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Center-Level Factors and Racial Inequity in Living Donor Kidney Transplant

The rate of new cases of kidney failure in Black patients is double that in White patients. Patients with kidney failure who receive living donor kidney transplant experience improved quality of live and excellent long-term graft survival. It is well established that, despite policy- and research-associated interventions, racial disparities in living donor kidney transplant persist.

According to **Lisa M. McElroy, MD, MS,** there are few data available on associations between transplant center-specific characteristics and catchment area population characteristics and living donor kidney transplant racial inequities. To identify targets for multilevel interventions, the researchers conducted a study to examine racial differences in rates of living donor kidney transplant relative to differences in waiting list, referral region, and center characteristics. Results were reported in *JAMA Network Open* [doi:10.1001/jamanetworkopen.2023.47826].

The retrospective cohort longitudinal study was completed in February 2023. The cohort included transplant centers in the United States with at least 12 annual living donor kidney transplants from January 1, 2008, to December 31, 2018. The centers were identified using the Health Resources Services Administration database linked to the US Renal Data System

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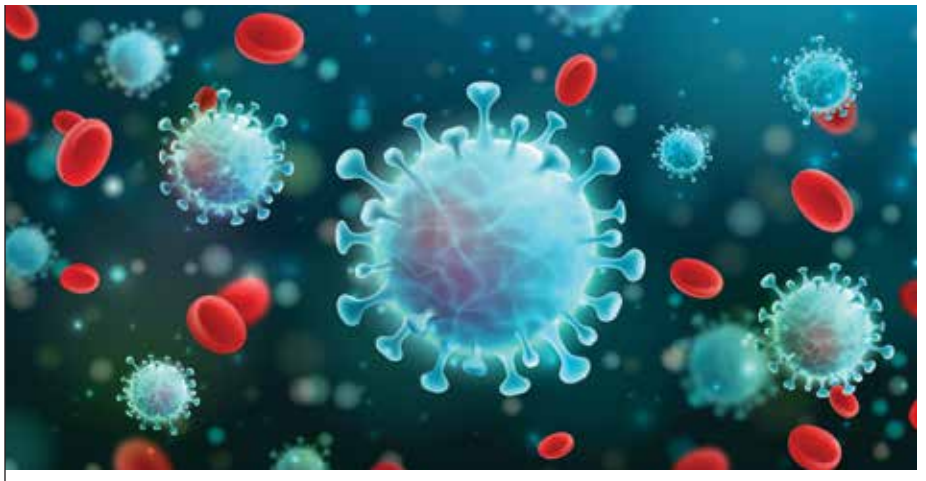

COVID-19 Infection and Disease Activity in Primary Glomerular Disease

Patients with primary glomerular disease who have COVID-19 face increased risk for severe adverse outcomes, including hospitalization, kidney replacement therapy (KRT), or death. Risk factors in that patient population include a higher prevalence of hypertension and diminished kidney function. Patients with glomerular disease are often treated with immunosuppression, which has been linked to attenuated response to COVID-19 vaccines, resulting in blunting the effectiveness of vaccines in mitigating COVID-19.

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Body Mass Index in Adolescents Related to Risk of Early CKD

The rates of adolescent obesity are increasing. One in five adolescents in the United States have a body mass index (BMI) at or above the 95th percentile for age and sex on the Centers for Disease Control and Prevention (CDC) growth chart. Adolescent obesity has been linked with adverse health outcomes later in life, including diabetes, cardiovascular diseases, cancer, and all-cause mortality.

There is a recognized link between obesity and chronic kidney disease (CKD) in adults. However, there are few data available on the link between adolescent obesity and early CKD. Further, it is unknown whether an association between adolescent obesity and early CKD is independent of other comorbidities, such as diabetes and hypertension.

Researchers, led by **Avishai M. Tsur, MD, MHA,** conducted a study to examine the association between adolescent BMI and early CKD in young adulthood, defined as under 45 years of age. Results of the retrospective cohort study were reported in *JAMA Pediatrics* [doi:10.1001/jamapediatrics.2023.5420].

The study linked screening data of mandatory medical assessments of Israeli adolescents to data from a CKD registry of a national health care system. The cohort included Israeli adolescents who were 16 to 20 years of age; born since

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COVID-19 Infection and Disease Activity

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There are concerns that COVID-19 may exacerbate glomerular disease and kidney function decline. In addition, acute kidney injury from severe COVID-19 is common among patients with glomerular disease and may increase the risk of kidney failure. There have also been reports of disease relapse after COVID-19 vaccination among patients with glomerular disease, which may result in vaccine hesitancy.

Chia-shi Wang, MD, MSc, and colleagues conducted a study designed to examine the association of COVID-19 versus COVID-19 vaccination with kidney function and glomerular disease activity. Results of the study were reported in the *American Journal of Kidney Diseases* [2024;83(1):37-46].

The National Institutes of Health-sponsored Cure Glomerulonephropathy (CureGN) observational cohort study included 71 centers and more than 2500 patients in the United States, Canada, and Europe with primary minimal change diseases, focal segmental glomerulosclerosis, membranous nephropathy, or IgA nephropathy. The study exposures were COVID-19 and COVID-19 vaccination.

The primary outcomes of interest were decline in estimated glomerular filtration rate (eGFR) and glomerular disease activity based on the degree of proteinuria. Worsening of glomerular disease was defined by doubling of the urinary protein-creatinine ratio (UPCR) to at least 1.5 g/g or increase in dipstick urine protein by two ordinal levels to 3+ (300 mg/dL) or above.

CureGN participants had study visits and data collection on COVID-19 and vaccination from July 1, 2021, to January 1, 2023. The median number of completed study visits per person with information on COVID-19 and vaccination was three. The overall cohort included 2055 participants. Of those, 44% (n=900) were female, and 72% (n=1477) had at least one comorbidity (52% hypertension [n=1056], 6% diabetes mellitus [n=129], 14% cardiovascular disease [n=278], 16% asthma/chronic obstructive pulmonary disease [n=335], 9% cancer [n=189], and 35% obesity [n=715]).

Thirty-five percent of participants (n=722) experienced COVID-19 infection, resulting in an incidence rate of 15.2 per 100 person-years since January 1. 2020. Patterns of first incidence of COVID-19 infection were similar between the CureGN cohort and US trends.

Of the 722 participants with COVID-19 infection, 13% (n=90) were hospitalized, including five who were admitted to the intensive care unit, and three died. One participant required acute KRT. Eight patients progressed to kidney failure after COVID-19 (median time of 322 days). Of those eight patients, seven were unvaccinated at the time of their COVID-19 episode.

Among the CureGN cohort, 68% (n=1407) reported receiving at least one COVID-19 vaccine. The proportion of vaccinated individuals remained relatively constant since the summer of 2021; the lowest uptake was among pediatric subgroups. By January 1, 2023, 65% of participants in the CureGN cohort were fully vaccinated against COVID-19.

Of the 722 participants in the CureGN cohort who developed COVID-19, 232 had at least two eGFR measurements prior to their illness and two after their illness. Follow-up was a median of 3.67 years prior to illness and 0.84 years after. The slope of eGFR prior to COVID-19 was –1.40 mL/min/1.73 m^2 per year (calculated based on a median of 13 measurements).

Following COVID-19 infection, slopes were calculated based on a median of three eGFR measurements. At 6 months post COVID-19, the eGFR slope was –4.26 mL/min/1.73 m^2 per year (the difference was not statistically significant from before COVID-19 infection). There were no statistically significant differences in slopes between patients who were vaccinated at the time of COVID-19 infection and those who were not vaccinated at the time of infection.

A total of 583 participants who experienced COVID-19 infection had at least two urine protein or dipstick measurements before and after their illness. Comparing glomerular disease activity between those who experienced COVID-19 and matched controls who did not experience COVID-19, there was an association between COVID-19 infection and subsequent worsening in glomerular disease (hazard ratio [HR], 1.35; 95% CI, 1.01-1.80; *P*=.04).

Of the 1407 CureGN cohort participants who received a COVID-19 vaccination, 705 had at least two eGFR measurements before and two after their illness. Median follow-up was 3.59 years before and 1.33 years after vaccination. There was no association between COVID-19 vaccination and decline in eGFR.

There were 1129 participants with at least two urine protein or dipstick measurements before and after COVID-19 vaccination. In comparisons of those who received a COVID-19 vaccine with matched controls who did not receive a vaccine, there was no association between vaccination and higher risk of subsequent worsening in glomerular disease (HR, 1.02; 95% CI, 0.79-1.33; *P*=.87). Further, there were no significant differences in worsening of glomerular disease between patients who were vaccinated at the time of their COVID-19 infection and those who were not vaccinated at the time of the infection.

Citing limitations to the study findings, the authors included incomplete sampling of CureGN participants (2055 of 2698 total participants), reliance on self-report and review of electronic health records for identification of cases of COVID-19, and the relatively short follow-up period, making associations with eGFR and glomerular disease activity among those with COVID-19 infection unclear.

In conclusion, the researchers said, "COVID-19 occurred commonly and was often severe in patients with primary [glomerular disease] from the CureGN cohort. COVID-19 infection [was] also associated with a higher risk of increased [glomerular] disease activity as defined by proteinuria. By contrast, COVID-19 vaccination was not associated with [glomerular] disease activity. Strategies to promote COVID-19 vaccination are critical to prevent COVID-19 infection and its major sequelae, including [glomerular disease] relapse and decline in kidney function." ■

TAKEAWAY POINTS

- Researchers conducted an observational cohort study to examine the associations of COVID-19 with longitudinal kidney function in patients with primary glomerular disease.
- Among patients with glomerular disease, COVID-19 infection was severe for one in eight cases and was associated with subsequent worsening of glomerular disease activity, defined by proteinuria.
- There were no associations between vaccination against COVID-19 and change in disease activity or decline in kidney function.

Body Mass Index in Adolescents

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January 1, 1975; medically evaluated for mandatory military service through December 31, 2019; and insured by the Maccabi Healthcare Services. Exclusion criteria were kidney pathology, baseline albuminuria, hypertension, dysglycemia, or missing data on blood pressure or BMI at the time of the baseline assessment. Individuals whose follow-up ended prior to the establishment of the CKD registry were also excluded.

The outcome of interest was a diagnosis of early CKD, based on at least two results of a urine albumin-creatinine ratio of 30 mg/g or greater within 6 months of a serum creatinine test that showed an estimated glomerular filtration rate of 60 mL/min/1.73 m^2 or greater (determined using the Chronic Kidney Disease Epidemiology Collaboration creatinine equation). Test results were automatically extracted, and the date of the first positive test result was determined as the date of early CKD.

High BMI late in adolescence was associated with early CKD in young adulthood, which can occur even in seemingly healthy individuals with high-normal BMI and before the age of 30 years.

BMI was calculated as weight in kilograms divided by height in meters squared and categorized by age- and sex-matched percentiles according to the CDC. Follow-up began at the time of medical evaluation or January 1, 2000 (whichever came last), and ended at early onset CKD, death, the last day insured, or August 23, 2020 (whichever came first). Data analysis was performed from December 18, 2021, to September 11, 2023.

A total of 629,168 adolescents were evaluated during the study. Of those, 5.6% were excluded from the analysis, resulting in a final cohort of 593,660 adolescents (54.5% [n=323,293] male and 45.5% [n=270,367] female). Of these, 5.9% (n=35,056) were categorized as underweight, 43.3% (n=256,968) had low-normal BMI, 35.3% (n=209,485) had high-normal BMI, 10.0% (n=60,516) were overweight, 4.3% (n=25,304) had mild obesity, and 1.1% (n=6331) had severe obesity. Mean age at study entry was 17.2 years and was similar across groups. Mean age at study entry was 17.3 years for males and 17.2 for females.

For both males and females, the normal BMI groups had the highest proportions of high residential socioeconomic status, high cognitive performance, complete education, and unimpaired health.

There was an interaction among BMI group, sex, and early CKD in adulthood. In males, the reported incidents of early CKD by adolescent BMI group were: underweight, 0.17% (n=40); low-normal BMI, 0.15% (n=211); high-normal BMI, 0.25% (n=263); overweight, 0.50% (n=169); mild obesity, 0.78% (n=135); and severe obesity, 0.93% (n=38). Mean follow-up was 13.4 years, including 4,316,217 person-years. Corresponding rates per 10,000 person-years were 1.25 for males who were underweight in adolescence, 1.10 for low-normal BMI, 1.86 for high-normal BMI, 4.10 for overweight, 6.54 for mild obesity, and 8.43 for severe obesity.

For females, the reported incidents of early CKD were: underweight, 0.38% (n=46); low-normal BMI, 0.30% (n=364); high-normal BMI, 0.41% (n=421); overweight, 0.68% (n=188); mild obesity, 0.79% (n=64); and severe obesity, 1.07% (n=24). Mean follow-up was 13.4 years. The corresponding rates per 10,000 person-years were 2.75 for females who were underweight in adolescence, 2.24 for low-normal BMI, 3.08 for high-normal BMI, 5.34 for overweight, 6.53 for mild obesity, and 9.64 for severe obesity.

Among males, the adjusted hazard ratios for early CKD were 1.8 (95% CI, 1.5-2.2) for adolescents with high-normal BMI, 4.0 (95% CI, 3.3-5.0) for those who were overweight, 6.7 (95% CI, 5.4-8.4) for those with mild obesity, and 9.4 (95% CI, 6.6-13.5) for those with severe obesity. Corresponding values among females were 1.4 (95% CI, 1.2-1.6), 2.3 (95% CI, 1.9-2.8), 2.7 (95% CI, 2.1-3.6), and 4.3 (95% CI, 2.8-6.5), respectively.

In subgroup analyses of cohorts limited to those who were seemingly healthy as adolescents, those surveyed up to 30 years of age, and those free of diabetes or hypertension at the end of the follow-up, results were similar.

Limitations to the study cited by the authors included the possibility of ascertainment bias, the lack of longitudinal clinical and lifestyle data, and the lack of serum creatinine measurements.

In summary, the researchers said, "In this cohort study, high BMI late in adolescence was associated with early CKD in young adulthood, which can occur even in seemingly healthy individuals with high-normal BMI and before the age of 30 years. Given the increasing obesity rates among adolescents, our findings are a harbinger of the potentially preventable increasing burden of CKD and subsequent cardiovascular disease." ■

TAKEAWAY POINTS

- Researchers reported results of a study designed to examine the association between body mass index (BMI) in adolescence and early chronic kidney disease (CKD) before 45 years of age.
- In the cohort study, there were associations between high BMI in adolescence and early CKD; the risk increased with increasing severity of obesity.
- There was also a risk in seemingly healthy individuals with high-normal BMI and before 30 years of age.

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and the Scientific Registry of Transplant Recipients.

The primary outcome of interest was center yearly living donor kidney transplant rate ratio (RR) between Black and White individuals. The researchers calculated the rate of living donor kidney transplant per eligible wait time for Black and White patients for each center in each year, then derived the ratio of those rates as the living donor kidney transplant RR between Black and White individuals. An RR of 1 indicated equal rate (racial equality) and lower than 1 indicated inequity for Black patients.

Modifiable and nonmodifiable covariates were derived at three levels: transplant referral region where the centers were located, center characteristics, and characteristics of the waitlisted patients. Nonmodifiable covariates included characteristics of patients waitlisted for kidney transplant and transplant referral region population. Characteristics of waitlisted patients included percentage female sex, calculated panel reactive antibody greater than 70%, less than postsecondary education, and type B blood. Transplant referral region characteristics included Black population prevalence, percentage uninsured, and interquintile range of the Area Deprivation Index.

Modifiable covariates at the center level included participation in the National Kidney Registry voucher or paired exchange programs, state Medicaid expansion, and percentage of total kidney transplants that were living donor transplants. Medicaid expansion was used as a proxy for care to the uninsured.

The final cohorts used to derive the living donor kidney transplant rate outcome included 394,625 adults who were waitlisted, of whom 33.1% were Black and 66.9% were White, and 57,222 adult living donor kidney transplant recipients, of whom 14.1% were Black and 85.9% were White. There were no additional racial or ethnic categories included in the study

There was an association between the prevalences of Black populations within a geographic transplant referral region and overall volume of living donor kidney transplants. Over time, there was a concave trend in the percentage of living donor kidney transplants that were United Network for Organ Sharing Kidney Paired Donation Program-matched runs.

During the study period, center-level living donor kidney transplant RRs between Black and White individuals ranged from 0.00 to 4.27. Among the 89 transplant centers included in the study, yearly medians ranged from 0.197 in 2015 to 0.305 in 2010. Those results indicated median lower rates of living donor kidney transplant among Black patients compared with White patients. When the estimation model included patient, center, and regional characteristics, estimated center-level RRs over the entire study period ranged from 0.577 to 0.771, and yearly medians of center RRs ranged from 0.216 in 2016 to 0.285 in 2010.

The estimated average living donor kidney transplant RR between Black and White individuals was 0.260 (95% CI, 0.227-0.298), indicating that, on average, racial equity in living donor kidney transplant rates was not achieved at these centers. More specifically, Black patients experienced inequity.

Across all centers, all study period years, and all levels of categorical variates, with numeric covariates fixed at observed mean values, the estimated average living donor kidney transplant RR between Black and White individuals was 0.260 (95% CI, 0.227-0.298), indicating that, on average, racial equity in living donor kidney transplant rates was not achieved at these centers. More specifically, Black patients experienced inequity.

In the hypothetical best-case scenario, model-based estimations resulted in little change in the minimum RR (from 0.0557 to 0.0559), but a greater positive shift in the maximum from 0.771 to 0.895. Relative to the observed 582 living donor kidney transplants in Black patients and 3837 in White patients, the 2018 hypothetical model estimated an increase of 423 living kidney donor transplants in Black patients (a 72.7% increase) and of 1838 living donor kidney transplants for White patients (a 47.9% increase).

There were some limitations to the study cited by the authors, including the use of national data registries, the discordant dates available for the transplant referral region-level covariate sources, and the derivation of the transplant referral regions based on hospital referral regions. In addition, the cohort design prevented the establishment of causality.

In conclusion, the researchers said, "The findings of this cohort study suggest that racial inequities in living donor kidney transplant persist despite decades of investigation and intervention. Our findings observed geographic but no temporal variation and suggest that center participation in national programs, such as the paired exchange and voucher programs, may help to mitigate living donor kidney transplant Black-White race inequities. Overall, our findings support the increasingly accepted notion that a strong program is multifactorial and many contributing factors remain unmeasured by national data systems. Achieving racial equity will require identification of living donor kidney transplant RRs related to the referral region conditions, and tailored interventions and goalsetting should be based on the center-specific barriers to achieve them." ■

TAKEAWAY POINTS

- Researchers reported results of a retrospective cohort longitudinal study evaluating center-level factors and racial equity in living donor kidney transplant during an 11-year time period.
- During the study period, Black-White mean living donor kidney transplant rate ratios (RRs) ranged from 0.216 in 2016 to 0.285 in 2010.
- There was no substantial improvement over time in either observed or covariate-adjusted estimated RRs.

Incidence of Clinical Outcomes After AKI During Hospitalization

Patients who experience acute kidney injury (AKI) while hospitalized face increased risk for morbidity and mortality after discharge. The increased risk of development and progression of chronic kidney disease (CKD) and death after an AKI event is associated with the severity, duration, and frequency of AKI episodes, as well as preexisting CKD and other comorbidities.

Previous studies of administrative databases have been limited to study populations that were elderly or had limited demographic and geographic diversity, were conducted in countries with universal medical coverage, or have lacked a control group of hospitalized patients without AKI.

Ivonne H. Schulman, MD, and colleagues conducted a retrospective, propensity score-matched cohort study designed to quantify various short- and long-term outcomes of hospitalization with AKI. Results were reported in the *American Journal of Kidney Diseases* [2023;82(1):63-74].

The study outcomes of interest were all-cause and selected-cause rehospitalizations and mortality within 90 and 365 days after index hospitalization. The researchers identified patients with prior continuous enrollment for at least 2 years hospitalized with and without a discharge diagnosis of AKI between 2007 and September 2020 in Optum Clinformatics, a national claims database.

A total of 471,176 patients hospitalized with AKI were propensity score-matched to 471,176 patients hospitalized without AKI. Following propensity-score matching, the cumulative incidence function method was used to estimate incidences of rehospitalization and death; Gray's test was used to compare the incidences between the two groups. Cox models for all-cause mortality were used to test the association of AKI hospitalization for each outcome.

The cumulative incidence per 100 patients of all-cause hospitalization within 90 and 365 days after discharge was significantly higher in the propensity score-matched cases than in controls. The cumulative incidences per 100 patients of all-cause hospitalization within 90 and 365 days after index discharge were significantly higher among patients with and without preexisting CKD in propensity score-matched cases than in controls (P<.001).

Cumulative incidence curves show that the incidence of all-cause rehospitalization with 365 days after index discharge was higher in patents hospitalized with AKI (propensity score-matched cases) than in patients hospitalized without AKI (propensity score-matched controls). It was also higher in patients with preexisting CKD than in patients without preexisting CKD (P<.01).

Results of the Cox model for cause-specific hazards demonstrated an association between AKI and an increased risk of rehospitalization within 90 days (hazard ratio [HR], 1.62; 95% CI, 1.60-1.65). Associations of AKI with rehospitalizations within 365 days after the index discharge were similar. There were no significant differences in the association of AKI with all-cause rehospitalization between those with preexisting CKD and those without preexisting CKD.

The cumulative incidences per 100 patients of nearly all select-cause rehospitalizations within 90 and 365 days of index discharge were significantly higher among the propensity score-matched cases than among controls. The most common causes of rehospitalization within 90 and 365 days for the propensity score-matched cases were sepsis, heart failure, AKI, and pneumonia. For the propensity score-matched controls, the most common causes were sepsis, heart failure, and pneumonia.

Among patients with preexisting CKD, with the exception of cerebrovascular accident (CVA), the cumulative incidence per 100 patients for select-cause rehospitalization was significantly higher in propensity score-matched cases than in controls (P<.001). While there was no significant difference between groups in the rates of CVA within 90 days after index discharge, the rate was significantly higher for propensity score-matched cases than for controls within 365 days after discharge (P<.01).

There were associations between AKI and higher rates of rehospitalization for end-stage renal disease (HR, 6.21; 95% CI, 1.04-36.92), heart failure (HR, 2.81; 95% CI, 2.66-2.97), sepsis (HR, 2.62; 95% CI, 2.49-2.75), pneumonia (HR, 1.47; 95% CI, 2.37-1.57), myocardial infarction (HR, 1.48; 95% CI, 1.33-1.65), and volume depletion (HR, 1.64; 95% CI, 1.37-1.96) at 90 days after index discharge compared with the group without AKI. Findings at 365 days after index discharge were similar.

The cumulative incidences per 100 patients of all-cause mortality were significantly higher in the group with AKI compared with the group without AKI within 90 and 365 days of index discharge (P<.01). The monthly cumulative incidences of mortality were also higher in the propensity score-matched cases than in controls with and without preexisting CKD (P<.01).

In the Cox model fitted for cause-specific hazards, there was an association between AKI and a significant increase in all-cause mortality. The association was stronger within 90 days (HR, 2.66; 95% CI, 2.61-2.72) compared with 365 days (HR, 2.11; 95% CI, 2.08-2.14). The association between AKI and all-cause mortality was significantly weaker in patients with preexisting CKD than in patients without preexisting CKD within both 90 days and 365 days after index discharge.

The researchers cited some limitations to the study findings, including the use of observational data that resulted in an inability to infer causal relationships between the AKI hospitalizations and the outcomes included in the study, the potential for bias from unmeasured confounding, the lack of data on inpatient creatinine values, and due to the use of data for an insured population, the findings may not reflect the uninsured population, who are particularly vulnerable and may experience worse AKI outcomes.

In summary, the authors said, "We confirm and extend prior studies in showing the association between a hospitalization with AKI and adverse short- and long-term clinical outcomes in a broad and diverse group of hospitalized patients with and without preexisting CKD. Although the best posthospitalization AKI clinical management regimen is yet to be determined, these results underscore the immediate need for close posthospitalization monitoring of individuals with AKI." ■

The cumulative incidences per 100 patients of all-cause hospitalization within 90 and 365 days after index discharge were significantly higher among patients with and without preexisting CKD in propensity score-matched cases than in controls (P<.001).

TAKEAWAY POINTS

- Patients who experience an episode of acute kidney injury (AKI) during hospitalization face increased risk of morbidity and mortality postdischarge.
- A recent study was designed to quantify various short- and long-term clinical outcomes after hospitalization with AKI among patients with and without preexisting chronic kidney disease.
- There was an association between AKI and an increased risk of 90- and 365-day all-cause and selected-cause rehospitalization and death.

Kidney Function Measures and Dementia and Cognitive Decline

Patients with chronic kidney disease (CKD) face increased risk of cognitive decline, and more advanced stages of CKD are associated with more severe cognitive decline. Results of previous studies have suggested an association between measures of kidney function and brain atrophy, cerebrovascular pathologies, and white matter abnormalities. Those studies characterized the brain damage as primarily driven by vascular causes and having a functional rather than structural nature.

There are no data available on the effects of CKD on structural outcomes. Further, most studies based estimates of glomerular filtration rate (GFR) on creatinine, which can be influenced by non-GFR determinants of creatinine such as unusual muscle mass, a diet rich in protein, or supplement intake.

Johannes B. Scheppach, MD, and colleagues recently conducted a cross-sectional study nested in a cohort study to evaluate the association of estimated GFR (eGFR) and urinary albumin-creatinine ratio (UACR) with structural brain abnormalities visible on magnetic resonance imaging (MRI). The researchers also sought to determine whether this association was altered when different filtration markers were used to estimate GFR. Results were reported in the *American Journal of Kidney Diseases* [2023;81(3):261-269].

The Atherosclerosis Risk in Communities (ARIC) study recruited 15,792 participants 45 to 64 years of age from four communities in the United States (Washington County, Maryland; Forsyth County, North Carolina; Jackson, Mississippi; and Minneapolis, Minnesota). Participants with evidence of cognitive impairment and a stratified random sample of the remaining participants were invited for a brain MRI scan at study visit 5 (2011-2013) as part of the ARIC Neurocognitive Study (NCS). The current cross-sectional analysis included all White or Black participants with complete data for brain MRI, eGFR, UACR, and covariates.

The outcomes of interest were brain volume reduction, infarcts, microhemorrhages, and white matter lesions. Predictors were log(UACR) and eGFR based on cystatin-C, creatinine, cystatin-C and creatinine in combination, or ß$_2$-microglobulin (B2M). The analysis utilized multivariable linear and logistic regression models fit separately for each predictor based on a 1-IQR difference in the predictor value.

The analysis included 1527 ARIC participants. Mean age was 76.4 years, 879 (57.6%) were women, and 417 (27.3%) were Black. Among all participants, 25.6% (n=391) had one and 2.6% (n=40) had two apolipoprotein E (APOE) e4 risk alleles. At the cognitive status assessment at the study visit, 60.6% (n=926) of the participants had no cognitive impairment, 34.4% (n=525) had mild impairment, and 5.0% (n=76) had dementia.

There was an association between lower eGFR and a higher prevalence of hypertension, diabetes, heart failure, and previous stroke. Those with an eGFR <30 mL/min/1.73 m^2 also had higher levels of albuminuria compared with the rest of the study cohort. Mean brain volume was 1016.0 cm^3, and cortex volume was 399.1 cm^3. Results of brain MRI scans revealed infarcts in 26.1% of participants (n=398) and microhemorrhages in 24.3% of participants (n=371).

There was an association between lower cystatin C-based eGFR and lower brain cortex volume, with a regression coefficient of –0.07 (95% CI, –0.12 to –0.02) per 1-IQR lower eGFR (equivalent to 26.10 mL/min/1.73 m^2). The association of decreased eGFR with brain atrophy in temporal lobe meta-regions of interest, which identify regions of the cortex usually susceptible to neurodegenerative disease, had a regression coefficient of –0.05 (95% CI, –0.11 to 0.1) per 1-IQR lower eGFR. Results were similar when eGFR was estimated with different equations based on cystatin C, creatinine, a combination of cystatin C and creatinine, or B2M.

In assessing cortex volume according to standard eGFR categories, there was an association between lower eGFR with brain cortex atrophy; the association was only statistically significant for participants with eGFR <30 mL/min/1.73 m^2 compared with the reference group with an eGFR of 60 to <90 mL/min/1.73 m^2. Higher levels of albuminuria were also related to lower brain volume; the regression coefficients per 1-IQR-fold greater value were similar to the regression coefficients per 1-IQR lower eGFR.

Associations of albuminuria with macrovascular damage were expressed in adjusted odds ratio (aOR) per 1-IQR-fold greater log(UACR). Participants with higher levels of albuminuria were more likely to have prevalent macrovascular brain damage, such as brain infarcts (aOR, 1.31; 95% CI, 1.13-1.52). This was also seen for the two types of brain infarcts examined in this study: cortical infarcts (aOR, 1.27; 95% CI, 1.05-1.53) and lacunar infarcts (aOR, 1.18; 95% CI, 1.00-1.39).

Higher levels of albuminuria were also associated with increased odds of brain microhemorrhages in general (aOR, 1.30; 95% CI, 1.12-1.51) and subcortical microhem-orrhages in particular (aOR, 1.32; 95% CI, 1.13-1.54). The effect estimate was similar in direction and magnitude but not statistically significant for lobar microhemorrhages.

Similar associations between reduced eGFR and greater albuminuria and microvascular white matter pathologies were seen in conventional MRI and diffusion tensor imaging. The volume of white matter hyperintensities, a sign of brain small vessel damage, was higher in participants with lower eGFR (regression coefficient, 0.07; 95% CI, 0.01-0.15) and higher log(UACR) (regression coefficient, 0.09; 95% CI, 0.03-0.15).

White matter fractional anisotropy (FA) is a measurement for the directional constrain of water diffusion with a unitless range from 0 to 1. In analysis of standard eGFR categories, white matter FA was lower in participants with eGFR <30 mL/min/1.73m^2 than in those in the reference group (regression coefficient,–0.30; 95% CI, –0.59 to –0.01).

The researchers cited some limitations to the study, including the cross-sectional design that did not allow for inference regarding longitudinal effects, the inability to assess the rate of brain atrophy over time, and the possibility of selection bias due to conducting MRI scans on only a part of the ARIC cohort at study visit 5.

In summary, the authors said, "A principal objective of ARIC-NCS is to characterize the morphological manifestations of dementia and cognitive decline. This study builds upon previous reports, which linked kidney function measures to dementia and cognitive decline, and confirms the association of UACR and eGFR with structural brain damage while also providing new information about its etiology as well as its localization in the brain. Future studies need to collect longitudinal data and confirm predictors as risk factors in increased clinical applicability." ■

TAKEAWAY POINTS

- Patients with kidney disease commonly develop cognitive decline. Researchers measured kidney function and albuminuria in participants from the Atherosclerosis Risk in Communities study.
- There were associations between both low kidney function and albuminuria and various structural brain pathologies,
- The results confirm the connection between kidney function and albuminuria with brain damage and provide new information regarding cause and localization in the brain.

Preserved Kidney Function and Nutritional Status in ADPKD

The prevalence of malnutrition among individuals with chronic kidney disease (CKD) is 30% to 40%, and the presence of protein-energy wasting malnutrition is a key predictor of increased risk for morbidity and mortality in that patient population. Results of previous studies have identified several nutritional factors, including serum albumin levels, creatinine levels, body mass index (BMI), and subjective global assessment (SGA) scores, as independent predictors of CKD mortality and treatment failure.

At 1 year following enrollment, 38.6% of the 236 participants with available follow-up data (n=91) had a decrease of >3 mL/min/1.73 m^2 in eGFR.

Among patients with autosomal dominant polycystic kidney disease (ADPKD), even in early stages of the disease, nutritional status may deteriorate due to external compression of the gastrointestinal tract from enlarged kidneys or liver. However, conventional anthropometric parameters, such as body weight and BMI, are ineffective in ADPKD settings.

Jinwoo Lee, MD, and colleagues in South Korea conducted a study to examine the association between good nutritional status and preservation of kidney function in a population of patients with ADPKD. Results were reported in the *Journal of Renal Nutrition* [2023;33(4):529-537].

The prospective, observational study enrolled ambulatory patients with ADPKD at nine tertiary medical centers in Korea from May 2019 to December 2021. Exclusion criteria were age less than 18 years, known end-stage kidney disease at time of enrollment, diagnosis of atypical ADPKD, and use of tolvaptan.

The primary outcome of interest was a decline in estimated glomerular filtration rate (eGFR) of >3 mL/min/1.73 m^2, based on nutritional status assessed by SGA score. Secondary outcomes included a decline in eGFR of >1 mL/min/1.73 m^2, an increase in urine protein-creatinine ratio (UPCR) >0, and an increase in UPCR >0.3, based on SGA score after the 1-year follow-up.

The odds ratio for the primary outcome was calculated using a logistic regression model. In addition, due to differences in several variables, including Mayo classification, serum hemoglobin, serum creatinine, and UPCR between groups stratified according to SGA score, the researchers matched propensity scores.

The final analysis included 236 typical patients with ADPKD with 1-year follow-up data on kidney function and urine proteinuria. Mean age was 45.0 years and 49.6% were female. Approximately 36% had Mayo class 1C ADPKD, 82% had a history of hypertension, and 4% had a history of diabetes. Participants were stratified according to SGA score: SGA 3-5, n=12; SGA 6, n=37; and SGA 7, n=187.

Overall, mean eGFR at baseline was 81.9 mL/min/1.73 m^2, and CKD stage 1 was the most common stage (42.8%). The three groups were similar in the proportion of use of angiotensin-converting enzyme inhibitor/angiotensin II receptor antagonist (ACEi/ARB). Of the baseline variables, there were significant trends only in Mayo classification, hemoglobin levels, basal renal function, UPCR, height-adjusted total kidney volume, height-adjusted total liver volume, and height-adjusted total kidney-liver volume (htTKLV).

At 1 year following enrollment, 38.6% of the 236 participants with available follow-up data (n=91) had a decrease of >3 mL/min/1.73 m^2 in eGFR. The rates of a 1-year eGFR decline >3 mL/min/1.73 m^2 were 53.1% in the SGA 3-6 group and 34.8% in the SGA 7 group (P=.029). The rates of a 1-year increase in UPCR >0.3 were 8.2% in the SGA 3-6 group and 2.7% in the SGA 7 group (P=.172).

In univariable logistic regression models, htTKLV and SGA 3-6 (vs SGA 7) were significant factors related to 1-year eGFR decline of >3 mL/min/1.73 m^2. In a subsequent multivariable regression model that included all independent variables as adjusting variables, the risk of a 1-year decline in eGFR of >3 mL/min/1.73 m^2 was higher in the SGA 3-6 group than in the SGA 7 group, irrespective of the adjustment.

In most subgroups, the preservation of kidney function in the SGA 7 group remained consistent. There was a significant benefit in patients with any of these criteria: age 60 or more years, male, BMI lower than 28, *PKD1* mutation, history of hypertension, absence of diabetes mellitus, and eGFR <60 mL/min/1.73 m^2. In contrast to other subgroups, among patients with a BMI greater than 28, there were no beneficial effects regarding preservation of kidney function associated with a well-nourished status (SGA 7).

The 1-year decline in eGFR of >3 mL/min/1.73 m^2 remained higher in the SGA 3-6 group regardless of proteinuria matching propensity scores.

In results of analysis of covariance, there was a significant association between larger abdominal muscle mass area (AMMA) and better preserved 1-year kidney function. The association remained significant after adjustment for factors such as sex, Mayo classification, history of hypertension, serum hemoglobin, serum albumin, baseline eGFR, baseline UPCR, use of ACEi/ARB, and htTKLV. As AMMA increased, the 1-year follow-up eGFR significantly increased. However, while there was a decreasing proteinuria trend based on AMMA, the trend did not reach statistical significance. In contrast to SGA and AMMA, as abdominal fat mass area increased, the 1-year follow-up eGFR significantly decreased.

In citing limitations to the study, the researchers included the prospective, observational cohort design that could not completely determine the causality between good nutritional status and preserved kidney function; the possibility of selection bias and residual confounding factors; the lack of various biochemical and setting parameters other than eGFR and UPCR in the 1-year follow-up data; and the inability to accurately reflect the trend or trajectory of change in renal function.

In conclusion, the authors said, "Good nutritional status is associated with better-preserved kidney function in nonobese typical ADPKD patients not taking tolvaptan, and these beneficial effects on preserving renal function were reinforced when accompanied by more muscle mass and less fat mass. Future randomized clinical trials should determine the causality between them, and the present results can serve as a foundation for these." ■

TAKEAWAY POINTS

- Malnutrition in patients with autosomal dominant polycystic kidney disease (ADPKD) is associated with increased morbidity and mortality.
- Researchers reported results of a study examining whether nutritional status is associated with the preservation of kidney function in a population of patients with ADPKD.
- There was an association between good nutritional status and better-preserved kidney function in nonobese patients with ADPKD who did not take tolvaptan.

Integrated Home Dialysis Model for Patients Initiating KRT

Selection of a dialysis modality is a crucial decision for patients requiring kidney replacement therapy (KRT). Patient autonomy can be enhanced with the selection of home hemodialysis or peritoneal dialysis, resulting in improved quality of life compared with in-center hemodialysis. Benefits associated with peritoneal dialysis compared with in-center hemodialysis include preservation of residual kidney function, the ability to travel, decreased risk of bacteremia, and reduced health care costs. However, up to 50% of patients cannot continue peritoneal dialysis beyond 2 years of treatment. In addition, compared with home hemodialysis, patients receiving peritoneal dialysis may face increased risk of hospitalization and mortality, particularly after the first year of treatment.

The integrated home dialysis model is designed to initiate dialysis using peritoneal dialysis with a plan to transition to home hemodialysis, incorporating initial lifestyle advantages and a home-based option following termination of peritoneal dialysis. According to **Louis-Charles Desbiens, MD, MSc,** and colleagues, there are few data available on direct comparisons of outcomes of patients transitioning from peritoneal dialysis to home hemodialysis with those of patients who initiated KRT with home hemodialysis.

The researchers performed an observational analysis of data from the Canadian Organ Replacement Register (CORR), a validated register that includes all adults initiating KRT in Canada. Results of the analysis were reported in the *American Journal of Kidney Diseases* [2023;83;(1):47-57].

The analysis included data on all patients who initiated peritoneal dialysis or home hemodialysis within the first 90 days of KRT between 2005 and 2018. The exposure was patients who transitioned from peritoneal dialysis to home hemodialysis (PD + HHD group) versus those who initiated KRT with home hemodialysis (HHD group). The outcomes of interest were (1) a composite of all-cause mortality and modality transfer (to in-center hemodialysis or peritoneal dialysis for 90 days) and (2) all hospitalizations (considered as recurrent events).

A total of 63,327 patients were identified in the CORR. At the 90th day of KRT, 745 patients received home hemodialysis and 18,726 received peritoneal dialysis. Of those, 4420 patients transitioned from peritoneal dialysis to in-center hemodialysis and 163 patients transitioned from peritoneal dialysis to home hemodialysis in less than 90 days following termination of peritoneal dialysis. Patients in the PD + HHD group remained on peritoneal dialysis for a median of 1.9 years and underwent a median of 4.0 days of in-center hemodialysis before transitioning to home hemodialysis.

Compared with those in the HHD group (n=711), patients in the PD + HHD group were younger (51 years vs 52 years), more often of minority race (41% vs 26%), and had a lower burden of comorbidity. Patients in the PD + HHD group were more likely to reside in western Canada and less likely to live in Ontario. Median follow-up time in the HHD group was 2.4 years compared with 1.9 years in the PD + HHD group. In each group, a median of two hospitalizations per patient occurred.

In the incident-match analysis, a median of 157 patients in the PD + HHD group were matched to 157 HHD patients. Following matching, the distribution of propensity scores was similar between the two groups. Patient characteristics were also similar between the two groups, with the exceptions of minority race (36.8% in the HHD group, 40.7% in the PD + HHD group), hemoglobin levels (102 g/L in the HHD group, 106 g/L in the PD + HHD group), and use of antihypertensive medications (72.6% in the HHD group, 78.5% in the PD + HHD group).

There was no statistically significant difference in the incidence of the composite event (modality transfer or death) between the groups: hazard ratio [HR], 0.88; 95% CI, 0.58-1.32 for PD + HHD vs HHD). The risk of hospitalization was also similar between the two groups: 0.89 hospitalizations per patient-year in the PD + HHD group versus 0.85 in the HHD group (HR, 1.04; 95% CI, 0.76-1.41). Results were comparable in analysis of individual components of the composite outcome and in joint modeling of the composite outcome and hospitalizations.

In the vintage-match analysis, follow-up of patients receiving home hemodialysis began after a KRT vintage equivalent to their PD + HHP counterpart at transition (median of 141 patient pairs). Baseline patient characteristics and propensity score distribution were similar between the groups, with the exception of hemoglobin levels and use of antihypertensive medications. The incidence of the terminal composite outcome was significantly lower in the PD + HHD group (HR, 0.61; 95% CI, 0.40-0.94), but comparable for recurrent hospitalizations (HR, 0.85; 95% CI, 0.59-1.24). When joint or individual modeling of outcomes was used, results were similar.

> The incidence of the terminal composite outcome was significantly lower in the PD + HHD group but comparable for recurrent hospitalizations.

The researchers cited some limitations to their findings, including the risk of survivor bias in the PD + HHD group, limits to the generalizability of the findings related to the inability to assess patients who intended but could not transition to home hemodialysis and to the matching process, the relatively small size of the group of patients in the PD + HHD group, the inability to account for eligibility for kidney transplantation, and not evaluating patients' quality of life.

In conclusion, the authors said, "This registry study showed that patients who transition from peritoneal dialysis to home hemodialysis have similar risks of hospitalization, modality transfer, and death compared with patients who initiate home hemodialysis within the first 90 days of KRT, and this is despite a higher dialysis vintage. At equivalent dialysis vintages, peritoneal dialysis plus home hemodialysis patients displayed longer survival than patients treated with home hemodialysis but had similar rates of hospitalization.

"This study reinforces the feasibility and safety of the integrated home dialysis model, capitalizing on the early lifestyle and economic benefits of peritoneal dialysis while preserving long-term clinical outcomes of home hemodialysis. However, our results are subject to survivorship bias and cannot be generalized to the entire peritoneal dialysis population intending to transfer into home hemodialysis. Future studies are required to optimize this KRT paradigm, with more personalized prediction of peritoneal dialysis ending and the identification of an optimal timing for the peritoneal dialysis-to-home hemodialysis transition." ■

TAKEAWAY POINTS

- Researchers compared outcomes of patients transitioning from peritoneal dialysis to home hemodialysis (PD + HHD group) with those of patients who initiated kidney replacement therapy with home hemodialysis (HHD group).
- In the incident-match analysis, the two groups had a similar risk of the composite outcome of all-cause mortality and modality transfer.
- In the vintage-match analysis, patients in the PD + HHD group had lower hazard for the composite outcome, but a similar risk for hospitalization compared with the HHD group.

Estimating Relative Survival Among Patients With Kidney Failure

Providers and policy-makers rely on population estimates of the attributable mortality risk associated with chronic diseases to make decisions regarding therapeutic choices and to justify funding for research. Disease mortality estimates also provide researchers with tools to identify disparities in care or improvements in treatment over time, and provide a more accurate estimate that can be compared across populations and over time.

Previous studies have developed methods to estimate disease-specific survival. However, according to **Margaret R. Stedman, PhD, MPH,** and colleagues, those methods have been underutilized in research focused on kidney disease. Relative survival is often used to measure disease-specific survival where information on cause of death is unavailable; however, there are few publications using US data that implement relative survival methods in kidney disease research.

Noting that estimates of mortality from kidney failure are misleading because mortality in patients with kidney failure is connected to mortality attributed to comorbid conditions, the researchers conducted a longitudinal cohort study to develop an alternative method to reduce the bias in estimating mortality due to kidney failure using life table methods. Results of the study were reported in the *American Journal of Kidney Diseases* [2024;83(1):28-36].

The study utilized data from the US Renal Data System and the Medicare 5% sample to identify an incident cohort of patients 66 years of age and older who had a first diagnosis of kidney failure in 2009 and a similar population cohort without kidney failure. The study exposure was kidney failure, and the outcome of interest was death.

The researchers estimated relative survival of patients with incident failure by creating comorbidity-, age-, sex-, race-, and year-specific life tables. The tables also provided an estimate of excess deaths related to kidney failure. The estimates were compared with those based on standard life tables (not adjusted for comorbidity).

A total of 53,612 patients with incident kidney failure had complete information on age, sex, and race. Following application of exclusion criteria, the final cohort with kidney failure totaled 31,944. Of those, 0.7% (n=251) had received a preemptive kidney transplant on or before the index date. Following similar exclusions and exclusion of patients with kidney failure, the 5% sample of Medicare beneficiaries yielded a cohort of 1,237,540 individuals without kidney failure.

Comorbidity scores were derived from a Cox proportional hazards regression model, predicting time to all-cause death from age, sex, designated race, and individual comorbidities. Designated race was grouped as Black, White, and other, and age was grouped into 5-year increments. Comorbidity models were stratified by diabetes. Log scaler comorbidity scores were categorized as low (≥0), medium (>0 to 0.5), or high comorbidity (≥0.5).

The proportion of Black patients in the kidney failure population was more than twice as high as that in the population without kidney failure (18% vs 7%, respectively). There were substantially more comorbidities in the kidney failure cohort compared with the cohort without kidney failure (71% in the high category vs 24% in the high category, respectively). Over follow-up of 8 years, 11% of the population with kidney failure survived compared with 70% of the population without kidney failure. Two percent of patients received a transplant during the follow-up period; this event was not censored.

Using standard life tables adjusted for age, sex, race, and year, without comorbidities, the 5-year relative survival was 31%. Using life tables adjusted for those factors, as well as for comorbidities, the 5-year relative survival was 36%. Relative survival from kidney failure was higher among patients with fewer comorbidities (47% for low comorbidity). Older age groups had lower relative survival (22% for patients 91 to 95 years of age). Men and women had similar relative survival (36%). Compared with White patients, relative survival was highest for Black patients and patients of other races (33% vs 48% vs 44%, respectively).

Compared with other chronic diseases, relative survival was lowest for patients with kidney failure. Kidney failure, dementia, and heart failure had the lowest relative survival (36%, 50%, and 61%, respectively) compared with stroke, lung disease, and peripheral arterial disease (78%, 79%, and 83%, respectively).

Patients with incident kidney failure ages 66 to 70 years of age had a survival comparable with adults without kidney failure roughly 86 to 90 years of age and 91 to 95 years of age, respectively.

The researchers cited some limitations to the study findings, including not including younger patients, the lack of data on patients with kidney failure not treated with dialysis or preemptive transplant, and the inability to compare relative survival to patients with kidney failure who pursue conservative, nonanalytic therapy. In addition, the authors said that relative survival estimates can be improved by narrowing the specificity of the covariates collected.

In summary, the researchers said, "Relative survival is an estimate of cause-specific survival, a measure that is adjusted for the differences in survival due to natural aging process and other causes of death. Relative survival using comorbidity-adjusted life tables gives us a less biased estimate of the mortality burden from kidney failure that may be easier to communicate to policy-makers and patients. Furthermore, it can be directly compared across age, sex, race, year, and comorbidity groups, which makes it ideal for national and international research where demographics vary. Our estimates help quantify the immense mortality burden due to kidney failure and underscore the importance of disease prevention efforts for older adults." ■

TAKEAWAY POINTS

- Researchers reported results of a study to develop an alternative method to estimate mortality due to kidney failure using life table models.
- Using standard life tables (adjusted for age, sex, race, and year), 5-year relative survival for patients with kidney failure was 31%.
- When standard life tables were also adjusted for comorbidities, the 5-year relative survival rate for patients with kidney failure was 36%.

Reporting of Sex and Gender in Trials Among Adults Receiving Hemodialysis

Sex is a biological construct defined by genetics, specialized cells, and distinct protein expression. Gender is a construct defined by social, environmental, cultural, and behavioral factors that influence a person's identity.

There are potential differences in disease epidemiology, pathophysiology, and prognosis across sex and gender, making sex and gender important considerations in randomized, controlled trials. There are also differences based on sex and gender in pharmacokinetics and pharmacodynamics. Considerations regarding sex and gender are required in funding and regulatory agency applications in the United States, Canada, and Europe; however, only sex is referred to in reporting guidelines for randomized, controlled trials.

Clinical responses to interventions in kidney disease and other chronic diseases may be influenced by sex and gender, which, according to **David Collister, MD, PhD,** and colleagues, should be considered when examining the efficacy and safety of interventions or assessing associations in observation studies. There may also be underrepresentation of female persons/women in randomized, controlled trials in kidney failure, as well as in trials of other chronic diseases such as cardiovascular disease, including acute coronary syndrome, heart failure, and primary-secondary prevention.

The researchers conducted a meta-epidemiologic study to characterize how sex and gender were incorporated in the design, conduct, and analysis of trials in adults with kidney failure undergoing maintenance dialysis. They also sought to determine whether the proportion of woman or female participants varied across trial characteristics. Results were reported in the *American Journal of Kidney Diseases* [2023;81(5):575-582].

The study included randomized, controlled trials in patients receiving maintenance dialysis published in high-impact general medicine, nephrology, and cardiology journals. The researchers sought to test the hypothesis that the proportion of women or female participants would be less than in the general dialysis population; would vary by study design, trial populations, and interventions; and that sex and gender considerations would be reported suboptimally.

The journals included were the *New England Journal of Medicine, The Lancet, JAMA, BMJ,* the *Annals of Internal Medicine, Kidney International (KI),* the *Journal of the American Society of Nephrology (JASN),* the *American Journal of Kidney Diseases (AJKD),* the *Clinical Journal of the American Society of Nephrology (CJASN), Nephrology Dialysis Transplantation (NDT), Circulation,* the *Journal of the American College of Cardiology,* and the *European Heart Journal*. The search included the terms "dialysis" and "randomized controlled trial" and was limited to publications from January 1, 2000, to December 3, 2020.

Inclusion criteria were studies restricted to people ≥18 years of age, those that included people with kidney failure treated with hemodialysis or peritoneal dialysis but not kidney transplantation or kidney replacement therapy for acute kidney injury, no secondary analyses or substudies, no long-term follow-up or extension studies, and those that did not have multiple interventions or sequential stages.

The search revealed a total of 1155 studies that met eligibility criteria. Of those, 561 randomized controlled trials were included in the current analysis. The majority of included studies were from core nephrology journals: *NDT* (n=176; 31.4%); *AJKD* (n=133; 23.7%); *KI* (n=86; 15.3%); *JASN* (n=77; 13.7%); and *CJASN* (n=55; 9.8%). The majority of the included studies were parallel in design (n=391; 69.7%) and had a median size of 60 participants. Most were from Europe (n=217; 38.6%) and North America (n=166; 29.5%). Median duration of follow-up was 154 days.

Most of the studies (80.6%) were conducted in populations of patients receiving maintenance hemodialysis. Twenty-five percent compared the treatment of interest with a placebo arm, 25% with a usual care arm, and 50% with an active alternative therapy arm. Thirty-seven percent were masked.

The mean proportion of women or female participants in the trials that reported the sex and/or gender of participants was 0.40. The highest proportion of women or female participants was in South America (0.46) and the lowest was in Europe (0.38). In countries participating in the DOPPS (Dialysis Outcomes and Practice Patterns Study), the proportion was highest in Italy (0.42) and lowest in Belgium (0.31). Of the studies that reported gender, none reported the inclusion of any transgender, nonbinary, or gender-diverse populations.

Region was the only trial characteristic that was independently associated with the proportion of women or female participants; with the exception of Asia, the proportions were similar in the reported regions. In the multivariable linear regression model, there was no other trial characteristic associated with the participation of women or female participants ($P \geq .05$ for all other covariates).

In referring to the sex/gender demographics of participants, 39.0% (n=219) used sex, 26.6% (n=149) used gender, and 3.4% (n=19) used both. Thirty-one percent of the trials (n=174) did not report sex or gender, but used a descriptor instead (ie, male/female or man/woman) with no specific reference to sex and/or gender.

Over time, the reporting of sex and gender varied, with an increased reporting of sex most recently. Participants were described as male/female in 56.2% of trials (n=315), man/woman in 25.3% (n=142), or both in 15.5% (n=87). Sex and/or gender was not reported in 3% (n=17) of the trials. The descriptors also varied over time.

Sex/gender was used as an inclusion criterion in 2.7% (n=15) of the trials, and as an exclusion criterion in 26.6% (n=149) (ie, related to pregnancy, breastfeeding, or contraception). Sex or gender were used in 4.5% of trials (n=25) as a factor for stratification or minimization during randomization. Sex/gender were used in 4.8% of trials (n=27) in subgroup analyses, and 15.7% (n=88) used sex/gender to adjust treatment effects.

Study limitations cited by the authors included the use of only high-impact journals, unawareness of specific journal policies regarding sex/gender reporting, the lack of any trials from Africa, the underrepresentation of other regions such as Eastern Europe or the Middle East, and the poor data quality for some study-level covariates.

In conclusion, the authors said, "Randomized controlled trials in dialysis are representative of the general dialysis population with regard to sex and gender, but they uncommonly report both and often do not include either in their reporting or analysis." ■

TAKEAWAY POINTS

- Researchers reported results of a meta-epidemiologic study examining how sex and gender concepts are incorporated into randomized, controlled trials in populations of adults with kidney failure receiving maintenance dialysis.
- The study included 561 randomized, controlled trials with a median size of 60 participants and a median follow-up period of 154 days.
- Results suggested that the trials were representative of the general dialysis population with regard to sex and gender, but reporting of both sex and gender was uncommon.

Physical Activity and eGFR in Kidney Transplant Recipients

The aging of the world's population has resulted in a dramatic increase in the prevalence of chronic kidney disease (CKD) worldwide. Further, the number of individuals receiving kidney transplantation is estimated to double by 2030. Successful transplantation reduces the mortality rate associated with end-stage kidney disease, and advances in immunosuppression therapy have improved short-term graft survival and reduced the risk of mortality among kidney transplant recipients.

However, according to **Takuya Ohata, PT, MS,** and colleagues, the rate of long-term graft survival has not yet reached a satisfactory level. Declines in estimated glomerular filtration rate (eGFR) following kidney transplantation are strongly linked to premature mortality as well as the incidence of graft failure.

Physical activity is a recognized modifiable lifestyle factor for patients with CKD. Previous studies have suggested that physical activity has beneficial effects on health-related outcomes in kidney transplant recipients. However, there are few data available on the effects of the type or intensity of physical activity and sedentary behavior on eGFR in that patient population. The researchers conducted a study designed to clarify the association between accelerometry-measured PA and sedentary behavior and eGFR in kidney transplant recipients. Results were reported in the *Journal of Renal Nutrition* [2023;33(6):755-763].

Physical activity before renal transplant was retrospectively measured using the International Physical Activity Questionnaire Short Form; the value was used as a covariable in the statistical analyses. The total physical activity was then calculated and presented as metabolic equivalents (METs) per minute per week.

All participants wore a triaxial accelerometer to measure physical activity for 24 hours per day over 10 consecutive days. Proprietary software packages were used to download the data from the accelerometers to quantify physical activity. For the data to be considered valid, at least 7 consecutive days within a 24-hour period of wear time per day were required. Within the valid period, any constitutive 7-day data were extracted for further analyses. Measured physical activity was classified based on intensity: (1) light physical activity; (2) moderate-to-vigorous physical activity; and (3) sedentary behavior.

Multiregression analyses of single-factor, partition, and isotemporal substitution models were used to examine the association of each type of physical activity with eGFR. The isotemporal model was applied to examine the estimated effects of substituting 30 minutes of sedentary behavior with an equal amount of light physical activity or moderate-to-vigorous physical activity on eGFR. Physical function was evaluated using four measures: (1) grip strength, assessed using a grip strength meter; (2) knee extensor muscle strength, measured using a handheld dynamometer; (3) gait speed, measured twice using a digital stopwatch; and (4) 6-minute walking test, evaluated according to the American Thoracic Society guidelines.

In multiple regression analyses, eGFR could be explained by sedentary behavior and moderate-to-vigorous physical activity. In the partition model, there was a positive association between moderate-to-vigorous physical activity and eGFR ($P<.05$). There was no positive association between sedentary behavior or light physical activity and eGFR. The isotemporal substitution model demonstrated that substituting time spent in sedentary behavior with moderate-to-vigorous physical activity led to beneficial changes in eGFR ($P<.05$). There was no significant improvement in eGFR substituting sedentary behavior with light physical activity.

In the partition model, there was a positive association between moderate-to-vigorous physical activity and eGFR ($P<.05$). There was no positive association between sedentary behavior or light physical activity and eGFR. The isotemporal substitution model demonstrated that substituting time spent in sedentary behavior with moderate-to-vigorous physical activity led to beneficial changes in eGFR ($P<.05$).

TAKEAWAY POINTS

- Recipients of kidney transplantation may experience a decline in estimated glomerular filtration rate (eGFR), a complication that is associated with premature mortality in that patient population.
- Researchers conducted a cross-sectional study to examine the association between accelerometry-measured physical activity and sedentary behavior and eGFR among recipients of kidney transplantation.
- There was an independent and positive association between moderate-to-vigorous physical activity and eGFR; replacing 30 minutes of sedentary behavior with moderate-to-vigorous physical activity may lead to improvements in eGFR among kidney transplant recipients.

The cross-sectional study included 82 kidney transplant outpatients. Of those, 65 were included in the final analyses. Average age of the 65 included patients was 56.9 years, 58.5% (n=38) were men, and mean body mass index was 21.7 kg/m^2. Mean time post-transplant was 83.0 months, and 63% (n=41) underwent dialysis prior to transplant. Comorbidities included diabetes (18.5%, n=12), hypertension (44.6%, n=29), dyslipidemia (12.3%, n=8), and hyperuricemia (6.2%, n=4). Mean eGFR at baseline was 42.5 mL/min/1.73 m^2.

Immunosuppression medications included calcineurin inhibitors (tacrolimus or cyclosporine, 98.5%, n=64), antiproliferative agents (mycophenolate mofetil or azathioprine, 96.9%, n=63), mTOR (mammalian target of rapamycin) inhibitor (everolimus, 50.8%, n=33), and steroids (prednisone, 100%, n=65).

The authors cited some limitations to the study findings, including the nonprospective and noninterventional design of the study, creating the possibility of biases that prevented the identification of the cause-and-effect relationship between physical activity and eGFR; not adjusting the statistical analyses for the renal function of the study population immediately following transplantation or for dietary data; and the small sample sizes for the subgroup analyses.

In conclusion, the researchers said, "The present study suggested that moderate-to-vigorous physical activity was an independent explanatory variable for eGFR in renal transplant recipients and replacing 30 minutes of sedentary behavior with moderate-to-vigorous physical activity after renal transplantation might lead to the maintenance or improvement of eGFR in renal transplant recipients." ■

Effect of an Intervention Designed to Improve Patient Access to Kidney Transplant

For patients with kidney failure, survival requires either ongoing dialysis treatment or a kidney transplant. Compared with dialysis, transplant is associated with improved quality of life and a possible gain of 10 or more years of life expectancy. In addition, over a 5-year period, transplant saves the health care system approximately $14.6 million USD, driven primarily by costs of dialysis. Compared with deceased donor kidney transplant, living donor transplants are associated with further advantages, including improved patient and graft survival.

Nevertheless, many eligible patients do not receive a kidney transplant. According to **Amit X. Garg, MD,** and colleagues, the reasons for the care gap are complex, and include barriers for patients, families, health care professionals, chronic kidney disease (CKD) programs, transplant centers, and health care systems.

Several countries have initiated interventions to address the barriers to care. Dr. Amit et al conducted the Enhance Access to Kidney Transplant and Living Donor Donation (EnAKT LKD) trial, a multicomponent intervention designed to target several barriers that prevent eligible patients from completing key steps toward receiving a kidney transplant. Results were reported in *JAMA Internal Medicine* [doi:10.1001/jamainternmed.2023.5802].

The pragmatic, two-arm, parallel-group, open-label, registry-based, superiority cluster, randomized clinical trial included all 26 CKD programs in Ontario, Canada. The programs care for patients with advanced CKD who are approaching the need for dialysis or are already receiving maintenance dialysis. The trial period was November 1, 2017, to December 31, 2021.

The intervention had four main components: (1) administrative support to establish a new local quality improvement team to manage local performance; (2) transplant education for health care staff, patients, and potential donors; (3) patient support in the form of transplant recipients and living donors sharing their experience; and (4) data and accountability, including program-level performance reports and oversight by administrative leaders.

The primary outcome of interest was the rate of steps completed toward receiving a kidney transplant. Each patient could complete up to four steps, and for each patient, the researchers only counted each step once. The steps were: (1) referred to a transplant center for evaluation; (2) had a potential living donor contact a transplant center for evaluation (if multiple donors initiated evaluations, only the first donor counted); (3) added to the deceased donor waitlist; and (4) received a transplant from a living or deceased donor.

There were five secondary outcomes that focused on living donor transplant: (1) donor evaluation or living donor transplant [step 2 or a subset of step 4]; (2) donor evaluation [step 2]; (3) referral and donor evaluation [steps 1 and 2]; (4) living donor transplant [subset of step 3]; and (5) preemptive living kidney donor transplant [a subset of step 4].

During the trial period, the 26 CKD programs cared for 20,375 patients with advanced CKD who were potential candidates for kidney transplantation. The intervention group included 9780 patients who entered the trial from 13 CKD programs, and the usual-care group included 10,595 patients from 13 CKD programs. All patients were included in the intention-to-treat analysis.

The two groups were similar in both patient and center characteristics. Median age in the overall cohort was 61 years, 38% (n=7786) were women, and 57% (n=11,517) had a history of diabetes. At trial entry, 51% (n=10,025) were nearing the need for dialysis; the remaining 49% were receiving maintenance dialysis. In the group nearing the need for dialysis, median estimated glomerular filtration rate (eGFR) was 16 mL/min/1.73 m^2, median random urine albumin-to-creatinine ratio was 162 mg/mmol, and the 2-year predicted risk of kidney failure was 45%.

Among the patients who entered the trial on November 1, 2017, already receiving maintenance dialysis, median duration of dialysis was 2.6 years. Of the patients who entered the trial nearing the need for dialysis, 48% initiated maintenance dialysis during the trial. Prior to entering the trial, 80% of patients had completed no steps toward receiving a kidney transplant.

During a median follow-up of 2.1 years, 1.4% (n=290) of the cohort emigrated from the province, 1.1% (n=225) recovered their kidney function, 13.7% (n=2789) became ineligible for a kidney transplant, and 16.8% (n=3432) died. The rates were similar in the two groups. Of the overall cohort, 5.4% of patients (n=484 in the intervention group [4.9%] and 621 in the usual care group [5.9%]) transferred to a CKD program in the alternate group.

There was no significant difference in the rate of the primary outcome between the intervention group (n=9780) versus the usual-care group (n=10,595): 5334 steps versus 5638 steps, 24.8 versus 24.1 steps per 100 patient-years; adjusted hazard ratio (aHR), 1.00; 95% CI, 0.87-1.15. During follow-up, 1.3% of patients in the intervention group (n=130) completed all four steps, 5.8% (n=572) completed three or more, 15.3% (n=1493) completed two or more, and 32.1% (n=3138) completed one or more steps. In the usual-care group, the corresponding numbers were 1.2% (n=129), 5.6% (n=589), 14.5% (n=1538), and 31.9% (n=3382).

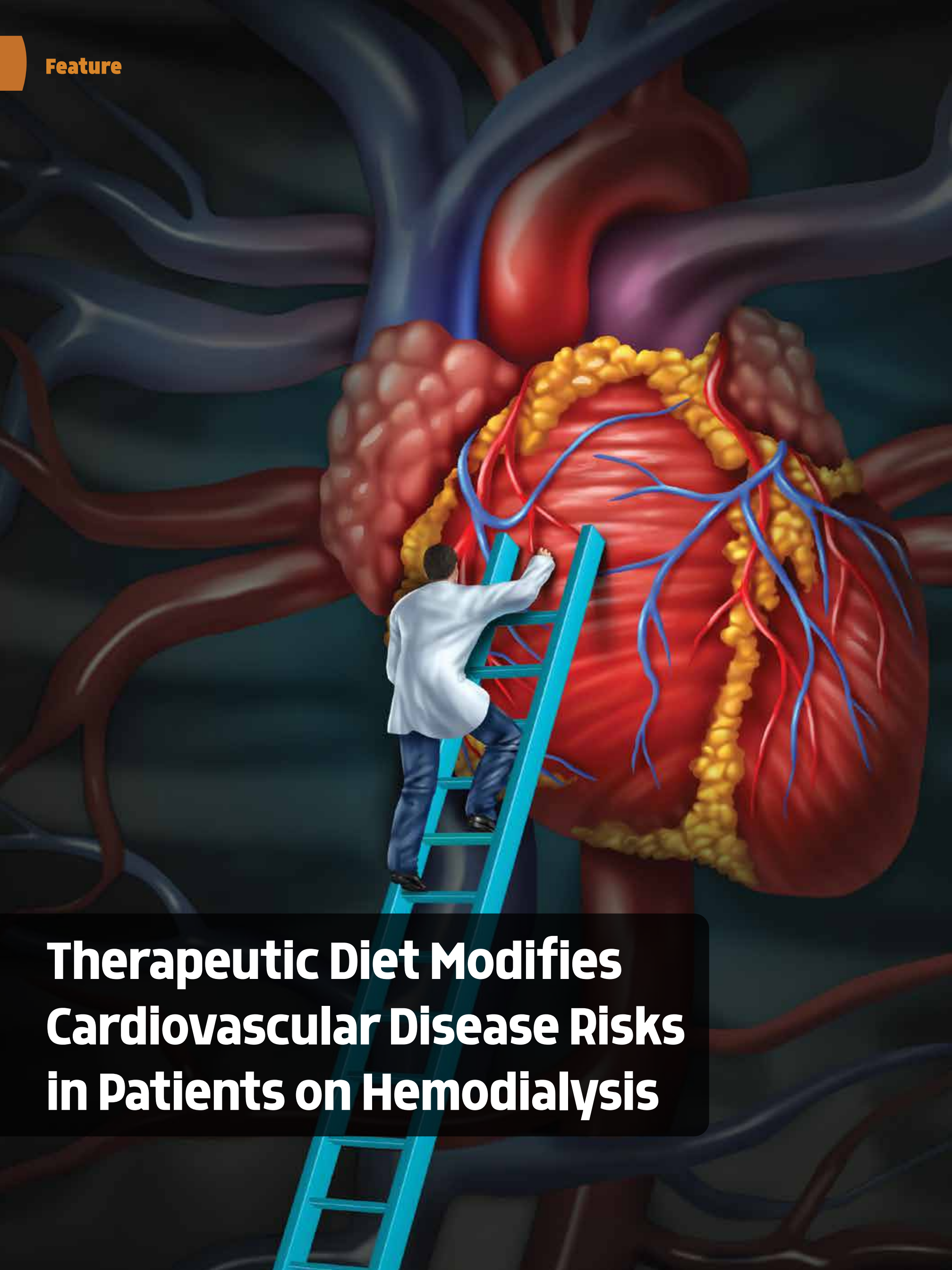
For the five secondary outcomes focusing on living donor kidney transplant, there were no notable differences between the two groups. The rate of starting a living donor evaluation (step 2) for patients with CKD who did not have one prior to trial entry was numerically higher, but not notably different between the two study groups: 923 in the intervention group versus 920 in the usual-care group; 4.9 versus 4.4 evaluations per 100 patient-years; aHR, 1.22; 95% CI, 0.97-1.54.

Limitations to the study cited by the authors included the impact of the COVID-19 pandemic on delivery of the intervention and a possible lessening of momentum for the initiative as health care priorities shifted to focus on the pandemic, and not addressing inequities in access to transplantation.

In conclusion, the researchers said, "The findings of this randomized clinical trial did not show that a novel multicomponent intervention significantly increased the rate of completed steps toward receiving a kidney transplant. Improving access to transplantation remains a global priority that requires substantial effort." ■

TAKEAWAY POINTS

- Researchers reported results of an intervention designed to help patients with advanced chronic kidney disease (CKD) complete key steps toward receiving a kidney transplant.
- Among 20,375 patients from 26 CKD programs in Canada, the intervention did not significantly increase the rate of steps completed toward kidney transplantation compared with usual care.
- There was no significant increase in overall access to kidney transplantation among transplant-eligible patients with advanced CKD.



Therapeutic Diet Modifies Cardiovascular Disease Risks in Patients on Hemodialysis

The leading cause of death among individuals with kidney failure is cardiovascular disease. Patients with kidney failure face various cardiovascular risk conditions, including complications related to abnormalities of chronic kidney disease–mineral and bone disorder, accumulated uremic toxin levels, protein-energy wasting, and inflammation.

Unhealthy diet is known to exacerbate nutritional and metabolic derangements, and nutritional therapy may help manage the uremic complications associated with cardiovascular risk in patients with kidney failure. According to **Wan-Chuan Tsai, MD, PhD,** and colleagues, there are few data available on how therapeutic diets with various dietary strategies act as modifiers of the diverse biochemical parameters related to cardiovascular disease in patients with kidney failure.

The researchers conducted a randomized crossover trial to test the hypothesis that a therapeutic diet that was dialysis-specific and included a combination of favorable dietary strategies and therapies would provide adequate nutrition while reversing cardiovascular risk conditions, including altered mineral metabolism, uremic toxin accumulation, and inflammation. Results of the trial were reported in the *Journal of Renal Nutrition* [2023;33(6):730-739].

The study was conducted at a hemodialysis unit of a tertiary teaching hospital between October 28, 2020, and December 10, 2020.

Subjects were recruited and invited to participate if they met inclusion criteria (age older than 20 years, having end-stage kidney disease and undergone hemodialysis three times a week for more than 3 months, having adequate dialysis, serum intact parathyroid hormone [PTH] levels <100 pg/mL, and good dietary compliance). Exclusion criteria were serum albumin level <2.5 g/dL; hospitalization within the past 4 weeks; use of prebiotics, probiotics, symbiotics, or antibiotics within the past 4 weeks; history of psychiatric disorder; mental disability; dislike of the study meals; soft diet requirement; or vegetarian status.

The study was designed to compare a therapeutic diet with usual diets for 7 days, separated by a 4-week washout period. The therapeutic diet was characterized by adequate calorie and protein amounts, natural food ingredients with a low phosphorous-to-protein ratio, higher portions of plant-based food, and high fiber content.

The primary outcome of interest was the mean difference in the change-from-baseline in intact fibroblast growth factor 23 (FGF23) level between the two diets during the 7-day study period. Secondary outcomes included changes in serum phosphate, calcium, intact PTH, and C-terminal FGF23 levels. Exploratory outcomes were changes in serum p-cresyl sulfate (PCS), indoxyl sulfate (IS), and high-sensitivity C-reactive protein (hs-CRP) levels.

Outcome measures were recorded at the beginning of each study period, after 2 days, after 5 days, and at the end of each study period (7 days). Eight repeated measurements for each participant were obtained to assess the changes in study outcomes at different time points.

A total of 150 patients were screened for eligibility. Of those, 22% (n=33) underwent randomization. Of the 33 randomized participants, three were excluded during the first study period. The remaining 30 participants (15 in each group) completed the first and second study periods.

Mean age was 62 years, 56% (n=18) were men, and mean dialysis vintage was 8 years. Mean dry weight was 61 kg, and mean body mass index was 24 kg/m^2. Approximately 97% of the overall cohort had arteriovenous fistula, and 84% used low dialysate calcium.

Relative to participants who consumed the usual diet, there were significant reductions in change-from-baseline intact FGF23, phosphate, intact PTH, and C-terminal FGF23 levels in those who consumed the therapeutic diet. There was significant elevation in the change-from-baseline calcium level among those in the therapeutic diet group. The therapeutic diet also tended to lower the total IS level compared with the usual diet (*P*=.07). There were no significant differences in change-from-baseline free IS, total PCS, free PCS, or hs-CRP levels between the two study diets.

The primary and secondary outcomes were analyzed at two other time points (2 and 5 days after dietary interventions). After 2 days of the dietary intervention, the therapeutic diet had a significant phosphate-lowering effect and tended to elevate the calcium levels (*P*=.09). There was no effect on intact FGF23, intact PTH, and C-terminal FGF23 levels relative to the usual diet. After 5 days of the intervention, the therapeutic diet was associated with significant reductions in phosphate and intact PTH levels, significant elevations in calcium levels, and tended to reduce intact FGF23 levels (*P*=.06). There was no effect on C-terminal FGF23 levels relative to the usual diet after 5 days.

Citing limitations to the study, the authors included the intent to examine only the short-term beneficial effects of therapeutic diets, not standardizing the usual diet, and limiting the type of foods included in the study menus, which may have affected the dietary adherence of the study participants.

In conclusion, the researchers said, "It is suggested that eating the right type of food in the right amounts is good for human health, and this is particularly true for patients on dialysis. In contrast to the previous published studies that modified a single dietary factor as the main approach, this study adopted a comprehensive dietary approach comprising a variety of favorable dietary strategies to modulate the diverse cardiovascular risks in patients on hemodialysis. Over a 7-day period, this dietary strategy showed promising effects on mineral metabolism and uremic toxins. In order to promote these diets among dialysis patients, future studies with longer durations of dietary interventions are warranted." ■

TAKEAWAY POINTS

- Researchers examined the effects of therapeutic diets with a variety of different dietary strategies on modifying diverse biochemical parameters related to cardiovascular disease in patients with kidney failure on hemodialysis.
- Compared with the usual diet, the therapeutic diet lowered intact fibroblast growth factor 23, reduced intact serum phosphate levels, and reduced intact parathyroid hormone levels,.
- The therapeutic diet also increased calcium levels and tended to lower total indoxyl sulfate levels. There was no significant effect on high-sensitivity C-reactive protein levels.

Dr. Sankar Niranjan to Receive Distinguished Service Award From NKF

The National Kidney Foundation (NKF) will honor **Sankar Niranjan, MD, FASN,** with its Medical Advisory Board (MAB) Distinguished Service Award in May at the NKF 2024 Spring Clinical Meetings in Long Beach, California.

Sankar Niranjan, MD, FASN

A practicing nephrologist in Connecticut, Dr. Niranjan has served as his state's MAB chair since 2009. He has been an attending physician and nephrologist at St. Francis Hospital and Medical Center in Hartford, Connecticut, since 2004 and has mentored young physicians and nephrology trainees as a community-based faculty member at the University of Connecticut School of Medicine in Farmington. He was previously an owner/partner at Greater Hartford Nephrology LLC and a medical director at DaVita Dialysis in Bloomfield, Connecticut.

The award recognizes Dr. Niranjan's outstanding educational activities and community service to advance the NKF's mission at a local level. To that end, he has advocated for the prevention and early detection of kidney disease as part of NKF's Kidney Early Evaluation Program in Connecticut and facilitated screenings at inner-city community events and minority places of worship. He has also conducted camps to screen patients for kidney disease in rural areas of Southern India.

"Dr. Niranjan is a shining example of excellence in action with his deep commitment to helping everyone, particularly diverse communities, to obtain optimal kidney health through prevention and early detection," said NKF president **Sylvia Rosas, MD, MSCE**.

AKF Announces Inaugural AMKD Awareness Day

The American Kidney Fund (AKF) has announced that April 30, 2024, has been designated AMKD Awareness Day. AMKD (APOL1-mediated kidney disease) is a spectrum of kidney diseases associated with mutations in the apolipoprotein L1 (APOL1) gene. AMKD has been linked to an increased risk for rapidly progressing kidney disease in individuals of Western and Central African descent.

All people have two copies of the APOL1 gene. However, those with Western and Central African ancestry, including those who identify as Black, African American, Afro-Caribbean, and/or Latina/Latino, are at increased risk of having a mutation in one or both genes. It is estimated that 13% of Black Americans have two mutations of the APOL1 gene and a one in five chance of developing kidney disease.

In a press release from AKF, **LaVarne A. Burton,** president and CEO, said, "The discovery of APOL1 variants less than 20 years ago was hailed as a significant breakthrough, and we now have a better understanding of how the APOL1 variants have played a role in health disparities in kidney disease. In the United States, people of color are at increased risk for developing kidney failure, with Black Americans being four times more likely to need dialysis or a transplant. Unfortunately, not nearly enough people know about AMKD. We believe it is critical to raise national awareness of AMKD so that people will better understand their risk, start a conversation within their families and communities, and are empowered to take action to protect their health, including consulting with a genetic counselor."

Amit Sachdev, chief patient and external affairs officer at Vertex Pharmaceuticals, said, "Establishing this inaugural annual AMKD Awareness Day represents a significant and proud moment for the Heaney health community. We are honored to support AKF in highlighting the importance of increasing awareness of this disease and driving efforts to expand access to education and genetic testing resources."

NKF to Honor Dr. Mary B. Leonard With Seldin Award

The NKF will honor pediatric nephrologist **Mary B. Leonard, MD, MSCE,** with the Donald W. Seldin Award in recognition of excellence in clinical nephrology. Dr. Leonard will receive the honor in May during the NKF 2024 Spring Clinical Meetings in Long Beach, California.

Mary B. Leonard, MD, MSCE

Dr. Leonard 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 chronic kidney disease.

In addition, Dr. Leonard has dedicated herself to clinical and translational research and mentoring junior physician-scientists. She was the private investigator of six National Institutes of Health Research Project grants and has published more than 200 peer-reviewed papers. She has also played a role in several national NKF initiatives and served as president of the American Pediatric Society.

"I'm grateful to the NKF for recognizing the unique needs of pediatric chronic kidney disease patients, which further fuels my commitment to advancing the understanding of kidney health and enhancing the lives of those affected by kidney-related conditions," Dr. Leonard said.

NKF's Shaul G. Massry Distinguished Lecture Award Will Go to Dr. Suzanne Watnick

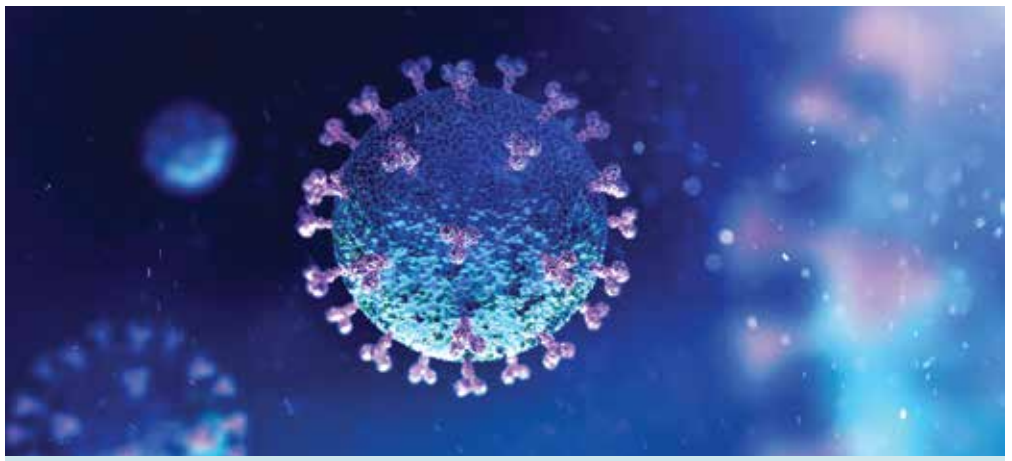
At the NKF 2024 Spring Clinical Meetings, **Suzanne Watnick, MD, FASN,** will receive the Shaul G. Massry Distinguished Lecture Award. The gathering will take place in May in Long Beach, California.

Suzanne Watnick, MD, FASN

"Dr. Massry was one of the most prominent leaders in our field, so I am truly humbled to be the recipient of the incredibly prestigious Shaul G. Massry Award," Dr. Watnick said. "Recognition from the NKF is particularly meaningful to me, given their patient-centered approach."

A professor of medicine at the University of Washington in Seattle and a practicing nephrologist at the Puget Sound Veterans Administration Medical Center, Dr. Watnick specializes in caring for patients with chronic kidney disease and providing oversight and care for end-stage kidney disease patients. 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 and Northwest Kidney Centers; and nephrology program director at Oregon Health & Science University. Dr. Watnick has served on several national advisory boards and has worked on many quality and payment issues related to dialysis.

"Dr. Watnick deserves this award because she's a role model to students, nephrologists, and investigators who have witnessed her dedication to finding ways to advance patients' health and improve outcomes for all kidney patients," said NKF president **Sylvia E. Rosas, MD, MSCE**. ■



COVID-19

COVID-19 Hospitalization Risk Among Solid Organ Transplant Recipients

JAMA Network Open. doi:10.1001/jamanetworkopen.2023.42006

Recipients of solid organ transplants are at increased risk of severe infection with SARS-CoV-2 compared with the general population. **Epiphane Kolla, MD, MPH,** and colleagues conducted a study to determine which health conditions and immunosuppressive drugs are associated with the risk of hospitalization related to COVID-19 in that patient population.

The study included 60,456 participants. Median age was 59 years, 63.7% were male, 68.6% (n=41,463) had kidney transplant, 23.9% (n=14,464) had liver transplant, 8.8% (n=5327) had heart transplant, and 4.6% (n=2823) had lung transplant. COVID-19-related hospitalization occurred in 12.7% of the kidney transplant recipients, 6.4% of liver transplant recipients, 12.9% of heart transplant recipients, and 18.0% of lung transplant recipients.

In kidney transplant recipients and liver transplant recipients, steroids and mycophenolic acid were associated with a high risk of hospitalization for COVID-19. In heart transplant recipients, steroids and mycophenolic acid, sirolimus, and everolimus were associated with an increased risk of hospitalization. In lung transplant recipients, only steroids were associated with a high risk of hospitalization.

In liver transplant recipients, tacrolimus was associated with a decreased risk of hospitalization. In heart transplant recipients, cyclosporine was associated with decreased risk.

"This study suggests that mycophenolic acid, sirolimus, and steroids are associated with an increased risk of COVID-19-related hospitalization in solid organ transplant recipients," the authors said. "These results should be considered by clinicians treating transplant recipients and may help inform epidemic-related decisions for this population in the future."

COVID-19-Related AKI and Mortality Rates Among Patients ≥80 Years of Age

Life. doi:10.3390/life14010086

The landscape of global public health has been reshaped by the COVID-19 pandemic. There are variations in the incidence and severity of adverse clinical outcomes among patients infected with the virus. **Alfredo Caturano, MD,** and colleagues in Italy conducted a study aimed at examining the specific impact of acute kidney injury (AKI) on in-hospital mortality among octogenarian patients with COVID-19.

The prospective observational cohort study included 23 COVID-19 hospital units in the Campania region in Italy. Exposure variables were collected during hospital admission and at discharge. Eligible patients were ≥80 years of age.

The study cohort included 197 patients; median age was 83.0 years, 51.5% were men, and median duration of hospitalization was 15.0 days. Following application of Šidák correction, results of the multivariable Cox regression analysis demonstrated that only the respiratory rate (hazard ratio [HR], 1.09; 95% CI, 1.04-1.14; $P<.001$) and development of AKI (HR, 3.40; 95% CI, 1.80-6.40; $P<.001$) were independently associated with the primary outcome of in-hospital mortality. In Kaplan-Meier analysis, there was a significantly different risk of in-hospital mortality between patients with and without AKI (log-rank: <.0001).

"In our investigation, we identified a significant association between AKI and mortality rates among octogenarian patients admitted for COVID-19," the authors said. "These findings raise notable concerns and emphasize the imperative for vigilant monitoring of this demographic cohort."

ACUTE KIDNEY INJURY

Predictors of Severe Outcomes in In-Hospital AKI

BMC Nephrology. doi:10.1186/s12882-024-03470-9

The rates of in-hospital AKI are increasing; patients who develop AKI are at risk for a poor prognosis. There are emerging biomarkers that may help identify early stages of AKI; however, accurate prediction of severe outcomes, such as the need for kidney replacement therapy (KRT), remains challenging.

According to **Rebecca Lehmann, MD,** and colleagues, blood gas analyses (BGA) are useful in diagnosing life-threatening complications associated with AKI. The researchers conducted a study designed to assess the role of BGA as a biomarker panel in emerging and established cases of AKI.

The retrospective, observational study included 202 patients with newly developed AKI to document venous and arterial pH, pCO_2, and actual bicarbonate levels at baseline (hospital admission) and at the onset of AKI. The primary end points of interest were in-hospital mortality, the need for KRT, and the recovery of kidney function.

Among the 202 participants, three variables were independent predictors of in-hospital survival: (1) admission arterial pH; (2) arterial pCO_2 at onset of AKI; and (3) arterial pCO_2 at AKI onset was identified as an independent predictor for the need of KRT.

"Our study suggests that blood gas analysis may have a potential role in predicting severe outcome variables in AKI," the researchers said. "The associated costs are minimal."

CHRONIC KIDNEY DISEASE

Sodium Bicarbonate Treatment and Bone Health in CKD

Journal of the American Society of Nephrology. 2024;35(1):57-65

Patients with chronic kidney disease (CKD) who develop metabolic acidosis are commonly treated with alkali to improve bone health. **Kalani L. Raphael, MD,** and colleagues performed a post hoc analysis of data from the BASE (Bicarbonate Administration to Stabilize eGFR) pilot trial (ClinicalTrials.gov, NCT02521181) to examine whether sodium bicarbonate affects serum levels of bone turnover markers and other hormones related to bone health in patients with CKD who have normal to slightly reduced total CO_2 (20-28 mEq/L).

The BASE trial included 194 individuals with CKD and serum total CO_2 20-28 mEq/L who were randomly assigned to placebo or one of two doses of sodium bicarbonate (0.5 or 0.8 mEq/kg lean body weight per day) for 28 weeks. At baseline, week 12, and week 28, serum measurements of bone-specific alkaline phosphatase (B-SAP), c-telopeptide,

continued on next page

procollagen type 1 intact N-terminal propeptide, intact parathyroid hormone (iPTH), intact fibroblast growth hormone 23 (FGF23), soluble klotho, 25-hydroxyvitamin D, 1,25-dihydroxyvitamin D, and tartrate-resistant acid phosphatase 5b were measured. Linear mixed models were used to determine the difference (sodium bicarbonate vs placebo) in mean change of each bone biomarker from baseline.

The post hoc analyses included data from 168 trial participants. At baseline, mean estimated glomerular filtration rate was 37 mL/min/1.73 m^2 and mean total CO_2 was 24 mEq/L. Compared with placebo, sodium bicarbonate induced a dose-dependent increase in soluble klotho levels. There was no significant effect of treatment with either dose of sodium bicarbonate on the other bone biomarkers, including iFGF23, iPTH, and B-SAP. The effects on bone biomarkers were similar in the group with serum total CO_2 <24 mEq/L and those with total CO_2 ≥24 mEq/L.

"In this pilot trial of individuals with CKD and total CO_2 20-28 mEq/L, sodium bicarbonate treatment increased serum klotho levels but did not affect other bone health markers over 28 weeks," the authors said.

DIABETES

Quantifying the Effect of Finerenone on Kidney and Cardiovascular Risk Reduction

Annals of Internal Medicine. doi:10.7326/M23-1023

Finerenone, a nonsteroidal mineralocorticoid receptor antagonist, has been shown to reduce cardiovascular and kidney failure outcomes in patients with CKD and type 2 diabetes. Finerenone also lowers urine albumin-to-creatinine ration (UACR). According to researchers, led by **Raijv Argarwall, MD, MS,** there are few data available on whether finerenone-induced change in UACR mediates cardiovascular and kidney failure outcomes.

The researchers conducted a post hoc analysis of pooled data from two phase 3, double-blind trials of finerenone to quantify the proportion of kidney and cardiovascular risk reductions over a 4-year period mediated by a change in kidney injury, as measured by the change in log UACR between baseline and month 4. The trials were conducted at clinical sites in 48 countries and included 12,512 patients with CKD and type 2 diabetes. The trials compared treatment effects with finerenone versus placebo.

The current analyses were conducted separately for the composite kidney outcome (kidney failure, sustained ≥57% decrease in estimated glomerular filtration rate [eGFR] from baseline, or kidney disease death) and the cardiovascular outcome (cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for heart failure).

Median UACR at baseline was 514 mg/g. In the finerenone group, 53.2% of participants (n=3338) had a reduction in UACR of ≥30% compared with 27.0% (n=1684) of the placebo group. When analyzed as a continuous variable, reduction in UACR mediated 84% of the treatment effect on the kidney outcome and 37% on the cardiovascular outcome. When change in UACR was analyzed as a binary variable (whether the guideline-recommended 30% reduction threshold was met), the proportion mediated for the kidney outcome was 64% and 26% for the cardiovascular outcome.

In summary, the authors said, "In patients with CKD and type 2 diabetes, early albuminuria reduction accounted for a large proportion of the treatment effect against CKD progression and a modest proportion of the effect against cardiovascular outcomes." Funding for the analyses was provided by Bayer AG.

Predicting Renal Outcomes in Patients With DKD

BMC Nephrology. doi:10.1186/s12882-024-03471-8

Worldwide, the most common cause of end-stage kidney disease (ESKD) is diabetic kidney disease (DKD). Results of studies have suggested that urinary podocyte stress biomarker (podocin:nephrin mRNA ratio), is a surrogate marker of podocyte injury in patients with nondiabetic kidney disease.

Researchers, led by **Lingfeng Zeng, PhD,** conducted a study of 118 patients with biopsy-proven DKD and 13 nondiabetic controls. Participants' urinary mRNA levels of nephrin, podocin, and aquaporin-2 (AQP2) were quantified. The outcome of interest was a renal event at 12 months, defined as death, the need for dialysis, or a 40% reduction in glomerular filtration rate.

In the group with DKD, urinary podocin:nephrin mRNA ratio was significantly higher than in the control group (P=.0019). There were no differences between the two groups in urinary nephrin:AQP2 or podicin:AQP2 mRNA ratios.

In the DKD group, there was a correlation between urinary podocin:nephrin mRNA ratio and the severity of tubulointerstitial fibrosis (r=0.254; P=.006). Urinary podocin:nephrin mRNA ratio was also associated with renal event-free survival (EFS) at 12 months (unadjusted hazard ratio [HR], 1.523; 95% CI, 1.157-2.006; P=.003). Following adjustment for clinical and pathological factors, there was a trend for urinary podocin:nephrin mRNA ratio as a predictor of renal EFS; however, the result did not reach statistical significance (adjusted HR, 1.327; 95% CI, 0.980-1.797; P=.067).

In conclusion, the authors said, "Urinary podocin:nephrin mRNA ratio has a marginal prognostic value in biopsy-proven DKD. Further validation is required for DKD patients without kidney biopsy."

DIALYSIS

Serum Creatinine Concentrations and Race/Ethnicity in Patients Receiving Hemodialysis

Journal of the American Society of Nephrology. 2024;35(1):66-73

According to **Cynthia Delgado, MD,** and colleagues, there are few data available on differences in serum creatinine concentration between Black and non-Black individuals. To date, those differences among groups defined by race and ethnicity have been attributed to differences in muscle mass.

The researchers conducted a data analysis to examine differences in serum creatinine by race and ethnicity in a cohort of patients receiving hemodialysis, and to determine whether the differences persisted following adjustment for proxies of muscle mass. The analysis included data on 501 participants in the ACTIVE/ADIPOSE (A Study to Investigate the Value of Exercise in ESKD/Analyses Designed to Investigate the Paradox of Obesity and Survival in ESKD) study. Eligible participants had been receiving hemodialysis for more than 1 year.

The researchers sought to examine the independent associations among race/ethnicity (Black, Asian, non-Hispanic White, and Hispanic), serum creatinine, and intracellular water (ICW; L/m^2; a proxy for muscle mass). The associations were identified using multivariable linear regression with adjustment for several demographic, clinical, and laboratory characteristics. ICW was derived by whole-body multifrequency bioimpedance spectroscopy. The association of race and ethnicity with serum creatinine concentration was examined with and without adjustment for ICW.

Serum creatinine concentrations were higher among Black, Asian, and Hispanic patients compared with non-Hispanic White patients (+1.68 mg/d; +1.61 mg/dL; +0.83 mg/dL, respectively). Overall, there was an association between ICW and serum concentration (0.26 ng/dL per L/m^2 ICW). The association was not statistically significantly different by race and ethnicity. After adjustment for ICW, the association between Black, Asian, and Hispanic race/ethnicity and serum creatinine concentration remained significant.

"Among patients receiving dialysis, serum creatinine was higher in Black, Asian, and Hispanic patients than in non-Hispanic White patients," the researchers said. "Differences in ICW did not explain the differences in serum creatinine concentration across race groups."

IGA NEPHROPATHY

Intensive Blood Pressure Control in Patients With IgA Nephropathy

Nephrology Dialysis Transplantation. 2024;39(1):55-63

Current guidelines recommend systolic blood pressure below 120 mm Hg in patients with chronic kidney disease. However, according to

Chen Tang, PhD, and colleagues, the renoprotective effect of intensive blood-pressure lowering in patients with immunoglobulin A nephropathy (IgAN) is unclear. The researchers conducted a study at Peking University First Hospital in China, to examine the effect of intensive blood pressure control on the progression of IgAN.

The study cohort included 1530 patients with IgAN. The researchers sought to define the relationship between baseline and time-updated blood pressure and composite kidney outcomes (development of end-stage renal disease or a 30% decline in eGFR). Multivariable causal hazard models and marginal structural models were used to model baseline and time-updated blood pressures.

During a median follow-up of 43.5 months, 24.0% of study participants experienced the composite kidney outcomes. There were no significant associations observed between baseline blood pressure and the composite outcomes.

Using marginal structural models with time-updated systolic blood pressure for analysis, there was a U-shaped association. Using systolic blood pressure 110-119 mm Hg as the reference, the HRs for the systolic blood pressure categories of <110, 120-129, 130-139, and ≥140 mm Hg were 1.48 (95% CI, 1.02-2.17), 1.13 (95% CI, 0.80-1.60), 2.21 (95% CI, 1.54-3.16), and 2.91 (95% CI, 1.94-4.35), respectively. The trend was more prominent in patients with proteinuria ≥1g/day and eGFR ≥60 mL/min/1.73 m^2. There was no similar trend observed in analysis of time-updated diastolic blood pressure.

In conclusion, the authors said, "In patients with IgAN, intensive blood pressure control during the treatment period may retard the kidney disease progression, but the potential risk of hypertension still needs to be considered."

TRANSPLANTATION

Sex Differences in Transplantation Survival Benefit

Nephrology Dialysis Transplantation. 2024;39(1):36-44

For patients with kidney failure who require renal replacement therapy, the preferred treatment is kidney transplantation. There are few data on whether the survival benefit is different for men and women.

Angelika Geroldinger, PhD, and colleagues conducted a study that included all patients receiving dialysis included in the Austrian Dialysis and Transplant Registry who were waitlisted for their first kidney transplant between 2000 and 2018. The researchers mimicked a series of controlled trials and applied inverse probability of treatment and censoring-weighted sequential Cox models to estimate the causal effect of kidney transplantation on 10-year restricted mean survival time.

The study cohort included 4408 patients. Of those, 33% were female and mean age was 52 years. In both women and men, the most common primary renal disease was glomerulonephritis (27% and 28%, respectively).

Over a 10-year follow-up, kidney transplantation led to a gain of 2.22 years (95% CI, 1.88-2.49) over dialysis. The effect was smaller in women than in men (1.95 years [95% CI, 1.38-2.41] vs 2.35 years [95% CI, 1.92-2.70], respectively). The survival benefit of transplantation over the follow-up period was smaller in younger women and increased with age. In both men and women, the survival benefit peaked at approximately age 60 years.

In summary, the authors said, "There were few differences in survival benefit by transplantation between females and males. Females had better survival than males on the waitlist receiving dialysis and similar survival to males after transplantation." ■