated with other illnesses (other-AKI). The flu-AKI group was older compared with the other two groups. There were more self-identified Black and Hispanic individuals in the COVID-AKI group (288 [29.2%] and 175 [17.7%], respectively) compared with the other two groups (52 [18.8%] and 34 [12.3%] for flu-AKI and 1236 [14.8%] and 798 [9.5%] for other-AKI, respectively). Compared with the other two groups, patients in the COVID-AKI group were slightly younger and had a higher baseline eGFR. They also had worse baseline comorbidity scores, higher markers of illness severity, and longer hospital stays.

Compared with the other-AKI group, the COVID-AKI group had lower MAKE (adjusted hazard ratio [aHR], 0.67; 95% CI, 0.59-0.75) due to lower all-cause mortality (aHR, 0.31; 95% CI, 0.24-0.39) and lower rates of worsened kidney function (aHR, 0.78; 95% CI, 0.69-0.88). The study authors posited that those who survive a bout of COVID-19 complicated by AKI may have intrinsic unmeasured characteristics that are associated with favorable longer-term outcomes.

The researchers noted several limitations to their study. First, there are likely residual unmeasured confounders that contribute to longitudinal eGFR trajectory. Because the study was retrospective, there is an absence of standardized follow-up and accurate tracking of postdischarge exposures. Additionally, ascertainment bias may be present. What's more, differential exposures during the follow-up period, such as starting renoprotective medications, could affect the kidney function trajectory. Changing trends in CKD care could also contribute to differing outcomes between the historic cohort and the COVID-19–era cohort. The researchers could not adjust for social determinants of health due to lack of data. Furthermore, GFR is estimated from creatinine, which is affected by muscle mass and nutritional status. Patients with critical illness and prolonged immobility experience muscle wasting, which may have affected results among the COVID-AKI group, which had a longer hospital stay and greater weight loss compared with the other groups.

In conclusion, however, the authors found their results reassuring because "COVID-AKI survivors experienced a rapid attenuation of their kidney function decline rate and had overall lower rates of long-term kidney progression compared with the other [two] groups. Replication in broader cohorts as well as assessment of the effects of other kidney dysfunction markers (eg, proteinuria) and the association of COVID-19–specific therapeutics with kidney function trajectory are worth investigating in future studies." ■

Effects of Ozone on ESRD Risk, Mortality in CKD

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with diabetes mellitus, 21.85% had hypertension, 29.42% had CKD stage 3, and 16.79% had advanced CKD with GFR less than 30 mL/min/1.73m^2.

The researchers obtained hourly O_3 concentrations from 533 air quality monitors between 2001 and 2016. They defined ozone concentration in terms of moving 8-hour averages (the average value of the 8-hour maximum O_3 concentration on a given day). During the study period, the mean concentrations of O_3 were 31.2 ppb. The time-series plot showed the national average daily 8-hour maximum O_3 concentration; there were days when air quality standard O_3 concentrations (60 ppb for each 8-hour average) were exceeded. The researchers divided personal exposure into two separate methods, one assigned to the individual's city, county, and district administrative entities according to their place of residence and the other using their address data to determine latitude and longitude coordinates. Researchers then determined personal exposure using the inverse distance weighting method.

The study outcome was cause-specific mortality and incidence of ESRD. During the study period, there were 5957 cases of ESRD and 6768 deaths. The researchers found that in both the district and individual-address models, the moving O_3 average was associated with an increased risk of ESRD and all-cause mortality. To adjust for the potential effects of other measured pollutants, the research team used a two-pollutant model. However, associations between O_3 exposure and study outcomes remained significant even after adjusting for nitrogen dioxide. The hazard ratio (HR) value for the district-level assessment was 1.025 (95% CI, 1.014-1.035); the HR value for the point-level assessment was 1.040 (95% CI, 1.035-1.045).

For the impact of ozone on ESRD, HR values were 1.049 (95% CI, 1.044-1.054) at the district level and 1.040 (95% CI, 1.031-1.050) at the individual address of the exposure assessment. The ozone HR for all-cause mortality was 1.012 (95% CI, 1.008-1.017) for administrative districts and 1.040 (95% CI, 1.031-1.050) for individual addresses.

In the district allocation model, the moving O_3 average for 365 days was associated with a higher risk of ESRD (HR, 1.034; 95% CI,1.031-1.036) and all-cause mortality (HR, 1.020; 95% CI, 1.018-1.023). This was also true in the point-allocation model for ESRD risk (HR, 1.019; 95% CI, 1.011-1.026) and all-cause mortality (HR, 1.047; 95% CI, 1.041-1.054).

The authors noted a few limitations of the study. Measurement error likely occurred due to the use of zip codes rather than the exact house address or place of death of each participant to determine exposure level. Selection bias may have resulted from most participants being in a specific metropolitan area. Data used in the study were at least 4 years old, so exposures and outcomes may not match current data. Finally, there was limited direct usage in model fitting due to the lack of information in the researchers' data that might correct for the lifestyle choices and health condition of patients with CKD.

"In conclusion," the authors wrote, "based on a large cohort of participants with CKD, long-term exposure to O_3 is associated with an increased risk of ESRD and mortality. Our findings highlight the need for better measures to control O_3 exposure and the emission of pollutants that contribute to the increase of O_3 in the atmosphere." ■

TAKEAWAY POINTS

- Some researchers have studied the effects of ozone (O_3) on cardiovascular and respiratory diseases in the general population, but data on renal outcomes and mortality in chronic kidney disease (CKD) are lacking.
- Ejin Kim and others investigated the association between long-term O_3 exposure and renal outcomes and mortality risk of patients with CKD using a two-pollutant model that reflected the mechanism of O_3 generation.
- In both single-pollutant and two-pollutant models, O_3 was associated with a higher risk of end-stage renal disease and all-cause mortality.

Conference Coverage

Long Beach, California | May 14-18, 2024

NATIONAL KIDNEY FOUNDATION

SPRING CLINICAL MEETINGS 2024

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 attended the 2024 NKF Spring Clinical Meetings in Long Beach, California, to learn about developments in all areas of nephrology practice and network with colleagues.

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

Renal Outcomes With Chlorthalidone Versus Hydrochlorothiazide

The Diuretic Comparison Project (DCP) previously demonstrated cardiovascular outcomes among individuals with and without chronic kidney disease (CKD; estimated glomerular filtration rate [eGFR] <60 mL/min) at baseline.

Researchers led by **Areef Ishani** evaluated renal outcomes from the DCP comparing chlorthalidone (CTD) with hydrochlorothiazide (HCTZ) in patients with hypertension. They presented results at the National Kidney Foundation Spring Clinical Meetings. Hypertension is a risk factor for the development and progression of CKD, and previous research has suggested there is a greater rate of progression of eGFR and a greater incidence of CKD with CTD versus HCTZ.

Participants were randomized to either continue HCTZ or switch to CTD at pharmacologically comparable doses. The primary outcome was CKD progression: doubling of creatinine, a terminal eGFR <10 mL/min, or kidney failure requiring treatment. Researchers also assessed the total slope of eGFR and incident CKD.

There were 12,024 (89%) patients with a baseline and at least one follow-up creatinine measurement (6002 receiving CTD, 6022 receiving HCTZ). The average baseline eGFR was 71 mL/min, and mean duration of follow-up was 2.4 years.

Primary composite renal outcomes between the 217 (3.6%) CTD patients and the 232 (3.9%) HCTZ patients did not differ (hazard ratio [HR], 0.94; 95% CI, 0.78-1.13; P=.5). Nor was there a difference between the CTD group (-0.6) compared with the HCTZ group (-0.6 mL/min/year; P=.4) in median total slope of eGFR change. Finally, there was no difference in the incidence of CKD between the CTD (16.5%) and HCTZ (16.8%) groups (P=.8).

In conclusion, among patients with hypertension, there was no difference in the primary outcome of CKD progression between the CTD and HCTZ groups. Similarly, the slope of eGFR progression and the incidence of CKD was similar in both groups.

Source: Ishani A, Hau C, Cushman W, Taylor A, Ferguson R, Leatherman S. Treatment with chlorthalidone vs hydrochlorothiazide and renal outcomes: the Diuretic Comparison Project (DCP). Presented at the National Kidney Foundation Spring Clinical Meetings 2024; May 14-18, 2024; Long Beach, California. doi:10.1053/j.ajkd.2024.03.004

Interim Analysis of APPLAUSE-IgAN Iptacopan Study

APPLAUSE-IgAN is a phase 3 study to determine the efficacy and safety of iptacopan versus placebo in patients with IgA nephropathy (IgAN). **Dana V. Rizk** and fellow researchers presented prespecified interim analysis (IA) results of the study during the National Kidney Foundation Spring Clinical Meetings.

The randomized, double-blind, placebo-controlled study evaluates iptacopan plus optimized supportive care in patients with biopsy-confirmed IgAN and proteinuria ≥1 g/g by urine protein-to-creatinine ratio (UPCR) from 24-hour urine collection (UPCR-24h) despite maximally tolerated renin-angiotensin system inhibitors for ≥3 months. The researchers randomized patients 1:1 to receive iptacopan 200 mg or placebo twice daily for 24 months.

At the prespecified IA, researchers evaluated 125 patients for iptacopan and 125 patients for placebo. The safety analyses included 222 patients for iptacopan and 221 for placebo. The baseline characteristics were balanced across treatment arms.

Iptacopan proved superior to placebo in reducing proteinuria (UPCR-24h) from baseline at month 9 (M9), with a reduction of 38.3% (95% CI, 26.0%-48.6%; one-sided P<.0001) versus placebo. UPCR from first morning void declined as early as week 2; the reduction from baseline at M9 with iptacopan versus placebo was 35.8% (95% CI, 22.6%-46.7%).

About twice as many patients on iptacopan reached UPCR-24h <1 g/g at M9 compared with the placebo group (marginal proportion, 42.5% [95% CI, 34.5%-50.5%] vs 21.9% [95% CI, 14.8%-29.0%], respectively). Adverse events prevented 2.7% of patients in each group from completing treatment. Otherwise, iptacopan was well tolerated with an infection rate not exceeding that of the placebo group.

The authors concluded that "APPLAUSE-IgAN demonstrated superiority of iptacopan versus placebo in proteinuria reduction at M9, with early onset and consistency of effect. Iptacopan was well tolerated with a favorable safety profile."

Source: Rizk DV, Kollins D, Papachristofi O, et al. Efficacy and safety of iptacopan in patients with IgA nephropathy (IgAN): interim analysis (IA) of the phase 3 APPLAUSE-IgAN study. Presented at the National Kidney Foundation Spring Clinical Meetings 2024; May 14-18, 2024; Long Beach, California. doi:10.1053/j.ajkd.2024.03.005

Comparison of eGFR Slopes in IgAN With Sparsentan, Irbesartan

Wu Gong and fellow researchers reported results of the PROTECT clinical trial in IgAN during the National Kidney Foundation Spring Clinical Meetings. The trial evaluated the long-term nephroprotective potential of sparsentan (SPAR) versus maximally titrated irbesartan (MT-IRB).

PROTECT compared 2-year eGFR total slopes between the SPAR and MT-IRB groups and standard of care (SoC) in the following populations with similar eligibility criteria: a real-world data setting (UK National Registry of Rare Kidney Diseases [RaDaR] patients with IgAN) and a comparable clinical trial population with physician-confirmed optimized SoC required prior to enrollment (NefigArd).

The researchers performed unanchored, matching-adjusted, indirect comparisons with matching based upon published clinical characteristics using the method of moments. They weighted patients in both groups to match key baseline characteristics of the comparator populations. Then, they calculated 2-year eGFR total slopes using random coefficients models. They used two-tailed z tests with pooled standard errors for indirect comparison.

Patients in both the MT-IRB and SPAR PROTECT groups had a significantly slower decline in kidney function compared with patients receiving SoC in the real-world setting of RaDaR and the clinical trial setting of NefigArd.

The results between clinical trials should be considered in the context of clinical practice.

Source: Gong W, Diva U, Bensink M, et al. Matching-adjusted indirect comparisons of eGFR slopes in the PROTECT study with UK RaDaR IgA nephropathy population and the control arm of NefigArd. Presented at the National Kidney Foundation Spring Clinical Meetings 2024; May 14-18, 2024; Long Beach, California. doi:10.1053/j.ajkd.2024.03.003

Utilization of Finerenone by Patients With T2D, CKD

Finerenone is a nonsteroidal mineralocorticoid receptor antagonist approved for use in adults with type 2 diabetes (T2D) and CKD to reduce the risk of sustained eGFR decline, end-stage renal disease (ESRD), cardiovascular death, nonfatal myocardial infarction, and hospitalization due to heart failure. Two years after its approval, researchers led by **Ajay Singh** studied the drug's utilization. They presented results at the National Kidney Foundation Spring Clinical Meetings.

Their observational, cross-sectional study examined patients who were prescribed finerenone between August 2021 and September 2023 and had 12 months of electronic health record activity prior to their first prescription date (index). Patient data came from practices across all 50 states and nearly 15% of US ambulatory care centers.

The study included 20,535 patients; mean age was 68 years, 44.3% were female, and 44.8% were White. Of patients with both eGFR and urine albumin-to-creatinine ratio lab results (n=4320), 71.1% had values that fell into the categories of high risk or very high risk according to Kidney Disease Improving Global Outcomes (KDIGO) standards. The percentage of patients with prescriptions for sodium-glucose cotransporter inhibitors, glucagon-like peptide-1 receptor agonists, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers was 40.5%, 29.0%, 23.7%, and 38.4%, respectively.

The proportion of patients prescribed finerenone by primary care physicians, nephrologists, endocrinologists, and cardiologists was 40.9%, 17.4%, 10.7%, and 8.8%, respectively; 82.8% received an initial dose of 10 mg. Despite being recommended by KDIGO and the American Diabetes Association, finerenone was highly underutilized, with the lowest utilization in the Midwest. The study authors believe future studies "should compare CKD in T2D patients with versus without finerenone, as well as associated outcomes."

Source: Singh A, Singh R, Du Y, et al. Utilization of nonsteroidal MRA finerenone: evaluation of real-world data in the United States, 2021-2023. Presented at the National Kidney Foundation Spring Clinical Meetings 2024; May 14-18, 2024; Long Beach, California. doi:10.1053/j.ajkd.2024.01.337

Health Care Use, Cost High for Patients With Undiagnosed CKD

Many patients do not realize they have CKD despite having laboratory values that support the diagnosis. **Rena Moon** and others studied this problem and presented results during the National Kidney Foundation Spring Clinical Meetings.

The researchers examined inpatient and outpatient discharge data from more than 1200 US hospitals to comprehend CKD status (diagnosed, undiagnosed, and at risk) and to measure the prevalence and burden of patients whose CKD was not diagnosed.

Participants were adults with an inpatient or outpatient visit during 2017-2021 with ≥1 serum creatinine (Cr) measurement and an eGFR <60 mL/min/1.73 m^2 or albuminuria (urine albumin-to-Cr ratio >30 mg/g). The researchers defined CKD stage ≥3 per KDIGO criteria: ≥2 eGFR <60 or albuminuria ≥3 months apart, or CKD-related diagnosis/procedure codes between 12 months prior to and 12 months after the index visit.

There were 2,847,086 eligible patients, 50% (n=1,422,492) of whom had CKD; 31% (n=440,749) had no diagnosis of CKD despite meeting the clinical criteria for CKD. More White patients (78% vs 72%) and female patients (63% vs 45%) were undiagnosed versus diagnosed. Most undiagnosed patients had CKD stage 3 (82%) and ≥1 comorbidity; 67% had hypertension, 46% hyperlipidemia, and 31% diabetes. This population had a high frequency of annual all-cause hospitalizations (26%), intensive care unit admissions (10%), and emergency department visits (43%). Their mean all-cause annual health care cost was $15,196 per patient.

The large proportion of patients whose CKD was undiagnosed despite having visited a medical provider points to the need for improved screening, diagnosis, and treatment. New educational and outreach materials and clinical decision support are merited.

Source: Moon R, Rosenthal N, Desai P, et al. Uncovering the burden of undiagnosed chronic kidney disease in US healthcare systems. Presented at the National Kidney Foundation Spring Clinical Meetings 2024; May 14-18, 2024; Long Beach, California. doi:10.1053/j.ajkd.2024.01.307

Cardiorenal Outcomes With SGLT2i Prescription in T1D

Sodium-glucose cotransporter-2 inhibitors (SGLT2is) have demonstrated cardiorenal benefits in individuals with CKD and type 2 diabetes. They are also approved in Europe for use in patients with type 1 diabetes (T1D) but are not yet approved for that purpose by the US Food and Drug Administration (FDA).

Mariangel Goitia and others conducted a retrospective study to determine whether SGLT2is have an association with cardiorenal benefits for patients with T1D. Their findings were presented during the National Kidney Foundation Spring Clinical Meetings.

Their study included 4114 patients with T1D seen at the Joslin Diabetes Center in Boston, Massachusetts, between January 2015 and December 2022; 39% had been prescribed an SGLT2i. Mean (SD) patient age was 44.0 (16.1) years, and duration of diabetes was 30.2 (14.2) years. The majority of subjects were White (88%), 51% were female, and 31% had CKD.

The average eGFR was 108.1 (13.8), and the median urine albumin-to-creatine ratio was 12.4 (interquartile range, 6.3-26.5). Those receiving an SGLT2i were younger (41.3 [15.8] vs 45.8 [16.0] years; $P<.001$). They also had higher eGFR (111.4 [13.9] vs 106.9 [13.7]; $P<.001$), higher serum albumin (4.21 [0.30] vs 4.16 [0.29]; $P<.01$), higher hemoglobin (13.80 [1.48] vs 13.60 [1.50]; $P=.4$), and lower diabetes duration (27.1 [12.2] vs 32.2 [15.1]; $P<.001$). HbA1c and CKD did not vary between the two groups.

The research team used multivariable logistic regression analysis to determine that albumin (odds ratio [OR], 1.64 [95% CI, 1.11-2.44]; $P=.01$), duration of T1D (OR, 0.98 [0.97-0.99]; $P<.001$]), and use of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (OR, 0.55 [0.44-0.69]; $P<.001$]) were associated with patients with T1D having a prescription for an SGLT2i.

In sum, the researcher determined that being prescribed an SGLT2i with T1D does not seem to be associated with CKD diagnosis or HbA1c control.

Source: Goitia M, Almanzar D, Rosas S. Factors associated with prescription of sodium-glucose cotransporter-2 inhibitor (SGLT2i) in individuals living with type 1 diabetes (T1D). Presented at the National Kidney Foundation Spring Clinical Meetings 2024; May 14-18, 2024; Long Beach, California. doi:10.1053/j.ajkd.2024.01.267

Does Renal Denervation Lower Nighttime BP?

Nocturnal hypertension (HTN) is associated with cardiovascular (CV) risk and is common in CKD. To help determine whether renal denervation (RDN) can lower nighttime blood pressure (BP) in patients with CKD and HTN, **Markus Schlaich** and others studied patients with uncontrolled HTN in the Global SYMPLICITY Registry (GSR) DEFINE. Their findings were presented at the National Kidney Foundation Spring Clinical Meetings.

There were 3331 patients enrolled in the study. All had uncontrolled BP and 24.2% had CKD. Those with CKD were 64 ± 12 years of age, 47.3% female, 54.9% with diabetes, and 56.9% with cardiac disease. Of those patients, 12.3% had an eGFR <30. The baseline nighttime systolic BP (NSBP) was higher for patients with CKD versus those without CKD (149 ± 23 mmHg vs 145 ± 21 mmHg; P=.0002), while they were prescribed 5.2 ± 1.7 versus 4.8 ± 1.7 (P<.0001) antihypertensive drugs, respectively.

All participants had radiofrequency RDN and were grouped by eGFR (mL/min/1.73m^2): <60 (CKD) or ≥60 (non-CKD). After 3 years of RDN, changes in NSBP were compared. NSBP declined significantly among those with CKD (-7.8 mmHg); this was similar to the non-CKD patients (-8.4 mmHg). Changes in eGFR were similar in both groups (CKD, -4.7 ± 17.4 vs non-CKD, -7.0 ± 17.0; P=.34). Daytime systolic BP, sodium, potassium, and creatinine changes were not significantly different between the CKD and non-CKD groups.

In sum, the researchers noted that, "RDN in addition to drugs may help to reduce risk of long-term CV events in this high-risk cohort."

Source: Schlaich M, Mahfoud F, Narkiewicz K, et al. Three-year nighttime blood pressure after radiofrequency renal denervation in patients with uncontrolled hypertension and chronic kidney disease. Presented at the National Kidney Foundation Spring Clinical Meetings 2024; May 14-18, 2024; Long Beach, California. doi:10.1053/j.ajkd.2024.01.431

Gastrointestinal Bleeding in CKD Stage 5, Kidney Transplant Patients

Mingyue He and other researchers studied the prevalence, etiology, interventions, and outcomes of gastrointestinal bleeding (GIB) in patients with stage 5 chronic kidney disease not on dialysis (CKD5ND), stage 5 CKD on dialysis (CKD5D), and patients who had kidney transplant (KT) versus a kidney-disease-free group (KDF). They presented results during the National Kidney Foundation Spring Clinical Meetings.

The population-based analysis included 527,640 adults with GIB from the 2019 National Inpatient Sample database. Incidence of GIB was much greater in the CKD5D group (adjusted odds ratio [aOR], 1.4; 95% CI, 1.3-1.4; P<.001) versus the others. When compared with the KDF group, patients in the CKD5ND group experienced the highest adjusted inpatient mortality (aOR, 2.3; 95% CI, 1.4-3.9; P=.001); the next highest was the CKD5D group (aOR, 1.9; 95% CI, 1.6-2.3; P<.001). Patients in the KT group had adjusted mortality comparable with the KDF group (P=.7).

The CKD5D group had endoscopy rates similar to those of KDF patients but had fewer early endoscopies (<24 hours) and more delayed endoscopies (>48 hours). CKD5D patients also had higher rates of angiograms, ventilation, vasopressor use, blood transfusion, and lengthy, expensive hospitalizations versus those in the KDF group (P<.05 for all).

Late endoscopy among CKD5D patients was associated with higher mortality rates (aOR, 1.6; 95% CI, 1.2-2.1; P=.001). Angiodysplasia was associated with increased GIB risk in CKD5ND and CKD5D patients (P<.001). The CKD5D group had more GIB attributed to ulcers and unspecified causes (P<.001), while the KT group had an increased risk of diverticular bleeding (P<.001).

Overall, despite comparable endoscopy rates, CKD5D patients had higher GIB prevalence, mortality, morbidity, and resource use. The researchers noted that further research is needed to identify barriers to endoscopy in these patients.

Source: He M, Desai S, Wang Y, Gillespie A, Friedenberg F. Gastrointestinal bleeding (GIB) in advanced chronic kidney disease and kidney transplant (KT) recipients: a national analysis. Presented at the National Kidney Foundation Spring Clinical Meetings 2024; May 14-18, 2024; Long Beach, California. doi:10.1053/j.ajkd.2024.01.272

Association of Short- and Long-term SZC Use With Hyperkalemia Hospitalization

Past research suggests that patients receiving long-term treatment with sodium zirconium cyclosilicate (SZC) experience lower rates of hyperkalemia (HK)-related hospitalizations compared with those receiving short-term SZC treatment. With funding from AstraZeneca, **Connie Rhee** and other researchers used real-world data to compare health care resource use between long-term and short-term users of SZC. Their results were presented at the National Kidney Foundation Spring Clinical Meetings.

The team used HealthVerity, a large US insurance claims database, to identify adults initiating SZC (index date) in the outpatient setting between July 2018 and December 2022. They matched patients with short-term SZC use (≤30 days) to those with long-term SZC use (>90 days) using exact and propensity score matching. There were 3133 matched patient pairs with a mean age of 64 years; 42% were female. Most patients in both cohorts (91%) had kidney disease; 30% had heart failure.

The researchers followed patients to the earliest of 6 months postindex, end of availability of data, other potassium binder use, or restarting of SZC after discontinuation. During follow-up, the investigators compared rates of a composite outcome of HK-related hospitalizations or emergency department (ED) visits and HK-related hospitalizations using generalized estimating equations.

Patients with long-term SZC use had a 40% lower rate of HK-related hospitalizations or ED visits than patients with short-term SZC use (mean [standard deviation] rates per person-year: 0.72 [1.93] vs 1.20 [4.13]) and a 36% lower rate of HK-related hospitalizations (0.55 [1.55] vs 0.87 [2.96]; both P<.001).

Source: Rhee C, et al. Hyperkalemia-related hospitalization associated with short-term vs. long-term outpatient SZC therapy: the GALVANIZE outcomes study. Presented at the National Kidney Foundation Spring Clinical Meetings 2024; May 14-18, 2024; Long Beach, California. doi:10.1053/j.ajkd.2024.01.340

2-Year Safety, Efficacy of Sparsentan for IgAN

The phase 3 PROTECT trial compared SPAR with IRB for treating adults with primary IgAN. An interim analysis at week 36 found a significant reduction in proteinuria with SPAR versus IRB (-49.8% vs -15.1%; $P<.0001$), leading to accelerated approval of SPAR by the FDA for patients at risk of rapid disease progression. Presenting at the National Kidney Foundation Spring Clinical Meetings, **Brad Rovin** and colleagues reported on 2-year safety and efficacy data from the trial.

PROTECT is a 110-week trial in adults with biopsy-proven IgAN at risk of progression to kidney failure despite optimized treatment with an angiotensin-converting enzyme inhibitor and/or angiotensin receptor blocker, urine protein excretion (UPE) ≥1.0 g/dL, and eGFR ≥30 mL/min/1.73 m^2. The double-blind, randomized, parallel-group trial compared SPAR 400 mg/dL (n=202) with maximum labeled IRB 300 mg/dL (n=202).

Rovin's team investigated complete remission of proteinuria (CR; UPE <0.3 g/d), absolute change in eGFR, rate of eGFR change (slope), and BP outcomes. Results were more positive for SPAR; with it, patients reached CR earlier and more often (31%) versus IRB (11%).

The absolute change in eGFR from baseline to week 110 with SPAR compared with IRB (-5.8 vs -9.5 mL/min/1.73 m^2) demonstrated long-term kidney preservation with SPAR (difference, +3.7 mL/min/1.73 m^2). Regardless of early treatment discontinuations or disease severity, the eGFR slope favored SPAR. Furthermore, SPAR was associated with minimal changes in BP and was well tolerated.

The researchers concluded that SPAR demonstrated clinically meaningful treatment benefits for preservation of kidney function compared with IRB over a 2-year period. The safety profile of SPAR supported its long-term use.

Source: Rovin B, Barratt J, Murphy E, Geletka R, Perkovic V. Sparsentan (SPAR) shows clinically meaningful treatment effects vs irbesartan (IRB) in patients with IgA nephropathy (IgAN) in the phase 3 PROTECT trial. Presented at the National Kidney Foundation Spring Clinical Meetings 2024; May 14-18, 2024; Long Beach, California. doi:10.1053/j.ajkd.2024.01.374

For more highlights from the NKF event, including exclusive interviews, go to nephtimes.com.

Higher Serum Bicarbonate Concentrations, Slower CKD Progression With Metabolic Acidosis

Oral alkali therapy can raise serum bicarbonate concentrations and has been associated with slowing CKD progression. Researchers led by **Bhupinder Singh** performed a post hoc analysis from the phase 3 VALOR-CKD trial to study the relationship between serum bicarbonate concentrations and CKD progression. They reported results at the National Kidney Foundation Spring Clinical Meetings.

VALOR-CKD was conducted to assess the safety and efficacy of veverimer, a nonabsorbed polymer that removes hydrochloric acid from the gastrointestinal tract. The randomized, double-blind, placebo-controlled trial included 1480 patients who had CKD (eGFR, 20-40 mL/min/1.73 m^2) and metabolic acidosis (serum bicarbonate, 12-20 mEq/L). Following single-blind active treatment for up to 8.0 weeks, randomized patient groups received either veverimer or placebo and were followed for a median of 24.5 months.

VALOR-CKD did not find a slowdown of CKD progression (defined as time to first kidney composite end point [KCE] of a confirmed reduction in eGFR ≥40%, end-stage kidney disease requiring dialysis or transplantation, or death due to kidney disease).

In their post hoc analysis, Singh's team used a Cox proportional hazards model to assess the relationships among three levels of average serum bicarbonate concentrations reached throughout the randomized treatment period (<20, 20 to <22, and ≥22 mEq/L) and the KCE. They found that patients with average serum bicarbonate concentrations 20 to <22 and ≥22 mEq/L had a reduced risk of KCE–HR, 0.67 (95% CI, 0.49-0.90); $P<.0078$ and HR, 0.50 (95% CI, 0.37-0.67); $P<.0001$, respectively–versus those with concentrations <20 mEq/L. This was true regardless of whether patients were receiving veverimer or placebo.

The researchers asserted that their results support that higher serum bicarbonate concentrations in patients with CKD and metabolic acidosis are associated with slower CKD progression.

Source: Singh B, Tangri N, Bushinsky D, et al. Serum bicarbonate concentrations and CKD progression in patients with metabolic acidosis: evidence from VALOR-CKD. Poster #352. Presented at the National Kidney Foundation Spring Clinical Meetings 2024; May 14-18, 2024; Long Beach, California. doi:10.1053/j.ajkd.2024.01.351

Markers for Lupus Nephritis

Hemapriya Gopal Reddy and others from Ascension St. John in Detroit, Michigan, described a case of diffuse class 4 lupus nephritis with normal complement levels at the National Kidney Foundation Spring Clinical Meetings.

A 35-year-old female presented with lower extremity swelling that was gradually worsening. The patient's medical history included significant hypertension, diabetes, hyperlipidemia, and lupus nephritis treated with cyclophosphamide. She was receiving a maintenance dose of mycophenolate mofetil 1000 mg twice a day and prednisone for the previous 6 months.

The patient's eVitals were stable, and a physical examination demonstrated lower extremity edema. Her laboratory results were 142.00 sodium, 4.70 potassium, 22.00 bicarbonate, 20.00 BUN, and 0.74 creatinine. Her hemoglobin was 12.6, white blood cell count 5.8, and platelets 234.0.

Low total complement hemolytic activity and decreased C3 and C4 levels are characteristic of lupus nephritis. This patient's complements were normal: C3, 119 and C4, 28. ANA was positive, and C-ANCA and P-ANCA were negative (proteinase-3 antibody <0.2, myeloperoxidase antibody <0.2). Urinalysis showed protein of 500.0 mg/dl and a urine protein-to-creatinine ratio of 3.6 g/g.

A biopsy found widespread endocapillary hypercellularity and cellular and fibrocellular crescents in 6/25 glomeruli. Immunofluorescence revealed granular deposits of C1q, C3, IgA, IgG, and IgM along the capillary walls in the mesangium. The biopsy indicated diffuse class 4 lupus nephritis. The patient was given methylprednisolone 500 mg intravenously for 3 days and rituximab 1 g twice daily; she also continued mycophenolate mofetil 1500 mg twice daily. After beginning therapy, she showed 0.5 g/g improvement in proteinuria.

Decreased complements are considered a reliable marker for disease activity in lupus nephritis. However, as this case shows, a patient may present with normal creatinine and normal complements but still have highly active disease requiring therapy. Clinicians should be aware of this and readily conduct a biopsy of patients with lupus even if they are seemingly stable.

Source: Reddy HG, Topf JM, Henderson H. A case of diffuse class 4 lupus nephritis with normal complement levels. Presented at the National Kidney Foundation Spring Clinical Meetings 2024; May 14-18, 2024; Long Beach, California. doi:10.1053/j.ajkd.2024.01.375

Awards and Honors

Health care professionals who have made significant contributions to the field of kidney disease were honored at the National Kidney Foundation (NKF) 2024 Spring Clinical Meetings.

Martin R. Pollak, MD

Martin R. Pollak, MD, accepted the David M. Hume Award, the highest honor given to a distinguished scientist-clinician in the field of kidney and urologic diseases. He is a professor of medicine at Harvard Medical School and chief of nephrology at Beth Israel Deaconess Medical Center. Dr. Pollak's research focus is to understand the genetic basis of kidney disease. He is a member of the American Society for Clinical Investigation, the Association of American Physicians, and the National Academy of Sciences.

David M. Charytan, MD, MSc

The J. Michael Lazarus Distinguished Award went to **David M. Charytan, MD, MSc.** The lectureship recognizes those whose research has yielded novel insights related to renal replacement therapy. Dr. Charytan is director of the nephrology division and the Norman S. Wikler Professor of Medicine at New York University (NYU) Langone Medical Center. He was a founding steering committee member of the National Institutes of Health Hemodialysis Novel Therapies Consortium. His research focus is chronic dialysis, diabetic kidney disease, and cardiovascular disease in the setting of chronic kidney disease (CKD).

Mary B. Leonard, MD, MSCE

Mary B. Leonard, MD, MSCE, received the Donald W. Seldin Award in recognition of excellence in clinical nephrology. She is the Arline and Pete Harman Professor and chair of the Department of Pediatrics at Stanford University, director of the Stanford Maternal and Child Health Research Institute, and physician-in-chief of Lucile Packard Children's Hospital. As a department chair at Stanford, she established an Office of Child Health Equity to address health disparities for children with chronic diseases, including CKD. She previously served as president of the American Pediatric Society.

Morgan Grams, MD, PhD

Morgan Grams, MD, PhD, was honored with the Garabed Eknoyan Award. Dr. Grams is the Susan and Morris Mark Professor of Medicine and Population Health in the Department of Medicine at NYU and co-director of NYU's Division of Precision Medicine. She also serves as co-chair of the Kidney Disease Improving Global Outcomes organization. Dr. Grams co-leads the global Chronic Kidney Disease Prognosis Consortium and maintains active research programs in multiomics of kidney disease as well as pharmacoepidemiology in CKD.

Suzanne Watnick, MD, FASN

The Shaul G. Massry Distinguished Lecture Award was presented to **Suzanne Watnick, MD, FASN.** Dr. Watnick is a professor of medicine at the University of Washington in Seattle and a nephrologist at the Puget Sound Veterans Administration Medical Center. Previously, she was chief medical officer at Northwest Kidney Centers in Seattle, the world's first dialysis organization; primary liaison for research operations between the Kidney Research Institute (KRI) and Northwest Kidney Centers; and nephrology program director at Oregon Health & Science University.

Kathy Schiro Harvey, MS, RDN, CSR

Kathy Schiro Harvey, MS, RDN, CSR, received the Joel D. Kopple Award for contributions in renal nutrition. Recently retired, she was director of nutrition for Puget Sound Kidney Centers (PSKC) in Snohomish County, Washington. She serves on the PSKC Foundation board. Harvey was instrumental in creating the Washington State Council on Renal Nutrition and the Northwest Renal Dietitians organization. She served on the Kidney Disease Outcomes Quality Initiative Chronic Kidney Disease Workgroup and the Centers for Medicare & Medicaid Services Technical Expert Panel on mineral bone health.

Robert A. Montgomery, MD, DPhil, FACS

The Excellence in Kidney Transplantation Award was given to **Robert A. Montgomery, MD, DPhil, FACS.** Dr. Montgomery is chair and professor of surgery at NYU Langone Health and the director of the NYU Langone Transplant Institute. He previously served as chief of transplant surgery and director of the Comprehensive Transplant Center at Johns Hopkins University. Dr. Montgomery was part of the team that developed the laparoscopic procedure for live kidney donation, now the standard throughout the world.

Sankar Niranjan, MD, FASN

Sankar Niranjan, MD, FASN, received the Medical Advisory Board Distinguished Service Award for his outstanding educational activities and community service to advance the NKF's mission at a local level. Dr. Niranjan is an attending physician and nephrologist at St. Francis Hospital and Medical Center in Hartford, Connecticut, and a community-based faculty member at the University of Connecticut School of Medicine in Farmington. He has participated in NKF's Kidney Early Evaluation Program in Connecticut and facilitated screenings at inner-city community events and minority places of worship.

Lisa Koester, ANP, CS, CNN-NP, MSN

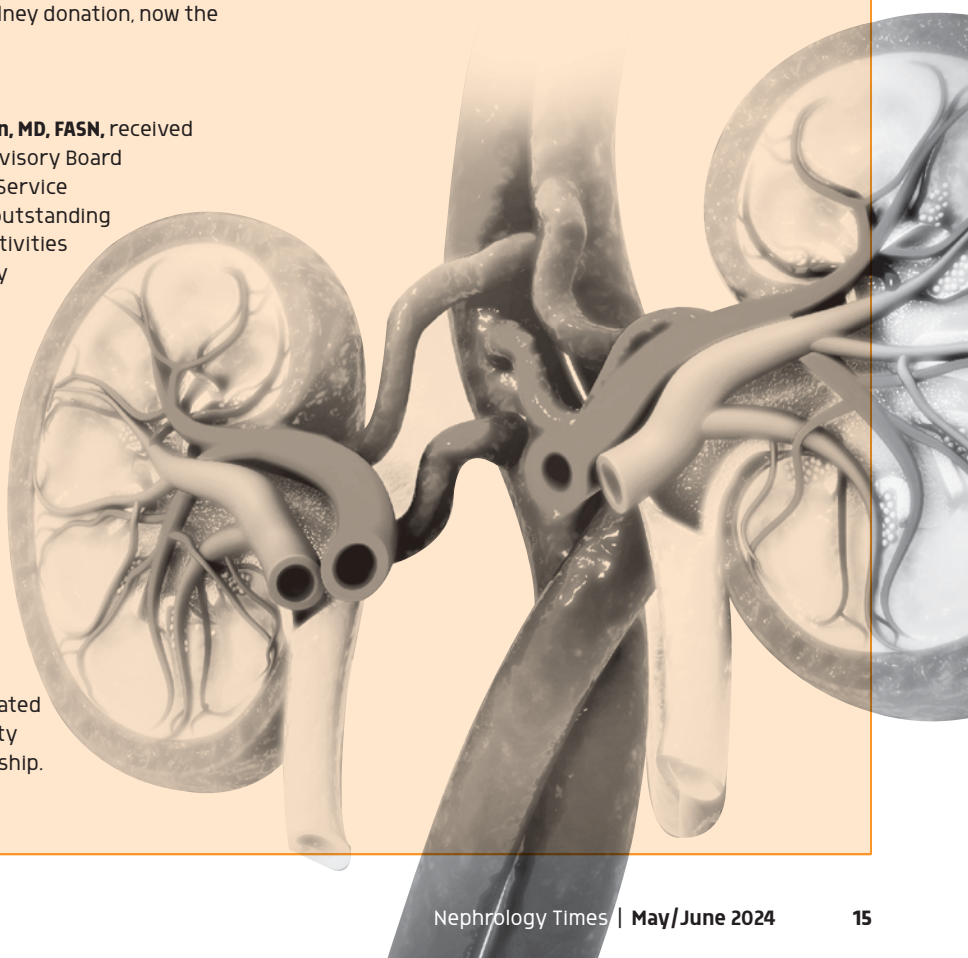
This year's recipient of the Carol Mattix Award, named for a home dialysis training nurse who worked tirelessly to improve patients' lives, was **Lisa Koester, ANP, CS, CNN-NP, MSN.** Koester started as a dialysis nurse in the 1990s and has held various roles related to dialysis. After receiving a master's degree in nursing and an adult nurse practitioner certification, she joined Washington University School of Medicine's renal division as a renal nurse practitioner, where she has worked for 24 years.

Glenda V. Roberts

Glenda V. Roberts received the Celeste Lee Award honoring her patient activism. In 2018, she joined the University of Washington Center for Dialysis Innovation and the KRI as director of external relations and patient engagement. Her role expanded to include chief operations and strategy officer for the university's Justice, Equity, Diversity, and Inclusion Center for Transformative Research. She was part of the NKF-American Society of Nephrology Taskforce Reassessing the Use of Race in Diagnosing Kidney Disease and has participated in many other kidney-related initiatives.

Suma Nair, PhD, MS, RD

Suma Nair, PhD, MS, RD, was the recipient of the Public Service Award. Dr. Nair is associate administrator for the Health Systems Bureau in the Health Resources and Services Administration (HRSA). She leads a portfolio of programs to improve access to care and strengthen public health and health care systems by increasing access to organ and blood stem cell donation and transplantation. Previously, she led the Office of Quality Improvement in the HRSA's Bureau of Primary Health Care.



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Comparing Palatability of Potassium Binders for Hyperkalemia Treatment

Guidelines for patients with chronic kidney disease (CKD) recommend treatment with renin–angiotensin–aldosterone system inhibitors (RAASi), but this regimen puts patients at high risk of hyperkalemia. However, discontinuing or down-titrating RAASi denies patients with CKD clinical benefits and increases their risk of cardiovascular events, hospitalization, and mortality.

Sodium and calcium polystyrene sulfonates (S/CPS) are traditional potassium (K+) binders used to treat hyperkalemia, but they are poorly tolerated and widely considered unpalatable, which can affect long-term adherence. Sodium zirconium cyclosilicate (SZC) and calcium patiromer sorbitex (patiromer) are recently approved K+ binders that are reported to be well tolerated in patients with hyperkalemia; they can also allow patients with CKD to maintain or increase their RAASi dose. However, published evidence of their palatability was lacking, so **David C. Wheeler, MB ChB, MD, FRCP,** and colleagues sought to determine the palatability of SZC, patiromer, and S/CPS in participants with CKD and hyperkalemia with the APPETIZE (NCT04566653) study. Results were reported in *BMJ Open* [doi:10.1136/bmjopen-2023-074954].

TAKEAWAY POINTS

- Treating chronic kidney disease with renin-angiotensin-aldosterone system inhibitors puts patients at high risk for hyperkalemia. Sodium and calcium polystyrene sulfonates (S/CPS) can treat hyperkalemia but are considered unpalatable, making adherence challenging.
- Researchers set out to uncover whether sodium zirconium cyclosilicate (SZC) and calcium patiromer sorbitex (patiromer) are more palatable alternatives to S/CPS.
- Their results found that SZC was more palatable than S/CPS and comparable with patiromer. The findings suggest that prescribing these newer, more palatable potassium binders for hyperkalemia may improve adherence.

The study took place in 17 centers across the United States, Canada, and a region of the European Union (EU) that included France, Spain, and Italy. Participants were aged 18 years and older with CKD (two estimated glomerular filtration rate measurements <60 mL/min/1.73 m^2, recorded at least 90 days apart) and hyperkalemia (serum K+ >5 mmol/L). Between October 23, 2020, and January 12, 2022, 234 participants were screened for eligibility and enrolled; 87 were excluded. The study randomized 147 participants; 144 from the United States (n=58), Canada (n=24), and the EU (n=62) completed the study and tasted each K+ binder. Of those 144, mean age was 66 years, 71% were male, and 53% were dialysis-dependent.

Eligible participants tasted the K+ binders in a randomized sequence. After tasting each product, they completed a questionnaire evaluating four palatability factors: taste, texture, smell, and mouthfeel; they also shared their willingness to take the product. Participants rated how much they liked or disliked each factor on a scale of zero to 10 (rational evaluation). Scores for each attribute were combined to obtain an overall rational palatability composite score (0-40 per product). Participants then indicated how they felt about each factor using AdSAM, a nonverbal, visual measure of emotional response.

In the rational evaluation, the overall palatability of SZC and patiromer was more appealing than that of S/CPS in each region. Among US participants, SZC performed much better than S/CPS (least squares [LS] mean [95% CI], 25.0 [22.7-27.2] vs 18.8 [16.6-21.1]; *P*<.001). Among participants from Canada, SZC performed much better than S/CPS (LS mean [95% CI], 27.2 [22.5-32.0] vs 15.8 [11.1-20.6]; *P*<.001). Among participants from the EU, SZC performed much better than S/CPS (LS mean [95% CI], 22.5 [19.9-25.1] vs 18.7 [16.1-21.3]; *P*=.017). There was no significant difference between SZC and patiromer in any of the geographic regions.

The emotional responses of participants in each region indicated a greater willingness to take SZC or patiromer once daily to manage K+ levels than S/CPS. Among US participants, the overall palatability of SZC was much more appealing than that of S/CPS (LS mean, 23.2 vs 18.9; nominal *P*<.001); the overall palatability of patiromer was more appealing than that of S/CPS (LS mean, 22.9 vs 18.9; nominal *P*<.001) and more engaging (LS mean, 17.7 vs 15.4; nominal *P*=.026. Participants from Canada found the overall palatability of SZC much more appealing than that of S/CPS (LS mean, 24.6 vs 16.4; nominal *P*≤.002); they found the overall palatability of patiromer to be much more appealing than that of S/CPS (LS mean, 22.7 vs 16.4; nominal *P*≤.002). Those from the EU found the overall palatability of SZC much more appealing than that of S/CPS (LS mean, 22.2 vs 18.9; nominal *P*=.013) and much more empowering (LS mean, 23.0 vs 20.0; nominal *P*=.018). Participants also found the overall palatability of patiromer more appealing than that of S/CPS (LS mean, 22.0 vs 18.9; nominal *P*=.017) and more empowering (LS mean, 23.6 vs 20.0; nominal *P*=.005).

There were several limitations to the study. Participants were blinded to study treatment, but site and sponsor personnel were not, and it is possible that this affected participant blinding. Participant numbers were reduced due to the early end of recruitment in Canada and France; the latter required merging data from France, Spain, and Italy to create one EU region. The researchers combined SPS and CPS into a single comparator group (S/CPS) for several reasons, which limited assessment of the individual products. The overall ranking of the products is not supported by statistical analyses and was limited by missing data. No product was ingested, which could have created new palatability experiences.

This exploratory study seems to be the first to use AdSAM to evaluate emotional responses in participants receiving different pharmacotherapies. Findings regarding the level of engagement in the emotional response rely on the level of appeal; high appeal and high engagement scores show a strong perceived benefit and strong positive motivation, while low appeal and high engagement scores indicate strong negative or agitated feelings. Therefore, engagement scores should be interpreted in terms of level of passiveness (lower scores) versus level of activation or intensity (higher scores). Finally, placing rational evaluation questions before the AdSAM measure can influence the emotional response because the unbiased emotional response is not captured prior to cognitive evaluation.

"Our results suggest that participants had an overall preference for SZC and patiromer over S/CPS, and that this preference is being driven by palatability," the authors concluded. "The palatability of SZC was superior to that of S/CPS and comparable [with] that of patiromer. These results offer promise that adherence to long-term treatment for hyperkalemia may be improved in patients prescribed newer, more palatable K+ binders." ■

SGLT-2is Reduce Mortality Risk in Patients With Type 2 Diabetes, AKD

Type 2 diabetes, acute kidney injury (AKI), and chronic kidney disease (CKD) are closely entwined. Type 2 diabetes is a risk factor for AKI, while both type 2 diabetes and AKI are risk factors for CKD. Recently, it has come to light that acute kidney disease (AKD) is a transitional stage between AKI and CKD, lasting 7 to 90 days after an incidence of AKI. Individuals with AKD have a higher risk of mortality, end-stage kidney disease, incident CKD, and progressive CKD, making it clear that managing AKD is crucial to preventing additional kidney damage and negative outcomes.

Sodium-glucose cotransport protein 2 inhibitors (SGLT-2is) have shown promise in terms of kidney-related and cardiovascular outcomes. They are a new class of oral hypoglycemic agents that inhibit the reabsorption of glucose and sodium in the kidneys, which results in reduced blood pressure, intraglomerular pressure, and albuminuria. In clinical trials, SGLT-2is were associated with slowing the progression of CKD, improving kidney function, and reducing the risk of death in patients with type 2 diabetes. Clinical trials also found that SGLT-2is may be associated with a lower risk of AKI in patients with type 2 diabetes.

To better understand the associations of SGLT-2is with mortality, major adverse kidney events (MAKEs), and major adverse cardiovascular events (MACEs) in patients with type 2 diabetes and AKD, a team of researchers led by **Heng-Chih Pan, MD,** conducted a longitudinal study using data from the global TriNetX database spanning from September 30, 2002, to September 30, 2022. Results were reported in *JAMA Network Open* [doi:10.1001/jamanetworkopen.2023.50050]. The researchers used propensity score matching (PSM) to select a cohort of patients, and follow-up was conducted with a maximum duration of 5 years or until the occurrence of an outcome or death. The primary outcome was mortality; secondary outcomes were MAKEs (redialysis, dialysis dependence, or mortality) and MACEs (cerebral infarction, hemorrhagic stroke, acute myocardial infarction, cardiogenic shock, or mortality).

The total cohort consisted of 230,366 patients with AKD with a mean (SD) age of 67.1 (16.4) years; 119,253 (51.8%) were men and 111,113 (48.2%) were women. Researchers identified 5319 individuals (2.3%) who were SGLT-2i users and did not undergo dialysis or die within 3 months of discharge. They also identified 225,047 patients who had type 2 diabetes and did not use SGLT-2is. The median follow-up duration for the full cohort was 2.3 (interquartile range, 1.2-3.5) years, with the 90th percentile extending to 4.3 years.

Using PSM, the researchers identified 5317 SGLT-2i users and 5317 nonusers as controls for analysis; mean (SD) age was 63.8 (12.3) years in the SGLT-2i group and 67.4 (15.5) years in the control group. The SGLT-2i group included 3181 (59.8%) men and 2136 (40.2%) women; most patients were White (3493 [65.7%]). The control group included 3175 (59.7%) men and 2142 (40.3%) women, most of whom were White (3496 [65.8%]). After PSM, the two groups had small and well-matched differences in age, sex, race and ethnicity, comorbidities, medication use, and most other lab results. The mean (SD) estimated glomerular filtration rates in the SGLT-2i and control groups were 76.9 (32.9) and 74.2 (40.5) mL/min/1.73 m^2, respectively. The SGLT-2i group had a greater percentage of angiotensin-converting enzyme inhibitor and angiotensin receptor blocker users compared with the control group.

After withdrawal from dialysis for AKI, the overall incidence rate was 13.9% for 5-year mortality, 15.3% for MAKEs, and 21.0% for MACEs. The 5-year all-cause mortality rate was 9.0% (481) in the SGLT-2i group and 18.7% (994) in the control group. Use of SGLT-2is was associated with a lower mortality rate (adjusted hazard ratio [aHR], 0.69; 95% CI, 0.62-0.77). Additionally, researchers noted a lower risk of MAKEs in the SGLT-2i group (504 [9.5%]) compared with the control group (1119 [21.0%]; aHR, 0.62; 95% CI, 0.56-0.69).

The baseline characteristics of the patients selected for MACE analysis were comparable with those observed in the primary analysis. In the SGLT-2i group, researchers observed a lower risk of MACEs (233 of 1732 [13.5%]) compared with the control group (690 of 2670 [25.8%]; aHR, 0.75; 95% CI, 0.65-0.88). These results further support the effectiveness of SGLT-2is in reducing the occurrence of MACEs.

Furthermore, researchers performed a subgroup analysis based on various comorbidities, such as advanced CKD and hypertension, and medication use. The use of SGLT-2is was associated with a lower risk of mortality, regardless of whether insulin or renin-angiotensin-aldosterone system (RAAS) blockers or diuretics were used. The association between SGLT-2i use and a lower risk of MAKEs was observed consistently among patients with advanced CKD and among those who used RAAS blockers or diuretics, although the association was more pronounced in patients without hypertension and those who were not receiving insulin or other oral hypoglycemic agents (OHAs). Researchers observed an association between a lower risk of MACEs and the use of SGLT-2is consistently among patients with hypertension and those using RAAS blockers, and particularly among those with advanced CKD and those who were not receiving insulin or other OHAs or diuretics.

The authors noted several limitations to their study. Most participants were White, potentially limiting generalizability of the results. Information bias may have occurred due to significant differences in comorbidities and medication use between the SGLT-2i users and nonusers. The use of diagnostic codes to classify diseases may have led to ascertainment bias by causing the researchers to underestimate the presence of mild conditions or those occurring outside the medical system. Misclassification bias and residual confounding could be present. The limitations of TriNetX's tools curbed the use of competing risk models, potentially biasing results. This was a retrospective study lacking raw data, which hampered a time-varying analysis. Cases with incomplete outcome data were excluded, which could have led to selection bias, and the dataset did not include detailed causes for redialysis or death.

"In this cohort study, we provide compelling clinical evidence supporting the associations of SGLT-2is in reducing the risk of mortality among patients with type 2 diabetes and AKD during a median follow-up period of 2.3 years," the authors summarized. "Use of SGLT-2is was associated with a lower risk of MAKEs and MACEs compared with nonuse. These findings highlight the potential benefit of SGLT-2is and suggest that clinicians should consider incorporating them into the management of type 2 diabetes with AKD." ■

TAKEAWAY POINTS

- Researchers sought to determine whether SGLT-2is are associated with mortality, major adverse kidney events (MAKEs), and major adverse cardiovascular events (MACEs) in patients with type 2 diabetes and acute kidney disease (AKD).
- In a cohort study of 230,366 patients, SGLT-2i use in those with type 2 diabetes and AKD was associated with reduced mortality, MAKEs, and MACEs compared with nonuse.
- The results highlight the potential benefits of SGLT-2i use in patient care after AKI. The authors believe clinicians should consider adding them to the management of type 2 diabetes with AKD.

Bariatric Surgery as a Path to Transplant for Obese Patients With ESRD

The age-adjusted prevalence of obesity among US adults was 42.4% in 2017 and 2018. Obesity is associated with outcomes and therapeutic options for patients with end-stage renal disease (ESRD). Elevated body mass index (BMI) correlates with several elements of kidney health; it is associated with the presence and emergence of proteinuria in people who do not have a kidney condition, reduced estimated glomerular filtration rate (GFR) and an accelerated decrease in GFR over time, and faster progression of chronic kidney disease (CKD).

However, obesity frequently poses a barrier for patients with ESRD in need of a kidney transplant. Obesity is often considered a contraindication for candidacy based on concerns about compliance, postoperative complications, worsening of comorbidities, and overall patient and graft outcomes.

The national kidney transplantation waiting list illustrates this issue. Data from Scientific Registry of Transplant Recipients records between 2015 and 2020 show that approximately 12% of transplant recipients were categorized as having class III obesity. However, 14% of transplant centers have fewer than 5% of such recipients and just 11% of centers exceed 20%. Moreover, there is a steep decline on the waiting list in patients with a BMI above 40.

To address this issue, **Shauna Levy, MD, FACS,** and colleagues at Tulane University School of Medicine designed a program in which transplant and metabolic bariatric surgery (MBS) teams collaborated to allow obese patients with ESRD to have weight-loss surgery before obtaining a kidney transplant. Their prospective cohort study followed the outcomes of patients referred to the program. The results were published in the *Journal of the American College of Surgeons* [2024;238(4):561-572].

From January 2019 to June 2023, the transplant team referred 183 patients with ESRD to the bariatric team; 115 dropped out. Another 64 (56%) could not complete the workup, 24 (21%) had insurance problems, five (4%) had medical issues that prevented MBS and transplant surgery, and 23 (20%) declined MBS at the start. In total, 36 patients underwent MBS. Most (55.6%) patients had Roux-en-Y gastric bypass (RYGB); 44.4% had sleeve gastrectomy (SG). Patients with a BMI higher than 45 were selected for RYGB due to a greater need for weight loss.

> Obesity is often considered a contraindication for candidacy based on concerns about compliance, postoperative complications, worsening of comorbidities, and overall patient and graft outcomes.

Mean age was 42.9 years (SD: 9.0); there were no significant age differences between the RYGB and SG groups (P=.398). Across the study, 66.7% of participants were female, but gender differences were not statistically significant (P=.406). Of the RYGB group, 75.0% (15) were female; of the SG group, 56.2% (9) were female. In the RYGB group, 60% (12) identified as Black and 40% (8) identified as White.

The primary outcomes were weight loss and improvement in comorbidities relevant to eligibility for transplant. Patients in both the RYGB and SG groups saw a significant decline in BMI. Those in the RYGB group experienced a constant reduction in BMI over 12 months, while the SG group's stabilized after about 6 months. HbA1c levels also improved, decreasing from 5.4 (interquartile range [IQR], 5.3-6.2) to 4.5 (IQR, 4.4-5.0) for the RYGB group and from 7.0 (IQR, 6.0-8.6) to 5.4 (IQR, 5.2-5.8) for the SG group. Changes were statistically significant for both groups (P=.038 and P=.061, respectively). Both RYGB and SG surgeries helped reduce blood pressure, and there was a median reduction in hypertension medications needed, from two (range, 2-4) presurgery to one (range, 1-3) postsurgery. The RYGB group required fewer medications (median, 1.0; IQR, 0.5-1.5) compared with the SG group (median, 2.0; IQR, 1.0-3.0) postsurgery (P=.189).

The mean starting BMI for all referrals was 46.4 kg/m^2, and it was 33.9 kg/m^2 at the time of transplant. Regarding transplant surgery, 29 patients were referred following MBS. Four resigned, two were found to be medically unsuitable for transplant, one had an insurance change requiring transplant at a different location, and one received a transplant out of state. Ten had deceased donor transplant, and the remainder are wait-listed.

The mean follow-up after transplant was 15.1 (1.0-36.0) months. During that period, there were no issues of organ rejection or infection and no patient or graft losses. All transplants are currently functioning, with a median creatinine level of 1.5 (1.2-1.6) mg/dL (GFR, 46 [36.3-71.0]).

There were a few limitations to the study. It is difficult to measure compliance after MBS and transplant. Many patients did not complete the protocol, likely due to unpreparedness. The study began before the widespread use of glucagon-like peptide-1 agonist drugs for weight loss, which offer an alternative to MBS.

In summary, the authors view collaboration between bariatric surgery and transplant teams as a pathway to transplant for morbidly obese patients with ESRD who would otherwise be ineligible. They wrote, "With increasing prevalences of obesity and ESRD in this country, we see this as a growing issue. A combined program helps alleviate disparities in health care and transplant access, especially for [Black individuals] and communities with socioeconomic barriers, who are more affected by obesity disease. ESRD patients may have unique complications post-MBS that bear further studies. MBS allows for optimization of patients' comorbidities, which allows for potential better long-term outcomes post-transplant." ■

TAKEAWAY POINTS

- High body mass index is a common reason that patients with end-stage renal disease are denied a kidney transplant. Metabolic bariatric surgery (MBS) is not widely available to these patients.
- A group at Tulane University School of Medicine created a program in which transplant and MBS teams collaborated to allow obese patients to undergo bariatric surgery before receiving a kidney transplant.
- Thirty-six patients underwent MBS and 10 had transplantation. They experienced a decrease in hypertension medications and better HbA1C levels. The collaborative approach seems to offer a path to transplant for patients with obesity.

Segregation Affects Living Donor Kidney Transplantation Access

With shorter wait times and better patient and graft survival, living donor kidney transplantation (LDKT) is the preferred method of kidney replacement therapy. However, the rate of LDKT is 4.3 times lower for Black patients than White patients, although Black individuals have a 3.8 times higher rate of end-stage kidney disease (ESKD). It is clear structural racism is at play, but examinations into the specifics of these disparities are lacking.

A group of researchers led by **Yiting Li, MPH,** looked at the problem from the perspective of segregation based on individuals' race or ethnicity. In a national cohort study of transplant candidates, the team researched the association between a candidate's access to LDKT and their residential neighborhood segregation and their transplant center's neighborhood segregation. The study results appear in *JAMA Internal Medicine* [2024;184(4):402-413].

> Both Black (aHR, 0.94; 95% CI, 0.89-1.00) and White (aHR, 0.92; 95% CI, 0.88-0.97) candidates listed at transplant centers in high-segregation neighborhoods had lower access to LDKT compared with their counterparts listed at centers in low-segregation neighborhoods (*P*=.64).

The study population included adults who were candidates for first-time kidney transplant (KT), including nonlisted patients who had LDKT between 1995 and 2021. These individuals were categorized by race and ethnicity as either non-Hispanic/Latino Black (Black) or non-Hispanic White (White). The categories were based on variables provided on Organ Procurement and Transplantation Network forms, and researchers obtained data from the Scientific Registry of Transplant Recipients. Race-specific population counts at the zip code level came from American Community Survey 5-year estimates from the US Census Bureau.

Researchers used the Theil H method to measure segregation tertiles in zip code tabulation areas. They used the Kaplan-Meier method to estimate the unadjusted aggregate incidence of the first LDKT by candidate race and tertiles of their neighborhood of residence and the transplant center's neighborhood segregation. Then they used the cause-specific hazards models to determine the likelihood of LDKT by tertiles of residential neighborhood and transplant center neighborhood segregation.

The researchers calculated the association of the residential neighborhoods' and transplant centers' neighborhood segregation by race and tested for trends over time. They confirmed the proportional hazards assumption using complementary log-log plots and Schoenfeld residuals, then looked at within-group differences in high-segregation neighborhoods, comparing mainly White neighborhoods (≥70% White) with multiracial neighborhoods (31%-69% White) and mostly minority neighborhoods (≤30% White), testing whether these associations differed by the patient's race. To validate the findings, the researchers used the Index of Concentration at Extremes–Race-Income measure as an alternative for segregation. Then they determined the strength of the estimates through various sensitivity analyses.

Among 162,587 candidates for KT, the mean (SD) age was 51.6 (13.2) years; 65,141 (40.1%) were female; and 80,023 (49.2%) were Black. Black transplant candidates residing in high-segregation neighborhoods had 10% (adjusted hazard ratio [aHR], 0.90; 95% CI, 0.84-0.97) lower access to LDKT compared with Black candidates living in low-segregation neighborhoods. This association was not present among White candidates (*P*=.01). High-segregation residential neighborhoods had a higher proportion of Black candidates relative to low-segregation residential neighborhoods. High-segregation residential neighborhoods had 69.2% Black candidates; medium-segregation neighborhoods, 47.2%; and low-segregation neighborhoods, 30.2% (*P*<.001).

Both Black (aHR, 0.94; 95% CI, 0.89-1.00) and White (aHR, 0.92; 95% CI, 0.88-0.97) patients at transplant centers in high-segregation neighborhoods had lower access to LDKT than those in low-segregation neighborhoods (*P*=.64). Of candidates listed at transplant centers in high-segregation neighborhoods, a greater proportion were Black (high-segregation, 62.7%; medium-segregation, 45.8%; low-segregation, 37.5%; *P*<.001).

In high-segregation transplant center neighborhoods, candidates listed at centers in mostly minority neighborhoods had 17% lower access to LDKT compared with candidates listed at centers in mostly White neighborhoods (aHR, 0.83; 95% CI, 0.75-0.92). Black candidates living in or listed at transplant centers in mostly minority neighborhoods had a 64% lower likelihood of LDKT compared with White candidates living in or listed at transplant centers located in majority White neighborhoods.

Limitations of the study included using zip codes, which may include diverse neighborhoods, as proxies for neighborhoods. This could result in spatial misclassification and modifiable areal unit problems that could cause systematic biases in the researchers' analysis. In addition, some race and ethnicity variables from the national registry were clinician-reported, which could result in misclassification bias. Lastly, using aggregated demographic information to define segregation may not completely capture the multidimensional aspects of structural racism in a neighborhood; future studies should consider other ways to measure structural racism.

"This national cohort study highlights the considerable role of racial and ethnic segregation in both the candidate's residential neighborhood and the transplant center's neighborhood in shaping access to LDKT," the authors said. They concluded that, "To promote equitable access, studies should assess targeted interventions (eg, community outreach clinics) to improve support for potential candidates and donors and ultimately mitigate the effects of segregation." ■

TAKEAWAY POINTS

- Researchers examined racial and ethnic segregation in residential and transplant center neighborhoods and its relationship to access to LDKT.
- In the cohort study of 162,587 transplant candidates, Black candidates living in or utilizing a transplant center in a high-segregation neighborhood had 10% and 6% lower access to living donor kidney transplant (LDKT), respectively, compared with Black candidates in low-segregation neighborhoods.
- Segregation in residential and transplant center neighborhoods could be a key driver of racial inequalities in LDKT access. Determining appropriate interventions is critical.

Major Adverse Kidney Events in Youth on CKRT

Because children, adolescents, and young adults with critical illness have a high risk of developing acute kidney injury (AKI) and disorders of fluid balance, they are increasingly treated with continuous kidney replacement therapy (CKRT). However, little has been reported about longer-term outcomes for this patient population, such as persistent kidney dysfunction, continued need for dialysis, or death.

To address this knowledge gap, **Dana Y. Fuhrman, DO, MS,** and fellow researchers sought to characterize the incidence and risk factors, including patterns of liberation from CKRT, associated with major adverse kidney events 90 days after CKRT initiation (MAKE-90) in young patients listed in the Worldwide Exploration of Renal Replacement Outcomes Collaborative in Kidney Disease registry. Their results appeared in *JAMA Network Open* [doi:10.1001/jamanetworkopen.2024.0243].

The researchers selected subjects aged 0 to 25 years and requiring CKRT due to AKI or fluid overload. They categorized patients into one of three liberation categories based on attempts to liberate within the first 28 days of CKRT: (1) liberated: patients who did not receive CKRT or another dialysis modality for 72 or more hours after discontinuing CKRT; (2) reinstituted: patients who resumed CKRT or another dialysis modality within 72 hours of attempting liberation; (3) not attempted: patients who did not attempt CKRT liberation within the first 28 days after initiating CKRT. The primary outcome was MAKE-90, including death or persistent kidney dysfunction (dialysis dependence or ≥25% decline in estimated glomerular filtration rate from baseline).

The study included 969 patients (529 males [54.6%]; median [IQR] age, 8.8 [1.7-15.0] years; 16 American Indian [1.9%]; 40 Asian or Pacific Islander [4.7%]; 127 Black [14.9%]; 652 White [76.4%]; and 160 Hispanic [18.6%]). MAKE-90 occurred in 630 (65%) patients. Of those, 368 (58.4%) patients fulfilled the MAKE-90 criteria via mortality, 91 (14.4%) were dialysis-dependent, and 262 (41.6%) had persistent kidney dysfunction. Patients with no prior comorbidities comprised the smallest proportion of the MAKE-90 population (85 [13.5%]). Patients with cardiac (145 [23.0%]), oncologic (161 [25.6%]), or immunologic (123 [19.5%]) comorbidities constituted the largest proportions of the MAKE-90 population.

Patients who successfully liberated from CKRT within 28 days had a 68% lower chance of meeting MAKE-90 criteria (adjusted odds ratio [aOR], 0.32; 95% CI, 0.22-0.48) compared with those who had CKRT reinitiated after attempting liberation. Patients who were successfully liberated had 98% lower odds of meeting the criteria for MAKE-90 compared with patients for whom liberation was never attempted (aOR, 0.02; 95% CI, 0.01-0.04). A longer period from intensive care unit (ICU) admission to initiation of CKRT was independently associated with increased chances of MAKE-90 (aOR for 6 days vs 1 day, 1.07; 95% CI, 1.02-1.13). Having a cardiac comorbidity was associated with 1.60-fold increased odds of MAKE-90 (aOR, 1.60; 95% CI, 1.08-2.37). The absence of any comorbidity was protective against MAKE-90 (aOR, 0.48; 95% CI, 0.30-0.76).

MAKE-90 incidence varied among the liberated group (110 [17.5%]), reinstituted group (179 [28.4%]), and not attempted group (341 [54.1%]). At 90 days, there was a statistically significant difference in mortality among patients who successfully liberated (26 [7.8%]), required reinstitution of CKRT after a liberation attempt (42 [14.6%]), and in whom liberation was not attempted (278 [77.9%]; $P<.001$). There was also a significant difference in mortality when comparing the successfully liberated group with the group that had CKRT reinstituted (log-rank $P=.006$). Individuals who successfully liberated had the lowest probability of MAKE-90 (33.6%; 95% CI, 25.6%-42.7%) compared with the not attempted group (95.6%; 95% CI, 93.3%-97.5%) and reinstituted group (61.0%; 95% CI, 51.2%-69.9%).

The study authors acknowledged several limitations. It is possible that liberation pattern does not directly contribute to MAKE but is instead a consequence of disease severity or that pathophysiologic mechanisms contributing to adverse outcomes after CKRT are independent of severity of illness. The study is retrospective, using data self-reported by participating centers, which could result in selection bias. The researchers included multiple markers of severity of illness in their analysis, but it is possible that there was residual confounding present. Only the first attempt at liberation was documented, so it is possible that the researchers missed patients who successfully liberated after a subsequent attempt. All hospitals included were tertiary or quaternary, which may have limited generalizability to resource-limited settings. The type I error rate may have surpassed the minimal level given that no adjustments for multiple testing were performed. Only multivariable results using complete data were reported, and 34 patients with missing data were excluded. Finally, the definition of liberation status may have introduced periods of immortal time during which patients could not experience the outcome, resulting in some bias in researchers' estimates.

In summary, the study found that MAKE-90 were common in young patients receiving CKRT, with more than two-thirds experiencing them. The researchers also successfully identified risk factors for MAKE-90, as they noted: "We found that successful liberation from therapy within 28 days was associated with lower odds of MAKE-90. Our study findings further suggest that cardiac diagnoses and increased duration between ICU admission and CKRT initiation contribute to MAKE at 90 days. Our study results support the need for future prospective studies exploring a causative relationship between CKRT parameters and clinically relevant outcomes in children, adolescents, and young adults." ■

TAKEAWAY POINTS

- Continuous kidney replacement therapy (CKRT) is increasingly used for young patients, but its long-term outcomes are unclear. Researchers sought to determine the frequency of major adverse kidney events at 90 days (MAKE-90) in youths receiving CKRT and to identify the associated risk factors.
- In the cohort study of 969 CKRT patients ages 0 to 25 years, MAKE-90, including death or persistent kidney dysfunction, occurred in 630 (65%) patients. Associated risk factors for MAKE-90 included time to CKRT initiation, failure to liberate from CKRT, and cardiac comorbidity.
- The study found a high incidence of MAKE-90 among youths receiving CKRT, emphasizing the need for future prospective studies to better comprehend liberation patterns and practices.

New CVAC System From Calyxo Gets FDA Clearance

Medical device manufacturer Calyxo, Inc., received FDA clearance for its new, redesigned CVAC System. This system enables a minimally invasive approach to kidney stone treatment. More than 50 patients have already undergone procedures using the new system.

The original CVAC Aspiration System has been used in steerable ureteroscopic renal evacuation (SURE) to treat more than 1500 patients in the United States. The device performs vacuum aspiration of stone fragments to improve clinical outcomes.

The new system, also used with SURE, is a complete stone clearance solution that integrates ureteroscopy, laser lithotripsy, irrigation, and aspiration in one device. It combines direct visualization with dedicated irrigation channels and a large aspiration lumen to aspirate kidney stones efficiently and effectively.

"The most commonly used kidney stone treatments today do not reliably remove all of the stone fragments and dust," said **Brian Eisner, MD,** director of the kidney stone program at Massachusetts General Hospital and founding clinical advisor of Calyxo. "We know that vacuum aspiration of stone fragments during ureteroscopy with laser lithotripsy under direct visualization provides unique advantages to enable better stone clearance for our patients who, in some cases, will experience a less invasive procedure with a decreased need for additional treatments."

KDIGO Releases New CKD Clinical Practice Guideline

Kidney Disease Improving Global Outcomes (KDIGO) released its *2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease,* which was also published as a supplement to *Kidney International* [2024;105(4S):S117-S314]. The guideline was last updated in 2012.

This resource is for health care professionals who provide kidney care, for people with suspected or diagnosed CKD and their caregivers, and for policy-makers and commissioners of CKD services. Its goal is to address relevant questions with actionable recommendations to guide clinical practice based on a formal evidence review and consensus-based practice points.

The new guideline addresses a wide range of topics, including optimal CKD evaluation and classification, kidney disease risk assessment, management of complications, medication management and drug stewardship in CKD, and strategies for delivering patient-centered care across diverse clinical settings. Highlights include guidance updates on the measurement of estimated glomerular filtration rate (eGFR) and albuminuria, utilization of CKD risk prediction equations, and personalized treatment recommendations for kidney and cardiovascular risk reductions tailored to individual patient needs and preferences.

Thermo Fisher Launches New Testing Service for Transplant Recipients

Thermo Fisher Scientific has announced the launch of the CXCL10 testing service, which will assist in the management of kidney transplant patients. The testing service is intended to make post-transplant care more convenient and less invasive for the nearly 250,000 people in the United States living with a kidney transplant.

The new test utilizes noninvasive urine sample collection and can produce results within 24 hours. It can detect the CXCL10 chemokine, which may provide valuable information faster than current tests. Elevated urinary CXCL10 levels have been associated with inflammation and early kidney transplant rejection.

Thermo Fisher hopes that the new service will improve current standards of care and provide increased specificity and sensitivity, resulting in fewer unnecessary and invasive biopsies or delayed results. The CXCL10 assay was developed and validated by Thermo Fisher's One Lambda Laboratories.

Print-only Content

Renal Device for Use in Cardiac Surgeries Gets FDA Breakthrough Designation

The JuxtaFlow Renal Assist Device (RAD) has received a Breakthrough Device designation from the FDA.

The device, developed by Roivios, aims to preserve kidney function in patients undergoing cardiac surgeries. JuxtaFlow RAD uses a gentle negative pressure technique on the kidneys' urine-collecting system to enhance function and protect against hypoxia-induced damage under acute conditions. It has the potential to reduce intensive care unit stays, lessen the need for emergency dialysis, and create substantial savings for health care providers.

Roivios shared preclinical data from the BIPASS-AKI study of JuxtaFlow RAD at the Society of Cardiovascular Anesthesiologists Annual Meeting and called the outcomes "encouraging." It plans to launch JuxtaFlow RAD in the United States in late 2025. Roivios also wants to expand the device's application beyond cardiothoracic surgery.

The FDA's Breakthrough Devices Program was created to provide patients and health care providers with timely access to medical devices by speeding up development, assessment, and review for premarket approval, 510(k) clearance, and de novo marketing authorization.

Federal Home Dialysis Bill Introduced

Reps. **Carol Miller (R-WV), Marilyn Strickland (D-WA), Earl Blumenauer (D-OR),** and **Mariannette Miller-Meeks (R-IA)** introduced a new bill in the US House of Representatives that could boost access to care and improve outcomes for some patients receiving dialysis. Companion legislation is expected to be introduced in the Senate soon.

The Improving Access to Home Dialysis Act (HR-8075) would:

- Require that patients be educated about all their dialysis options
- Expand the number of health care providers who can provide home dialysis training to decrease the burden on nursing staff and cut down on wait times for training
- Cover the costs of in-home support staff for patients when they are starting home dialysis

Only 14% of US patients receiving dialysis do so at home, although evidence shows that it may be a better option for some patients. Often, this is because patients are unaware of at-home options. ■

ADPKD

Classification System for Predicting Outcomes in ADPKD

Clinical Journal of the American Society of Nephrology. 2024:19(5):591-601

The Mayo imaging classification (MIC) tool was created to predict the rate of disease progression in patients with autosomal dominant polycystic kidney disease (ADPKD). **Thomas Bais** and other researchers working on behalf of the DIPAK consortium evaluated MIC to validate its ability to predict kidney outcomes in a large, multicenter ADPKD cohort. They included patients with ≥1 height-adjusted total kidney volume (HtTKV) measurement and ≥3 estimated glomerular filtration rate (eGFR) values during ≥1 year follow-up.

Measurements included Mayo HtTKV class stability, kidney growth rates, and eGFR rates of decline. The research team compared the observed eGFR decline with predictions from the Mayo Clinic future eGFR equation and tested the future eGFR prediction equation for nonlinear eGFR decline. They used Kaplan-Meier survival analysis and Cox regression models to evaluate time to kidney failure using Mayo HtTKV class as a predictor variable.

The study included 618 patients with a mean age of 47 ± 11 years and mean eGFR of 64 ± 25 mL/min/1.73 m^2 at baseline. Most (82%) stayed in their baseline Mayo HtTKV class. During a mean follow-up of 5.1 ± 2.2 years, mean TKV growth rates and eGFR decline were 5.33 ± 3.90 %/year and −3.31 ± 2.53 mL/min/1.73 m^2/year, respectively. Kidney growth and eGFR decline overlapped considerably between the classes. The observed annual eGFR decline was not significantly different from the predicted values for classes 1A, 1B, 1C, and 1D, but it was significantly slower for class 1E.

Ninety-seven (16%) patients developed kidney failure during follow-up. MIC predicted the development of kidney failure, although the sensitivity and positive predictive values were limited. Although the MIC showed acceptable stability and predicted kidney failure and eGFR decline rate, there was considerable interindividual variability in the rate of disease progression within each class.

ANEMIA

Iron Replacement With Ferric Citrate Hydrate

Clinical and Experimental Nephrology. doi:10.1007/s10157-023-02455-6

Because iron deficiency anemia (IDA) increases levels of C-terminal fibroblast growth factor 23 (cFGF23) and platelet count (PLT), both associated with cardiovascular events, **Kyoko Ito** and others hypothesized that iron replacement with ferric citrate hydrate (FC) would decrease cFGF23 levels and PLT in patients with IDA. To test this theory, they conducted a randomized, open-label, multicenter, 24-week clinical trial.

They randomized patients with nondialysis-dependent chronic kidney disease (CKD) and non-CKD complicated by IDA (8.0 ≤ hemoglobin <11.0 g/dL; serum ferritin <50 ng/mL [CKD] and <12 ng/mL [non-CKD]) 1:1 to FC-low (500 mg: elemental iron approximately 120 mg/day) or FC-high (1000 mg: elemental iron approximately 240 mg/day). Treatment was discontinued if adequate iron replacement had been achieved after 8 weeks.

The researchers assigned 73 patients to FC-low (CKD, n=21; non-CKD, n=15) and FC-high (CKD, n=21; non-CKD, n=16). FC increased serum ferritin and transferrin saturation, did not change intact cFGF23 or serum phosphorus, and decreased cFGF23 regardless of CKD status. In the FC-high group, median changes in cFGF23 from baseline to week 8 were −66.00 RU/mL in CKD and −649.50 RU/mL in non-CKD. In the FC-low group, the median changes were −58.00 RU/mL in CKD and −725.00 RU/mL in non-CKD. By week 8, FC treatment regularized PLT in all patients with high PLT at baseline (>35.2 × 10^4/μL; FC-low: 1 CKD, 8 non-CKD; FC-high: 3 CKD, 8 non-CKD).

The results showed that iron replacement with FC decreased elevated cFGF23 levels and normalized elevated PLT in patients with IDA regardless of CKD status.

CHRONIC KIDNEY DISEASE

Racial Disparities in CKD Kidney Failure, Death

Journal of the American Society of Nephrology. 2024;35(3):299-310

Black adults in the United States have a higher incidence of kidney failure than White adults. To help determine to what extent this disparity is due to factors present at the time of CKD onset, **Guofen Yan** and other researchers analyzed racial differences in kidney failure and death from onset of CKD using the race-free 2021 CKD Epidemiology Collaboration equation.

The national cohort included 547,188 US veterans (103,821 non-Hispanic Black and 443,367 non-Hispanic White) aged 18 to 85 years. All subjects had new-onset CKD between 2005 and 2016 and were followed through 10 years or May 2018 for incident kidney failure with replacement therapy (KFRT) and pre-KFRT death.

The cumulative incidence of KFRT was two-and-a-half times higher for Black veterans versus White veterans. In addition, Black veterans had more than two times higher hazards of KFRT throughout follow-up (overall hazard ratio [HR], 2.38; 95% CI, 2.31-2.45) but had 17% to 48% decreased hazards of pre-KFRT death. These differences decreased after accounting for racial differences in age at CKD onset; Black veterans were an average of 7.8 years younger than their White counterparts at CKD onset.

The authors concluded that the greater cumulative incidence of kidney failure in Black adults was due to a combination of higher hazards of progression to kidney failure and lower hazards of the competing risk of death. Both can be largely explained by the younger age at CKD onset in Black adults compared with White adults.

DIALYSIS

Muscle Mass, Fat, and Mortality in Hemodialysis Patients

Nephrology Dialysis Transplantation. 2024;39(2):286-296

A group of investigators led by **Sho Kojima** examined the associations among muscle mass, intramuscular fat, and abdominal fat measured by abdominal computed tomography (CT) and mortality in hemodialysis patients. High body mass in this population is associated with low mortality, while abdominal obesity is associated with increased mortality.

The team conducted a two-center, retrospective cohort study of hemodialysis patients who had abdominal CT between January 2013 and December 2018. Researchers used CT images at the third lumbar vertebral level to measure skeletal muscle mass index (SMI), muscle radiation attenuation (MRA) as an index of intramuscular fat, and the ratio of visceral fat to subcutaneous fat (VSR). They used the multivariate Cox proportional hazards model to determine independent predictors of all-cause, cardiovascular, and noncardiovascular mortality.

Of the 344 patients in the study (median age, 71.0 years; 33.7% female), 145 died during a median follow-up of 4.9 years (46 from cardiovascular causes, 99 from noncardiovascular causes). Lower MRA (HR, 0.71; 95% CI, 0.58-0.87; *P*=.001) and higher VSR (HR, 1.17; 95% CI, 1.01-1.37; *P*=.04) were independently associated with higher all-cause mortality but were not associated with lower SMI (HR, 0.87; 95% CI, 0.68-1.11; *P*=.26). Lower MRA (HR, 0.51; 95% CI, 0.35-0.73; *P*<.001) and higher VSR (HR, 1.29; 95% CI, 1.09-1.54; *P*=.003) were also associated with cardiovascular and noncardiovascular mortality, respectively.

The researchers concluded that intramuscular fat and abdominal fat as measured using abdominal CT in hemodialysis patients are stronger independent predictors of mortality than muscle mass.

Trends in Automated Peritoneal Dialysis Prescriptions

Clinical Journal of the American Society of Nephrology. doi:10.2215/CJN.0000000000000436

In the largest analysis of incident automated peritoneal dialysis (APD) prescriptions in the United States to date, **Harold E. Giles** and other researchers examined variations in peritoneal dialysis (PD) prescriptions among patients with incident APD who remain on PD for ≥120 days.

The retrospective analysis included data from a large dialysis organization on patients who initiated PD with APD between 2015 and 2019. Prescription data were categorized by calendar year, timing of PD, and residual renal function. Researchers assessed changes in prescriptions from PD initiation (day 1) to day 120.

The cohort included 11,659 patients. Mean age at PD initiation increased from 2015 (56 [15] years) through 2019 (58 [15] years). Most other variables showed no clear temporal change. Most patients (86%) were prescribed nighttime

PD, with an average of 4.9 (1.3) cycles per day, a mean total treatment volume of 9.3 (2.5) L, and a median daily total dwell time of 7 (6.0-9.5) hours. Relative to day 1 nighttime prescriptions, there were small increases in the proportion of patients receiving three or fewer cycles per day and those receiving six or more cycles per day; a 100-mL mean increase in fill volume per exchange; and a mean 0.5-L increase in total nighttime treatment volume at day 120. Changes in nighttime APD prescriptions were evaluated at the patient level; 49% of patients had day 120 prescriptions that were unchanged from their initial prescription.

The study authors concluded that most patients were prescribed nocturnal PD only, with limited variability across the first 4 months of therapy.

END-STAGE KIDNEY DISEASE

Age, Race, Sex Differences in ESKD Incidence Over Time

Journal of the American Society of Nephrology. 2024;35(4):456-465

Believing that assessments of changes in end-stage kidney disease (ESKD) incidence among Black and White Americans of different ages in recent decades were lacking, **Chyng-Wen Fwu** and fellow researchers analyzed United States Renal Data System data from 1980 to 2019 to determine ESKD incidence trends among Black and White Americans. They looked at adolescent (ages 13-17 years), adult (ages 18-64 years), and older adult (≥65 years) populations and used the National Cancer Institute Joinpoint Regression Program to estimate annual percent change in ESKD incidence and define points at which a statistically significant change in annual percent change slope occurred for each group.

They found that ESKD incidence for all groups increased after 1980, although trends differed (P<.001). By 1993, growth in incidence had slowed for most groups. By 2006, the annual percent change in ESKD incidence had decreased for all groups except White adults; their rates continued to increase (P<.05). Both Black and White adolescents experienced a return to near 1980 levels of ESKD incidence by 2019, but no other group's rates improved to that degree. In every age group, ESKD incidence among Black individuals exceeded that of White individuals.

In summary, the investigators identified distinct patterns in ESKD incidence among patients of different ages, sexes, and races. These patterns may reflect access to preventive care, changes in dialysis acceptance rates, incidence of diabetes mellitus, implementation of evidence-based guidelines for CKD treatment, or other factors. There may be an opportunity to apply population-specific strategies to alter the growth of the ESKD patient population and address racial disparities.

GLOMERULONENEPHRITIS

SGLT2i in Primary, Secondary Glomerulonephritis

Nephrology Dialysis Transplantation. 2024;39(2):328-340

The role of sodium-glucose cotransporter 2 inhibitors (SGLT2i) in the management of glomerular diseases with proteinuria in real-world clinical settings is unclear. So, **Fernando Caravaca-Fontán** and other researchers conducted a retrospective, observational, international cohort study of adult patients with biopsy-proven glomerular diseases. The study's main outcome was the percentage reduction in 24-hour proteinuria from SGLT2i initiation to 3, 6, 9, and 12 months. Secondary outcomes included percentage change in eGFR, proteinuria reduction by type of disease, and reduction of proteinuria ≥30% from SGLT2i initiation.

The study included 493 patients (median age, 55 years) with background therapy with renin-angiotensin system blockers. Proteinuria from baseline changed by –35%, –41%, –45%, and –48% at 3, 6, 9, and 12 months after SGLT2i initiation; eGFR changed by –6.0%, –3.0%, –8.0%, and –10.5% at 3, 6, 9, and 12 months, respectively. The results were similar regardless of the underlying disease. There was a correlation between body mass index (BMI) and percentage proteinuria reduction at last follow-up.

By using a mixed-effects logistic regression model, the researchers determined that serum albumin at SGLT2i initiation is a predictor of ≥30% proteinuria reduction (OR for albumin <3.5 g/dL, 0.53; 95% CI, 0.30-0.91; P=.02). They observed a slower eGFR decline in patients achieving a ≥30% proteinuria reduction: –3.7 versus –5.3 mL/min/1.73 m²/year (P=.001). The overall tolerance to SGLT2i was good.

The researchers concluded that the use of SGLT2i is associated with a significant reduction of proteinuria, and the percentage change is greater in patients with higher BMI. Also, higher serum albumin at SGLT2i onset is associated with a higher probability of reaching a ≥30% reduction in proteinuria.

PEDIATRIC NEPHROLOGY

Stratification in Determining Bias in GFR Estimating Equations

Pediatric Nephrology. doi:10.1007/s00467-024-06318-4

Determining bias is important when assessing glomerular filtration rate (GFR), and stratification by subgroups can show where equations perform differently. Stratifying on the level of only eGFR and measured glomerular filtration rate (mGFR) is widespread but can lead to erroneous conclusions.

Therefore, **Derek K. Ng** and other researchers compared and contrasted biases (eGFR relative to mGFR) with 95% CI within strata of mGFR only, eGFR only, and the average of mGFR and eGFR using data from the Chronic Kidney Disease in Children study.

A total of 304 participants provided 843 GFR studies with a mean mGFR of 48.46 (SD=22.72) and mean eGFR of 48.67 (SD=22.32). Correlation was 0.904. Although there was strong agreement, eGFR greatly overestimated mGFR when mGFR was <30 (+6.2%; 95% CI, +2.9% to +9.7%); eGFR vastly underestimated mGFR when mGFR was >90 (–12.2%; 95% CI, –17.3% to –7.0%).

There were also significant biases in the opposite direction when stratifying by eGFR only. Conversely, when stratifying by the average of eGFR and mGFR, biases were not significant (+1.3% and –1.0%, respectively), consistent with strong agreement.

The study authors concluded that, although it is common, stratifying only by mGFR or eGFR to assess eGFR biases can lead to inappropriate inference because of intrinsic statistical issues highlighted by their research. Instead, they recommend using the average of eGFR and mGFR for valid inferences in evaluations of eGFR biases.

TRANSPLANTATION

Effect of Consent for High-KDPI Deceased Donor Transplants

Journal of the American Society of Nephrology. 2024;35(5):630-641

Many kidney transplant candidates die while on the waiting list for transplantation. At the time of waiting list placement, candidates may consent to receive donor kidneys with lower expected survival (eg, kidney donor profile index [KDPI] >85%). It is believed that consent may increase the likelihood and timeliness of donor offers for transplantation. However, the impact of consent on access to transplantation is unclear.

Jesse D. Schold and others evaluated the characteristics of candidates consenting to high-KDPI donor kidneys and their likelihood of receiving a deceased donor transplant (DDTX) based on consent over time. The researchers utilized data from the Scientific Registry of Transplant Recipients between 2015 and 2022 (n=213,364) and assessed the likelihood of consent using multivariable logistic models and time to DDTX with cumulative incidence plots accounting for competing risks and multivariable Cox models.

High-KDPI consent was 41% and was higher among individuals who were Black or Hispanic, older, had higher BMI, had diabetes, had vascular disease, and had 12 to 48 months prelisting dialysis time, with significant center-level variation. High-KDPI consent was associated with higher rates of DDTX (adjusted HR, 1.15; 95% CI, 1.13-1.17), but there was no difference in the likelihood of DDTX from donors with KDPI <85%. The effect of high-KDPI consent on higher rates of DDTX was higher among candidates ages >60 years and diabetic candidates, and it varied based on center characteristics.

In sum, the study authors noted that there is significant variation of consent for high-KDPI donor kidneys and a higher likelihood of transplantation associated with consent. ■

Sarah Tolson

Navigating the Aftermath: Mitigating Risks From Clearinghouse Disruptions in Renal Care

Chances are, if you are reading this column, you have heard about the ransomware attack on Change Healthcare that occurred on February 21, 2024. In the ever-evolving landscape of health care, where technology plays an increasingly crucial role, this recent event has sent shockwaves through the industry. At the time of this writing, Change Healthcare's systems were not yet fully restored.

The repercussions extend far beyond the realms of data breaches and system downtime, bringing revenue to a screeching halt for many providers. For nephrology practices and dialysis programs whose sole clearinghouse is Change Healthcare, reimbursement may be limited to the advance payments available from Medicare Administrative Contractors and United Health Group. In this column, we will discuss the operational challenges the Change Healthcare attack has posed as well as some methods for mitigating the impact of future clearinghouse outages.

Nephrology practices and dialysis facilities rely entirely on timely and accurate claim submissions for revenue generation. Dialysis programs generally submit one claim per patient per month. Losing the ability to obtain their monthly reimbursement has the potential to jeopardize operations for small dialysis programs. With the attack on Change Healthcare's systems, renal providers have been confronted with a harsh reality: Their revenue streams are vulnerable to yet another external threat beyond their control.

Considering the technology utilized in the health care industry, some of the challenges related to the Change Healthcare attack may appear trivial. For instance, many of the insurance companies no longer accept paper claims. When there are no barriers to submitting electronic claims, eliminating paper claims seems like a great idea. However, if there is no mechanism to process paper claims and no pathway to submit claims electronically, there is no way to reimburse providers and facilities for the services they are providing to their patients. Another challenge presented by the Change Healthcare attack is that a sizable number of insurance companies can accept claims exclusively from Change Healthcare. Again, this is not a problem if all systems are running at full capacity. As an industry, we now understand more than ever the importance of redundancy in every aspect of a nephrology practice or dialysis program.

The company I work for is incredibly fortunate that our clearinghouse of choice was not Change Healthcare. However, we still felt the impact of the attack on Change Healthcare as several of our clients submit large volumes of claims to payers that only accept claims from Change Healthcare or the electronic connection was routed through Change Healthcare by our clearinghouse. Thankfully, we already had access to alternate claim submission methods for most of the insurance companies to which we submit claims. While these alternate submission methods were not as efficient as sending all the claims to our clearinghouse, we were still able to keep the revenue cycle moving.

The importance of maintaining contingency plans for claim submission in the event that a nephrology practice or dialysis program's main method of submission is compromised has been driven home by the attack on Change Healthcare. The alternate claim submission methods available are dependent on each insurance company's accepted methods for claim submission and it can take anywhere from minutes to weeks to gain access. Examples of alternate claim submission methods are direct submission of an electronic claim file to the insurance company's online provider portal, electronic claim submission via direct access to alternate clearinghouses, and direct data entry of claims into the insurance company's online provider portal.

In conclusion, the ransomware attack on Change Healthcare underscores a critical lesson for the health care industry about the pitfalls of relying solely on a single electronic claim submission method without backup submission methods. As we move forward, it is imperative for health care organizations to implement comprehensive contingency plans, ensuring redundancy in their operations to protect against future disruptions. This attack serves as a reminder of the need for continuous improvement in cybersecurity measures and the importance of adaptable and resilient infrastructure in safeguarding the financial stability and operational continuity of nephrology practices and dialysis programs. ■

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