Nephrology Times

Practical News, Trends, and Analysis

November/December 2024

VOLUME 16, NUMBER 7

Association Between Inflammatory Skin Diseases and IgA Nephropathy

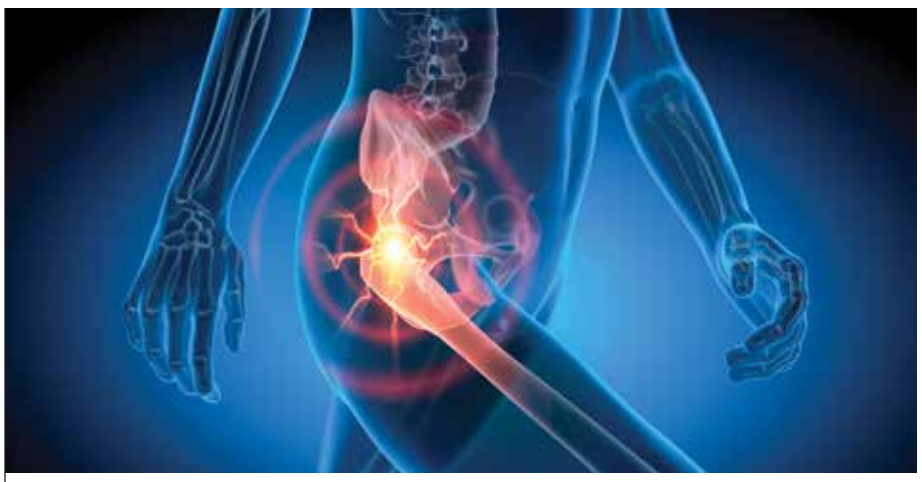
Research has shown an association between chronic kidney disease and inflammatory skin diseases (ISDs), such as atopic dermatitis (AD), acne, and psoriasis. However, research is lacking regarding a potential link between IgA nephropathy (IgAN), the predominant primary glomerular disease, and ISDs.

To address this knowledge gap, **Wenlong Cao** and **Jing Xiong** conducted a study using bidirectional Mendelian randomization (MR) to examine causality between ISDs and IgAN. Their findings were published in *Frontiers in Genetics* [doi:10.3389/fgene.2024.1402302].

The researchers' MR design was based on three assumptions: (1) instrumental variables (IVs) must strongly correlate with exposure; (2) IVs cannot be affected by any confounding factors; (3) IVs must relate to outcomes through exposure only and through no other causal pathway. Once those parameters were established, the researchers used bioinformatics methods to study the potential mechanism by which ISDs may cause an increased risk of IgAN.

Exposures included AD, acne, and psoriasis, with IgAN as the outcome; conversely, IgAN was the exposure with AD, acne, and psoriasis as outcomes. All data were based on independent genome-wide association studies (GWAS). IVs of AD, acne, and

continued on page 4



Examining the Relationship Between CKD and Osteoarthritis

Chronic kidney disease (CKD) and osteoarthritis (OA) are common chronic diseases that share several similar risk factors, such as older age, overweight/obesity, hypertension, and longtime use of nonsteroidal anti-inflammatory drugs. OA is prevalent among CKD patients receiving dialysis, and research indicates an increasing comorbidity between the two conditions. Therefore, a better understanding of the relationship between CKD and OA should help advance more

continued on page 4

Determining Causal Effect of Kidney Function on Cancer Incidence

Patients receiving kidney replacement therapy (KRT) have a 1.5 to two times greater risk of cancer and cancer-related death. The extent of this heightened risk depends on the type of cancer and KRT. Research shows that even patients with lower-stage chronic kidney disease (CKD) may experience a higher cancer risk. However, the reasons for this remain unclear. There may be a causal relationship, the association could be due to factors such as immune suppression and inflammation, or it could result from distortion of the analyses from unidentified variables (confounding).

To shed light on the relationship between kidney function and cancer risk, a group of researchers led by **Ellen Dobrijevic, MD,** performed a two-sample Mendelian randomization (MR) analysis to examine a potential causal relationship between kidney function and cancer risk. MR randomly assigns genetic variants at birth to investigate causal relationships as they reflect natural randomization, are fixed from birth, and are unaffected by clinical confounders or reverse causation. The study results were published in the *American Journal of Kidney Diseases* [doi:10.1053/j.ajkd.2024.05.016].

Study outcomes included overall cancer incidence, cancer-related mortality, and site-specific colorectal, lung, and urinary tract cancer incidence. The exposures were estimated glomerular filtration rate (eGFR) and urine albumin-to-creatinine

continued on page 5

What Is Ailing Nephrology?

Ajay K. Singh, MBBS, FRCP, MBA
Brigham and Women's Hospital and Harvard Medical School
BOSTON, MASSACHUSETTS

As we return from another American Society of Nephrology (ASN) meeting brimming with new knowledge and excited by the range of advances in therapies, there is no better time to be a nephrologist. So, why does nephrology remain unattractive to medical students and residents?

Ten years ago, Jeff Berns and colleagues[1] noted declining interest in nephrology among medical students and residents and identified an urgent need to better define the subspecialty and its scope of practice and to rethink fellowship training programs and training requirements. However, not much has changed, as an editorial by Farouk and Sparks[2] points out, and the basic structures and limitations of nephrology training endure.

The nephrology brand is still dominated by the idea that most clinicians focus on treating dialysis patients, and that these patients are complicated and difficult, leading to drudge work. In short, the life of a clinical nephrologist is exhausting and very different from the life of a cardiologist or an oncologist. Newer super-subspecialities of nephrology, such as critical care nephrology, onco-nephrology, and interventional nephrology, have emerged over the past decade or so, but have not caught the eye of would-be nephrology trainees. Nor has the approval of many new, exciting treatments to keep patients off dialysis increased interest in nephrology. At my hospital, the Brigham and Women's Hospital in Boston, Massachusetts, the most popular subspecialties remain cardiovascular medicine, oncology, and gastroenterology. (In some hospitals, dermatology is part of internal medicine and in others it is not, so I haven't listed it in my top three.)

Some evidence from the Kidney Disease Screening and Awareness Program[3] suggests that an effort to increase awareness among medical students might help change the situation. The 10-year review of this program by Jiang and colleagues[4] is encouraging and worth consideration. For several years, the ASN, National Kidney Foundation, and National Institutes of Health have committed to supporting young investigators in pursuing a career in nephrology.

There is also a global perspective to consider. Sozio and colleagues[5] recently reported on the global crisis in the nephrology workforce. In the US and Europe, they estimated that there are about 25 nephrologists per 1 million in the population. In South Asia, the number is one per 1 million and in sub-Saharan Africa it is estimated to be 0.5 per 1 million. The disparity is stunning as kidney disease is rampant in South Asia and sub-Saharan Africa, in large from the impact of type 2 diabetes, which is in epidemic proportions, and CKD of unknown origin, where exposure to regional environmental factors may be significant.

With respect to caring for dialysis patients and changing the negative impression of this work, we need more innovation. In several editorials published here, I have waxed lyrical about the US government funding a "Dialysis Moonshot" like the Biden Cancer Moonshot. The surge in funding for innovations in dialysis is well overdue. Large and midsized dialysis providers are focused on the business aspects of dialysis—ensuring financial returns to their shareholders. Surely, it is the government's role to fund research into better ways to treat dialysis patients. These new strategies will likely reduce mortality and improve the quality of life for our patients.

We need to change the brand by infusing in our trainees the excitement we all feel about recent advances in nephrology.

While the developed world must consider attracting more trainees to nephrology, we also need to think globally. North America and Europe must contribute to training nephrologists in the developing world in a way that does not exacerbate the dire nephrology workforce situation there. Organizations like the World Bank and the United States Agency for International Development must have nephrology workforce issues on their radar.

Our national and international societies can help by bringing this to their attention. Solutions can include incentivizing trainees to return to their country of origin so that the massive shortage of nephrologists in South Asia and Africa is not worsened by a nephrology "brain drain." Local funding to South Asian and African countries like what the Gates Foundation has done in maternal health could spur innovation in low- to middle-income countries. These innovations can include reducing the need for nephrologists and focusing instead on training physician extenders. This has been done successfully in many centers in the United States.

Turning to the developed world, what ails nephrology? Part of the problem is the nephrology brand—the way trainees think about our specialty. We need to change the brand by infusing in our trainees the excitement we all feel about recent advances in nephrology. The treatments that until now were unthinkable are becoming a reality and have been transformational for our patients. These treatments will keep patients off dialysis!

As Winston Churchill said, "To improve is to change; to be perfect is to change often." The workforce challenges, branding issues, and innovation in our specialty are inextricably linked. We need to tackle all three, while also taking a global view of this problem. Simply fixing the problems in our own backyard is not enough. ■

REFERENCES

1. Berns JS, Ellison DH, Linas SL, Rosner MH. Training the next generation's nephrology workforce. *Clin J Am Soc Nephrol*. 2014;9(9):1639-1644. doi:10.2215/CJN.00560114

2. Farouk SS, Sparks MA. Reenvisioning the adult nephrology workforce: the future of kidney care in the United States. *Adv Chronic Kidney Dis*. 2020;27(4):279-280. doi:10.1053/j.ackd.2020.08.006

3. Hsiao LL, Wu J, Yeh AC, et al. The Kidney Disease Screening and Awareness Program (KDSAP): a novel translatable model for increasing interest in nephrology careers. *J Am Soc Nephrol*. 2014;25(9):1909-1915. doi:10.1681/ASN.2013090928

4. Jiang M-Y, Song R, Chen R, Tuot DS, Heung M, Hsiao L-L. Addressing the nephrology workforce shortage via a novel undergraduate pipeline program: the Kidney Disease Screening and Awareness Program (KDSAP) at 10 years. *Kidney Int*. 2021;100(6):1174-1178. doi:10.1016/j.kint.2021.10.007

5. Sozio SM, Pivert KA, Caskey FJ, Levin A. The state of the global nephrology workforce: a joint ASN-ERA-EDTA-ISN investigation. *Kidney Int*. 2021;100(5):995-1000. doi:10.1016/j.kint.2021.07.029

Nephrology Times
Practical News, Trends, and Analysis

Contents

November/December 2024 VOLUME 16, NUMBER 7

www.nephtimes.com

AMC MEDIA GROUP

630 Madison Avenue
Manalapan, NJ 07726

Nephrology Times (ISSN 1940-5960) is published bi-monthly by AMC Media Group, at 630 Madison Avenue, Manalapan, NJ 07726. Printed in the U.S.A.
 Subscription information and orders: Physicians who are listed with AMA/AOA as having a primary or secondary specialty related to nephrology within the US are eligible for a free subscription. If you are not currently receiving the publication, send an email with your name, address, and specialty to Charlotte Robinson at: carobinson@amcmediagroup.com. For customer service on your free subscription, please call 732.490.5530. Annual subscription rates: US: $99 individual, $200 institution.

Postmaster: Send address change to: ***Nephrology Times,*** 630 Madison Avenue, 2nd Floor, Manalapan, NJ 07726.

Conference Coverage

KIDNEY WEEK 2024

The American Society of Nephrology Kidney Week 2024 included presentations and posters highlighting the latest findings in kidney health research, as well as sessions on advances in the care of patients with kidney and related disorders.


6

Feature

Kidney Failure, Mortality With Rare Kidney Diseases Versus CKD


12

News

News Focus on Transplantation

News Briefs

Abstract Roundup

From the Field

The Relationship Between CKD and Osteoarthritis
continued from page 1

comprehensive management of both.

Kuiliang Gao and colleagues used logistic regression to assess the relationship between CKD and OA, utilizing data from the National Health and Nutrition Examination Survey (NHANES). Their findings were published in *BMC Nephrology* [doi:10.1186/s12882-024-03672-1].

The study authors relied on demographic data, laboratory results, examination records, and questionnaire responses from NHANES between 2011 and 2020. Of an original pool of 26,280 adult participants aged ≥20 with complete demographic, physical examination, and health questionnaire data, 15,690 were included in the study after applying exclusion criteria.

The study excluded patients with unavailable information on weight and socioeconomic factors; missing data on urine albumin, urine creatinine, or blood creatinine concentrations; incomplete, unreliable, or uncertain data on arthritis; and unreliable assessment criteria for diabetes and hypertension. Mean age was 48.48 (± SE 16.95) years, and 49% of participants were male.

OA was the predictor variable in the analysis, and CKD was the outcome variable in the associative research. The relationship between CKD and OA was further examined after adjusting for covariates and effect sizes (β) and calculating 95% CIs. To further ensure the accuracy of results, the researchers conducted age- and sex-stratified subgroup analyses. To evaluate the performance of indicators, $P<.05$ (two-tailed) represented statistical significance.

Among study participants, 26.69% of OA patients developed concurrent CKD. In non-OA participants, 13.83% developed CKD.

Overall, CKD was found to be significantly related to OA (odds ratio [OR], 2.269; 95% CI, 2.266–2.271; $P<.01$). The relationship was even more significant in those with moderate-to-severe CKD (OR, 2.622; 95% CI, 2.610–2.634; $P<.01$). Even after adjusting for demographic factors, socioeconomic factors, body mass index, smoking status, alcohol consumption, physical activity, diabetes, and hypertension, the relationship between CKD and OA was strong (OR, 1.031; 95% CI, 1.030–1.033; $P<.01$), and the relationship between moderate-to-severe CKD and OA became even more pronounced (OR, 1.178; 95% CI, 1.173–1.184; $P<.01$).

Because there was no osteoporosis data in the NHANES database for some years, the researchers conducted a regression analysis with osteoporosis as a new covariate based on the years with available osteoporosis data. That analysis showed a strong relationship between CKD and OA, both in stages 1-3 CKD (OR, 1.065; 95% CI, 1.063–1.066; $P<.01$) and in stages 4-5 CKD (OR, 1.446; 95% CI, 1.436–1.45; $P<.01$).

The authors propose that metabolic dysfunction and inflammation, possible associations in the molecular cell field, and the effects of hypertension, diabetes, hormone levels, and physical inactivity may contribute to the association between OA and CKD.

TAKEAWAY POINTS

- Chronic kidney disease (CKD) and osteoarthritis (OA) share several similar risk factors. This study utilized data from the National Health and Nutrition Examination Survey 2011-2020 to assess the association between CKD and OA using logistic regression.
- Among study participants, CKD had a significant relation to OA after adjustments. The relationship remained significant in subgroup analyses based on age. Women demonstrated a higher risk of developing CKD than men.
- The results imply that the association between OA and CKD needs further study. The authors suggest that patients with OA pay extra attention to their kidney health.

Even after adjusting for common factors for OA and CKD, the association between OA and CKD remained statistically significant.

There was a higher proportion of Non-Hispanic White with OA patients (81.83%) than those without OA (63.92%). Patients with OA were of a significantly older age ($P<.01$) than those without OA. Patients aged 60 years and older demonstrated an increased CKD risk compared to those aged 20 to 39 years (OR, 3.706; 95% CI, 3.700-3.712). Stratified analyses showed an increasing correlation between OA and CKD with age.

There were more females with OA (66.1%) than males (33.9%). In subgroup analyses, the relationship between OA and CKD went in opposite directions for males (OR, 0.869; 95% CI, 0.867-0.871; $P<.01$) and females (OR, 1.178; 95% CI, 1.177-1.180; $P<.01$).

Limitations acknowledged by the authors include the retrospective nature of the study, potential underestimation or overestimation of CKD prevalence, possible self-reporting and recall biases, and failure to consider medication usage.

In conclusion, the authors wrote, "The results of this study, based on a nationally representative survey, reveal a strong association between CKD and OA. The likelihood of CKD is significantly higher in patients with OA compared to those without, particularly among women. We suggest that OA be considered a predictor of CKD. Alongside other predisposing factors, OA should be taken into account in annual CKD screening protocols." ■

TAKEAWAY POINTS

- While there is evidence that chronic kidney disease is associated with inflammatory skin diseases, the association between inflammatory skin diseases and IgAN has rarely been studied.
- Researchers utilized Mendelian randomization to examine the causality between IgAN and atopic dermatitis, acne, and psoriasis.
- Of the three skin diseases studied, only atopic dermatitis was associated with a higher risk for IgAN. Thus, properly managing atopic dermatitis may help prevent the occurrence and progression of IgAN.

Inflammatory Skin Diseases and IgA Nephropathy
continued from page 1

psoriasis were obtained from the FinnGen Consortium and IVs of IgAN came from an available GWAS.

An MRPRESSO test was used to detect and remove any outlier that may cause horizontal pleiotropy. A leave-one-out analysis determined whether there is an association driven by a single nucleotide polymorphism (SNP). Cochran's Q test and funnel plot were used to evaluate heterogeneity. An MR-Egger intercept of MR-Egger was utilized to assess pleiotropy. Causal associations between exposure and outcome were presented with odds ratios and 95% confidence intervals.

After the heterogeneity and pleiotropy tests, bidirectional causality was evaluated by an inverse variance weighted (IVW) model along with four other approaches: simple mode, weighted mode, weighted median, and MR-Egger. IVW was the primary approach, while the other four methods were supplemental. Three datasets related to AD were retrieved from the GEO database and combined. In the combined dataset, expression of galactose-deficient IgA1-associated genes were compared in atopic dermatitis patients versus healthy controls. These genes included GALNT2, GALNT12, C1GALT1, C1GALT1C1, and ST6GALNAC2.

In a two-sample MR examining the causal effect of ISDs on IgAN, AD was associated with an increased risk of IgAN (IVW: OR, 1.054; 95% CI, 1.014–1.095; $P=.0069$). There was no significant association between acne or psoriasis and an increased risk of IgAN. No reverse causality was found in reverse MR between AD and IgAN (OR=1.035; 95% CI=0.873–1.227; $P=.693$). The IVW method indicated that IgAN may be a risk factor for psoriasis (OR=1.273; 95% CI=1.012–1.602; $P=.040$). However, the other four methods identified no significant association. Therefore, the evidence does not conclusively show that IgAN can increase psoriasis risk. In the combined microarray dataset, the expression levels of GALNT12 and C1GALT1C1 among patients with AD were significantly lower than in controls ($P=2.3e^{-9}$; $P=.00067$), which may contribute to an increase in abnormal IgA1 synthesis.

The authors acknowledge some limitations. The GWAS data used for MR were based on a European population, and results were not validated in an Asian population. Pleiotropy cannot be excluded completely. Bioinformatics methods were used to examine the potential mechanism by which AD increases the risk of IgAN. Basic research is needed to confirm the hypothesis.

"In summary," the authors wrote, "among ISDs, only AD was found to be a risk factor for IgAN. Potential mechanism may be linked to the aberrant expression of Gd-IgA1-related genes. Our findings may provide new insights into the pathogenesis of IgAN and innovative strategies for the prevention and treatment of IgAN." ■

Effect of Kidney Function on Cancer Incidence
continued from page 1

ratio (UACR). The researchers obtained genome-wide association studies (GWAS) summary statistics for eGFR (n=567,460; mean age 50.1 years; 48.2% male) and UACR (n=127,865; mean age 56.0 years; 45.1% male) for participants of European ancestry from the CKDGen Consortium. Estimates of the association between the genetic variants and cancer outcomes (cancer incidence and cancer-related death) came from individual-level, deidentified data from the UK Biobank database (n=407,329; mean age 56.9 years; 45.9% male) for participants recruited between 2006 and 2010.

Univariate and multivariable MR were conducted for all outcomes using inverse-variance weighted methods. MR was conducted for each of the two exposures (eGFR and UACR) and the outcomes of overall cancer incidence, colorectal cancer incidence, urinary tract cancer incidence, lung cancer incidence, and cancer-related death. These types of cancer were selected for the analysis because they are the most common cancer types among patients with CKD.

There were 98,093 cases of cancer observed. Of them, 6,664 were colorectal, 3,584 were lung, and 3,271 were urinary tract. There were 15,850 cases of cancer-related death.

The genetic instruments for eGFR and UACR comprised 34 and 38 variants, respectively. Neither genetically predicted eGFR, UACR, nor a combination of eGFR and UACR were found to have a causal association with overall cancer incidence, cancer-related death, or site-specific lung or colorectal cancer incidence.

The odds ratios (95% CI; *P* value) of genetically predicted eGFR for overall cancer incidence, overall cancer-related death, lung, colorectal, and urinary tract cancer incidences were 0.88 (0.40-1.97; *P*=.76), 0.92 (0.24-3.53; *P*=.91), 0.48 (0.03-8.49; *P*=.62), 0.93 (0.11-7.99; *P*=.95), and 0.22 (0.02-2.72; *P*=.24), respectively. The odds ratios (95% CI; P value) of genetically predicted UACR on overall cancer incidence, cancer-related death, lung cancer, colorectal cancer, and urinary tract cancer were 0.90 (0.78-1.04; *P*=.16), 0.96 (0.76-1.20; *P*=.70), 1.07 (0.65-1.75; *P*=.79), 0.74 (0.50-1.07; *P*=.11), and 0.93 (0.59-1.46; *P*=.76), respectively.

No causal association between genetically predicted kidney function and cancer outcomes (cancer incidence and cancer-related death) was found during MR analyses.

The associations between the genetic variants and cancer outcomes came from generalized linear mixed-effects regression models adjusted for age, sex, and the first 10 genetic principal components. Sensitivity analyses were also performed.

Among CKDGen participants, mean eGFR and median UACR were 91.4 mL/min/1.73m^2 and 9.32 mg/g, respectively. For the UK Biobank participants, mean eGFR and median UACR were 90.4 mL/min/1.73m^2 and 9.29 mg/g, respectively.

There was no evidence of a causal association between eGFR and cancer in a stratified MR. In sum, no causal association between genetically predicted kidney function and cancer outcomes (incidence and cancer-related death) was found during MR analyses.

Notably, the GWAS and UK Biobank data comprised participants who were generally healthy and included only a small proportion of CKD or KRT patients. Slight variations in kidney function due to the genetic variants analyzed in this study may be insufficient to cause cancer. The effects of reduced kidney function on cancer risk may be limited to those with more advanced kidney disease.

Although a causal relationship was not identified, there was evidence of a nonlinear relationship between eGFR and cancer with an inflection point at an eGFR of 75. However, stratified MR did not show an association between genetically predicted eGFR and cancer, suggesting that increased cancer risk observed in kidney transplant recipients or patients with chronic glomerulonephritis may be related to factors such as prolonged use of maintenance immunosuppression rather than reduced kidney function.

Limitations acknowledged by the authors include the use of a smaller GWAS for UACR, which reduced the strength of the instrument and potentially introduced population stratification. The authors did this to prevent overlapping samples.

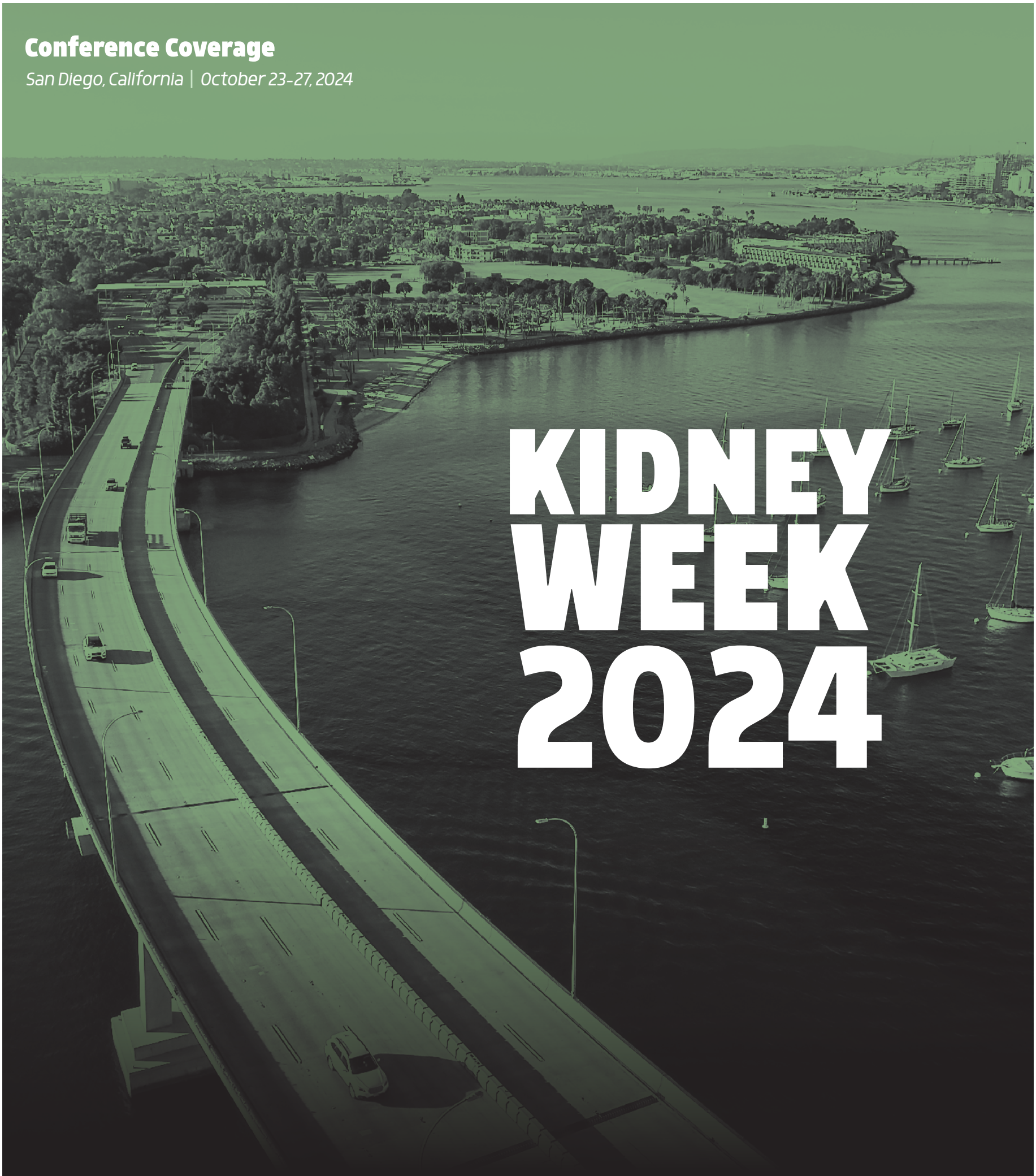
"In conclusion," the authors wrote, "we did not find evidence of a causal effect of kidney function on overall cancer incidence, cancer-related death, or site-specific lung, colorectal cancer, or urinary cancer incidence. Associations with cancer observed in patients with mild to moderate stage CKD may reflect residual confounding in the observational evidence. Strategies to reduce the excess risk of cancer observed in patients with more advanced stage CKD or those with kidney transplants should focus on other mediating factors such as chronic immunosuppression use." ■

TAKEAWAY POINTS

- People with chronic kidney disease have a greater risk of cancer and cancer-related death but it is unclear whether kidney disease is causally related to cancer.
- Researchers used Mendelian randomization analysis to assign genetic variants to subjects at birth to investigate causal relationships between kidney function and cancer incidence or mortality without confounding from measured and unmeasured confounders.
- The study found no evidence for causality between reduced kidney function and cancer.

Conference Coverage

San Diego, California | October 23-27, 2024



KIDNEY WEEK 2024

The American Society of Nephrology Kidney Week 2024 included presentations and posters highlighting the latest findings in kidney health research, as well as sessions on advances in the care of patients with kidney and related disorders. This is part one of our coverage of Kidney Week 2024. Part two will appear in our January/February 2025 issue.

Examining the Safety and Efficacy of Semaglutide in Nondiabetic CKD

Semaglutide, a glucagon-like peptide 1 receptor agonist, is approved as a treatment for patients with type 2 diabetes and CKD. The treatment reduces albuminuria and the risk of kidney failure in this patient population.

During an oral session at ASN Kidney Week 2024, **Hiddo Jan L. Heerspink, PhD,** and colleagues presented results of a study designed to examine the effects of semaglutide in patients with overweight/obesity and albuminuria CKD without diabetes. The session was titled *Effects of Semaglutide on Kidney Parameters in Patients With Obesity and Nondiabetic CKD*.

The multicenter, randomized, placebo-controlled trial included adults with CKD (defined as eGFR ≥25 mL/min/1.73 m^2 and UACR ≥30 and <3500 mg/g). Eligible participants had a body mass index of ≥27 kg/m^2 and hemoglobin A1c <6.5%, with no use of hypoglycemic agents.

Patients were randomized to receive 24 weeks of treatment with subcutaneous semaglutide 2.4 mg per week or placebo, in combination with renin-angiotensin-system inhibition when indicated. The primary endpoint was change from baseline in UACR at week 24. Secondary endpoints included change in iohexol measured GFR (mGFR), eGFR, body weight, and systolic blood pressure. Throughout the study period, participants were monitored for safety measures.

A total of 125 patients were screened for study participation. Of them, 101 were randomized to either the semaglutide or placebo group. Mean age of the overall cohort was 55.8 years, 39.6% (n=40) were female, median UACR was 251 mg/d, and median eGFR was 65.0 mL/min/1.73 m^2. The most common CKD etiologies were chronic glomerulonephritis (n=25) and hypertensive CKD (n=27).

At week 24, the placebo-corrected geometric mean change from baseline in UACR in the semaglutide group was -52.1% (95% CI, -65.2- to -34.1; *P*<.0001). The change in mGFR at week 24 was -1.9 mL/min/1.73 m^2 (95% CI, -8.0 to 4.3) in the semaglutide group compared to the placebo group. Corresponding changes in eGFR-creatinine and eGFR-cystatin C were -1.1 (95% CI, -4.8 to 2.6) and +2.1 mL/min/1.73 m^2 (95% CI, -1.7 to 5.9), respectively.

Compared to placebo, semaglutide changed body weight by -9.1 kg (95% CI, -11.1 to -7.1) and systolic blood pressure by -6.3 mmHg (95% CI, -11.1 to -1.5). More patients in the semaglutide group reported gastrointestinal events than patients in the placebo group (30 vs 15, respectively).

In conclusion, the researchers said, "Treatment with semaglutide for 24 weeks in patients with overweight/obesity and CKD without diabetes resulted in a robust and clinically meaningful reduction in UACR. These results support further trials to assess long-term efficacy and safety of semaglutide in these patients."

Source: Heerspink HJL, Apperloo EM, Jongs N, et al. Effects of semaglutide on kidney parameters in patients with obesity and nondiabetic CKD. FR-OR102. Abstract of an oral presentation at the American Society of Nephrology Kidney Week 2024; October 25, 2024; San Diego, California. Funding for the study was provided by Novo Nordisk.

Results of Open-Label Extension of the ORIGIN Phase 2b Study of Atacicept

Researchers have identified B-cell activating factor (BAFF) and a proliferation-inducing ligand (APRIL) as key factors in the pathogenesis of IgA nephropathy (IgAN). During a late-breaking oral session at ASN Kidney Week 2024, **Jonathan Barratt, PhD,** of the University of Leicester, Leicester, United Kingdom, presented long-term results from the ORIGIN study. The presentation was titled *Long-Term Results From the ORIGIN Phase 2b Study of Atacicept for the Treatment of IgA Nephropathy (IgAN)*.

Atacicept is a humanized TACI-Fc fusion protein that inhibits BAFF and APRIL. It is self-administered subcutaneously at home. The primary endpoint of the ORIGIN phase 2b study was met at week 24 with a statistically significant and clinically meaningful reduction in urine protein-creatinine ratio (UPCR) versus placebo. There was additional reduction and stabilization in eGFR over 36 weeks. The late-breaking session reported 96-week results from the open-label extension (OLE).

Study participants with IgAN in either the atacicept or placebo arm in the 36-week phase 2b, randomized, blinded study period were enrolled in the OLE and received atacicept 150 mg for an additional 60 weeks. Efficacy outcomes of interest were changes in galactose-deficient IgA1 (Gd-IgA1), percentage of participants with hematuria, UPCR, and eGFR over 96 weeks. The researchers also examined long-term safety data.

The OLE cohort included 113 patients who received ≥1 dose of atacicept. During the 96-week period, there were sustained reductions in Gd-IgA1 (-65.9%), and in the percentage of participants with hematuria (-75.0% in those with hematuria at baseline) and UPCR (-52.2%). Of note, long-term eGFR remained stable at near baseline levels (mean annualized sloe of -0.6 mL/min/1.73 m^2/year at 96 weeks).

Analysis of safety data demonstrated that atacicept was generally well tolerated.

In summary, the authors said,"Gd-IgA1, hematuria, and UPCR reduction with eGFR stabilization through 96 weeks demonstrate that atacicept offers a potentially safe, long-term, disease-modifying treatment for IgAN. Specifically, the conversion of an eGFR profile in patients with IgAN from one of steady decline to one representative of the general population without kidney disease [Baba M. *PloS One*. 2015.] supports the potential of atacicept to decrease the high lifetime risk of kidney failure in patients with IgAN."

Source: Barratt J, Barbour S, Brenner RM, et al. Long-term results from the ORIGIN phase 2b study of atacicept for the treatment of IgA nephropathy (IgAN). SA-OR102. Abstract of an oral presentation at the American Society of Nephrology Kidney Week 2024; October 26, 2024; San Diego, California. Funding for the study was provided by Vera Therapeutics, Inc.

Comparing Functional Patency of Acellular Tissue Engineered Vessel With AVF

The preferred method for vascular access in patients requiring hemodialysis is arteriovenous fistula (AVF). AVF failure is associated with increased use of catheter access, and the related increase in morbidity and mortality. According to **Mohamad Anas Hussain, MD, PhD,** and colleagues, there is a need for an alternative option for vascular access that provides the benefits of AVFs, such as low infection rate, while reducing the associated maturation failure possibility.

During an oral session at ASN Kidney Week 2024, the researchers presented results of a phase 3 trial assessing the safety and efficacy of an acellular tissue engineered vessel (ATEV) compared to autologous AVF. (CLN-PRO-V007; ClinicalTrials.gov, NCT03183245). The presentation was titled *Prospective Randomized Trial of Humacyte's Acellular Tissue Engineered Vessel vs Autologous Arteriovenous Fistula for Hemodialysis Access*.

The phase 3, prospective, multicenter, two-arm, randomized controlled trial included 242 individuals undergoing surgical vascular access creation for hemodialysis. Participants were randomized to receive either the ATEV (n=123) or autologous AVF (n=119). Primary outcomes of interest included 6-month functional patency and 12-month secondary patency following access creation. Secondary outcomes were comparisons of access usability and infection rates.

The mean age of the overall cohort was 58.6 years and 29% were female. Participants in the ATEV group had higher rates of functional patency at both six months (81% vs 68% for AVF) and 12 months (68% vs 62% for AVF), *P*=.0071; joint test for the coprimary endpoints. The mean duration of ATEV use was significantly higher than duration of AVF use (7.5 months vs 6.1 months, respectively; *P*=.0162).

In the subgroup of female participants, the rates of 6-month functional patency were higher among ATEV users compared to those with AVF access (89% vs 55%, respectively), as were 12-month functional patency rates (81% vs 49%, respectively); *P*<.001; joint test).

Infection rates related to the access type were comparable (5.8% ATEV vs 4.1% AVF). No unexpected safety events were observed.

"Humacyte ATEV had better access functional patency and usability versus AVFs at one year," the authors said. "Female subjects experienced improved outcomes, supporting ATEV consideration as a novel access option for subjects at high risk for AVF non-maturation."

Source: Hussain MA, Ozaki CK, Moore EE, Khondker Z, Parikh SJ, Niklason, LE. Prospective randomized trial of Humacyte's acellular tissue engineered vessel vs autologous arteriovenous fistula for hemodialysis access. SA-OR95. Abstract of an oral presentation at the American Society of Nephrology Kidney Week 2024; October 26, 2024; San Diego, California. Funding was provided by Humacyte Global, Inc.

SC0062 Effective and Safe in Patients With IgA Nephropathy

In patients with IgA nephropathy (IgAN) there are associations between both endothelin-1 upregulation and endothelin receptor type A (ETA) activation and proteinuria, inflammation, and fibrosis. The 2-SUCCEED trial was designed to identify the efficacy, safety, and optimal doses of SC0062 for the treatment of patients with IgAN (NCT05687890).

During a late-breaking oral session at ASN Kidney Week 2024, **Hiddo Jan L. Heerspink, PhD,** reported results of the phase 2, randomized, placebo-controlled, double-blind trial. The presentation was titled *SC0062, a New Selective Endothelin Receptor Type A Antagonist in IgA Nephropathy.*

Study participants included adults with biopsy-proven IgAN and eGFR ≥30 mL/min/1.73 m^2 with urinary UPCR ≥75 g/g or proteinuria ≥1 g/24 hours. Eligible patients were being treated with maximum tolerated doses of angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers. Participants were randomized 1:1:1:1 to receive SC0062 at 5 mg, 10 mg, or 20 mg or matching placebo once daily.

The primary outcome of interest was the percentage change from baseline in UPCR in 24-hour urine samples following 12 weeks of treatment. Change in eGFR over time was a secondary outcome. Treatment-emergent adverse events and serious adverse events were recorded throughout the study period.

The overall study cohort included 131 patients with a median age of 42 years, mean eGFR 72 mL/min/1.73 m^2, and median 24-hour UPCR 1.2 g/g. The four study arms were SC0062 5 mg (n=33), SC0062 10 mg (n=32), SC0062 20 mg (n=32), and placebo (n=34).

Throughout the treatment period, there were reductions in UPCR with SC0062 versus placebo. At week 12, the placebo-corrected geometric mean changes in UPCR from baseline were -27.8% in the 5 mg arm, -20.4% in the 10 mg arm, and -38.1% in the 20 mg arm. The proportion of participants with a reduction in UPCR ≥30% from baseline was 33.3% in the placebo arm, 48.5% in the 5 mg arm, 62.5% in the 10 mg arm, and 71.0% in the 20 mg arm. There were no differences in eGFR among the treatment groups.

In safety analyses, the proportion of participants with treatment-emergent adverse events or serious adverse events was balanced among the groups. The rates of peripheral edema were 3%, 0%, and 0% in the SC0062 5 mg arm, 10 mg arm, and 20 mg arm, respectively, compared with 14.7% in the placebo arm.

The authors said, "In patients with IgA nephropathy and significant proteinuria, the novel ETA selective antagonist SC0062 showed a clinically meaningful reduction in proteinuria and a favorable safety profile with no risk of peripheral edema."

Source: Heerspink HJL, Du X, Xu Y, et al. SC0062, a new selective endothelin receptor type A antagonist in IgA nephropathy. SA-OR103. Abstract of an oral presentation at the American Society of Nephrology Kidney Week 2024; October 26, 2024; San Diego, California. Funding for the study was provided by Biocity Biopharmaceutics Co., Ltd.

Final Results of the IGNAZ Study of Felzartamab for IgA Nephropathy

During a late-breaking oral session at ASN Kidney Week 2024, **Jonathan Barratt, PhD,** of the University of Leicester, Leicester, United Kingdom, reported final 24-month data from the IGNAZ study. The presentation was titled *Felzartamab for IgA Nephropathy: Final Results of the IGNAZ Study.*

The likely source of pathogenic galactose-deficient IgA1 (Gd-IgA1) and autoantibodies in IgA nephropathy (IgAN) is CD38. Felzartamab, a monoclonal antibody, binds to CD38 on plasma cells in patients with IgAN. IGNAZ is a randomized, double-blind, placebo-controlled phase 2a study that examined the efficacy and safety of felzartamab versus placebo in patients with IgAN.

The study cohort included patients 18 to 80 years with biopsy-confirmed IgAN, proteinuria ≥1.0 g/d (≥0.5 g/d for Japanese patients), and eGFR ≥30 mL/min/1.73 m^2 who were using renin-angiotensin inhibitors ≥3 months. In part one of the trial, patients were randomized 1:1:1:1 to placebo (n=12) or felzartamab in one of three arms: (1) two doses in 15 days (M1; n=12); (2) five doses in 2 months (M2, n=11); or (3) nine doses in 5 months (M3, n=13). In part two of the study, Japanese patients received open-label M3.

Of the overall cohort, 67% were men, mean age was 41.6 years, mean urine protein-creatinine ratio (UPCR) was 1.7 g/g, and eGFR was 74.6 mL/min/1.73 m^2. Forty of the 48 patients in part one completed the study treatment. Participants in the felzartamab arms had rapid, clinically meaningful reductions in UPCR compared to those in the placebo arm. The greatest effect was observed in the M3 arm. Compared to the placebo arm, mean eGFR declined less in the three felzartamab arms. In the felzartamab arms, reductions in IgA were rapid and durable, lasting 19 months after the last dose. IgG recovered by six to nine months. The efficacy in part two was similar to that in the part one M3 arm.

In general, treatment-emergent adverse events were grade 1 or 2 and were not dose dependent. Infusion-related reaction (IRR) was the most common treatment-related adverse event and occurred usually on dose one. There was one serious treatment-related adverse event of IRR, and five patients discontinued study participation due to IRR/hypersensitivity. All three arms had similar incidence of infection, and all were grade 1 or 2 and nonserious.

In summary, the researchers said, "Felzartamab was generally well tolerated and led to sustained proteinuria reduction and reduced eGFR decline versus placebo, indicating potential disease modification in patients with IgAN. Investigation of felzartamab in patients at high risk for loss of kidney function is warranted."

Source: Barratt J, Floege J, Lafayette RA, et al. Felzartamab for IgA nephropathy: final results of the IGNAZ study. SA-OR101. Abstract of an oral presentation at the American Society of Nephrology Kidney Week 2024; October 26, 2024; San Diego, California. Funding for the study was provided by Human Immunology Biosciences, Inc., a Biogen Company.

FLOW Trial Results Categorized by CKD Severity

The FLOW trial was designed to assess the effect of semaglutide versus placebo on the progression of renal impairment in people with type 2 diabetes and chronic kidney disease (NCT03819153). Results demonstrated an association between treatment with semaglutide and reduction in risks of major kidney outcomes, cardiovascuair events, and death from any cause in patients with type 2 diabetes and chronic kidney disease.

During an oral session at ASN Kidney Week 2024, **Katherine R. Tuttle, MD,** and colleagues presented results of an analysis of data from the FLOW trial assessing kidney outcomes by baseline CKD severity. The presentation was titled *Semaglutide Reduced Risks of Major Kidney Outcomes Irrespective of CKD Severity in the FLOW Trial.*

Eligible patients had type 2 diabetes with eGFR 50-75 mL/min/1.73 m^2 and UACR >300 to <5000 mg/g, or eGFR 25 to <50 mL/min/1.73 m^2 and UACR >100 to <5000 mg/g. Trial participants were randomized to receive semaglutide 1 mg subcutaneously once per week or placebo.

The primary outcome of interest was a composite of kidney failure (defined as eGFR <15 mL/min/1.73 m^2 or initiation of chronic kidney replacement therapy), ≥50% decline in eGFR, or death related to kidney or cardiovascular causes. Participants were stratified based on baseline eGFR and UACR.

Of the 3,533 study participants, 1,069 (30%) were women. Mean age at baseline was 67 years, mean eGFR was 47 mL/min/1.73 m^2, and median UACR was 568 mg/g. Over a median of 3.4 years, for the primary outcome of composite of kidney failure, ≥50 decline in eGFR, or kidney or cardiovascular death, the hazard ratio was 0.76 in the semaglutide group versus placebo (95% CI, 0.66-0.88). Results were consistent across categories of eGFR and UACR.

"Semaglutide safely reduced risks of major kidney outcomes irrespective of CKD severity defined by baseline eGFR or UACR in participants with type 2 diabetes and CKD in the FLOW trial," the authors said.

Source: Tuttle KR, Mann JF, Sokareva E, et al. Semaglutide reduced risks of major kidney outcomes irrespective of CKD severity in the FLOW trial. SA-OR93. Abstract of an oral presentation at the American Society of Nephrology Kidney Week 2024; October 26, 2024; San Diego, California. Funding for the study was provided by Novo Nordisk.

FLOW Trial Subanalysis: Effect of Semaglutide on Mortality Outcomes

During a late-breaking oral session at ASN Kidney Week 2024, **Richard E. Pratley, MD,** presented results of a subanalysis of data from the FLOW trial. The trial was designed to assess the effect of semaglutide versus placebo on the progression of renal impairment in people with type 2 diabetes and chronic kidney disease (NCT03819153). The session was titled *Effect of Semaglutide on Mortality Outcomes in the FLOW Trial.*

Eligible adults ≥18 years were randomized 1:1 to receive either once-weekly subcutaneous semaglutide 1.0 mg or placebo. Study results demonstrated an association between a reduction in the risk of major kidney and cardiovascular events and treatment with semaglutide. For the current analysis of the effect of semaglutide on mortality outcomes, cause of death was confirmed by an event adjudication committee.

Compared to those in the placebo group, the risk of all-cause mortality was reduced among those in the semaglutide group (HR, 0.80; 95% CI, 0.67-0.95). There were also reductions in the risk of cardiovascular death (HR, 0.71; 95% CI, 0.56-0.89) and death of undetermined cause (HR, 0.62; 95% CI, 0.42-0.91) in the semaglutide group compared to the placebo group.

The most common causes of cardiovascular death were sudden cardiac death (2.8% in the semaglutide group vs 3.8% in the placebo group) and heart failure (0.3% in the semaglutide group vs 0.7% in the placebo group). There was no effect of semaglutide on noncardiovascular death or nonkidney-related death. Infection (3.3% in the semaglutide group vs 3.7% in the placebo group) and malignancy (1.4% in the semaglutide group vs 1.2% in the placebo group) were the most common causes of noncardiovascular and nonkidney-related death.

In summary, the researchers said, "In FLOW, semaglutide reduced the risk of all-cause and cardiovascular death by 20% and 29%, and death of undetermined cause by 38%, relative to placebo."

Source: Pratley RE, Mahaffey KW, Mann J, et al. Effect of semaglutide on mortality outcomes in the FLOW trial. FR-OR109. Abstract of an oral presentation at the American Society of Nephrology Kidney Week 2024; October 25, 2024; San Diego, California. Funding for the study was provided by Novo Nordisk.

VALIANT Trial of Pegcetacoplan for C3G or IC-MPGN

During an oral session at ASN Kidney Week 2024, **Carla M. Nester, MD,** of the University of Iowa, Stead Family Children's Hospital, Iowa City, presented results of the VALIANT trial. The session was titled *VALIANT: A Randomized, Multicenter, Double-Blind, Placebo (PBO)-Controlled, Phase 3 Trial of Pegcetacoplan for Patients With Native or Post-Transplant Recurrent Glomerulopathy (C3G) or Primary Immune Complex Membranoproliferative Glomerulonephritis (IC-MPGN).*

The trial was designed to examine the efficacy and safety of pegcetacoplan (PEG), a C3/C3b inhibitor, in adolescents (≥12 years of age) and adults with native or post-transplant recurrent C3G or primary IC-MPGN. The primary endpoint of interest was log-transformed ratio of urine protein creatinine ratio (UPCR) at week 26 from baseline as a measure of proteinuria reduction with PEG versus placebo.

Study participants were randomized to receive PEG subcutaneously two times per week (n=63) or placebo (n=61). At week 26, the primary endpoint was met in the PEG group (-67.3%) versus placebo (3.2%); relative reduction, 68.3%; 95% CI, -76.3 to -57.7; $P<.001$. Results were consistent across all subgroups (disease type, age, and transplant status). There were robust reductions in C3c staining as well as clinically meaningful stabilization in eGFR in the PEG group compared to the placebo group.

Overall, there were four serious infections: three in the PEG group and one in the placebo group. None of them were attributed to encapsulated bacteria. There was one death in the PEG arm; cause of death was COVID-19 pneumonia, unrelated to PEG.

In summary, the authors, said, "PEG, a C3/C3b inhibitor, is the first therapy to achieve significant and clinically meaningful reductions in proteinuria (68.3% vs placebo) and C3c staining and eGFR stabilization, compared with placebo in patients ≥12 years with C3G or primary IC-MPGN and was well tolerated."

Source: Nester CVM, Bomback AS, Ariceta I, et al. VALIANT: a randomized, multicenter, double-blind, placebo (PBO)-controlled, phase 3 trial of pegcetacoplan for patients with native or post-transplant recurrent glomerulopathy (C3G) or primary immune complex membranoproliferative glomerulonephritis (IC-MPGN). SA-OR92. Abstract of an oral presentation at the American Society of Nephrology Kidney Week 2024; October 26, 2024; San Diego, California.

Treatment for Primary Membranous Nephropathy: Feasibility Study Results

Researchers have identified Bruton tyrosine kinase (BTK) as playing an important role in modulation of B cells, providing a potential therapeutic target for the treatment of primary membranous nephropathy (PMN), an antibody-driven glomerular disease.

During a poster session at ASN Kidney Week 2024, **Richard A. Lafayette, MD,** and colleagues presented results of a phase 2/3 study examining the efficacy and safety of zanubrutinib in patients with PMN. The poster was titled *Zanubrutinib for the Treatment of Primary Membranous Nephropathy (PMN): Results of a Single-Arm Feasibility Study.*

Zanubrutinib is a highly selective inhibitor of BTK. The two-part, open-label study included 30 patients. Eligible patients had anti-phospholipase A2 receptor (PLA2R) antibody ≥50 RU/mL and urinary protein-creatinine ratio (UPCR) >3.5 g/g. Following a 12-week run-in period that included optimal supportive care, participants received zanubrutinib 160 mg twice a day for 64 weeks. The treatment phase was followed by a 40-week observation period.

The primary endpoint of interest was the change in UPCR from baseline at week 24. Secondary outcomes included anti-PLA2R antibody titer, serum albumin level, overall remission rate, and safety.

Of the 30 participants, 66.7% were men and 93.3% were Asian. Baseline values were median UPCR 7.5 g/g, serum albumin 23.5 g/L, and eGFR 85.2 mL/min/1.73 m^2. Median duration of exposure as of July 15, 2024, was 26.5 weeks, and 20 patients had completed the week 24 visit (five patients discontinued early).

Median change from baseline in UPCR at 24 weeks was -1.5 g/g. Six patients (30%) had partial remission, defined as UPCR 0.3-3.5 g/g and ≥50% decrease from baseline, and stable eGFR. The immunological response rate, defined as anti-PLA2R titer reduction to <14 RU/mL, was 60%.

In safety measures, 87% of patients (n=26) had treatment-emergent adverse events, primarily upper respiratory tract infections (27%), rash (20%), and hypokalemia (17%). Four participants had severe treatment-emergent adverse reactions. One of those was treatment-related.

In summary, the authors said, "Zanubrutinib appears to be generally well tolerated and shows activity in patients with PMN."

Source: Lafayette RA, Barbour S, Chen Y, et al. Zanubrutinib for the treatment of primary membranous nephropathy (PMN): results of a single-arm feasibility study. TH-P01204. Abstract of a poster presented at the American Society of Nephrology Kidney Week 2024; October 24, 2024; San Diego, California. Funding for the study was provided by Bei-Gene Co., Ltd.

FINEARTS-HF Prespecified Analysis Results: Finerenone and Renal Outcomes

Finerenone provides renoprotective effects in patients with CKD and type 2 diabetes, but there are few data available on kidney outcomes among patients with heart failure (HF) with and without diabetes and/or CKD.

During an oral presentation at ASN Kidney Week 2024, researchers, led by **Finnian R. McCausland, MD,** reported prespecified analysis results from FINEARTS-HF. The presentation was titled *Finerenone and Kidney Outcomes in Patients With Heart Failure: The FINEARTS-HF Trial.*

The global, randomized clinical trial compared finerenone to placebo in a study population of patients with HF and mildly reduced or preserved ejection fraction. Outcomes of interest included a sustained decline of ≥50% in eGFR or kidney failure, defined as sustained eGFR decline ≤15 mL/min/1.73 m^2, initiation of chronic dialysis, or renal transplant. During the session, the researchers reported the effects of finerenone on sustained ≥57% eGFR decline or kidney failure and changes in urine albumin-to-creatinine ratio (UACR).

The study included 6,001 patients. Mean eGFR was 62 mL/min/1.73 m^2, and 48% had eGFR <60 mL/min/1.73 m^2. Of the 6,001 patients, 5,797 had baseline UACR data: median 18 mg/g; 61% had UACR <30 mg/g; 30% had UACR 30 to <300 mg/g; and 10% had UACR ≥300 m/g.

During a median of 2.6 years of follow-up, the incidence of the composite kidney outcome was low and not affected by finerenone (75 vs 55 events; HR 1.33; 95% CI, 0.94-1.89). Results were similar for ≥57% decline in eGFR or kidney failure (41 vs 31 events; HR, 1.28; 95% CI, 0.80-2.05). In the finerenone group at six months, UACR was reduced by 30% (95% CI, 25%-34%) compared to placebo. The effect persisted throughout follow-up in patients with and without diabetes ($P_{interaction}$=.48). In patients with baseline UACR ≤300 mg/g, the risk of new-onset of macroalbuminuria was reduced by 38% with finerenone (HR, 0.62; 95% CI, 0.53-0.73), in patients with and without diabetes ($P_{interaction}$=.96).

"Finerenone did not modify eGFR-based kidney outcomes but led to early and sustained reductions in albuminuria and reduced the risk of new-onset of macroalbuminuria among patients in FINEARTS-HF at low risk of adverse kidney outcomes," the researchers said.

Source: McCausland FR, Vaduganathan M, Claggett B, et al. Finerenone and kidney outcomes in patients with heart failure: the FINEARTS-HF trial. FR-OR100. Abstract of an oral presentation at the American Society of Nephrology Kidney Week 2024; October 25, 2024; San Diego, California. Support for the study was provided by Bayer.

Print-only Content

Kidney Failure, Mortality With Rare Kidney Diseases Versus CKD

Patients with rare kidney diseases account for only 5% to 10% of those with chronic kidney disease (CKD). However, they comprise more than 25% of patients receiving kidney replacement therapy (KRT). In addition, more than 50% of children and adults younger than 20 years receiving KRT have a rare kidney disease. Glomerulonephritis accounts for more UK adults receiving KRT than any common causes of CKD, including diabetes.

The reasons for this are poorly understood, and having more insight into these questions may help with prognosis and therapies. To help address this need for information, **Katie Wong, MBBS,** and colleagues conducted a retrospective cohort study using data from the National Registry of Rare Kidney Diseases (RaDaR), established by the UK Kidney Association. Their findings were published in *The Lancet* [2024;403:1279–89].

Data spanned from January 18, 2010, to July 25, 2022, and included 27,285 patients aged 0 to 96 with 28 rare kidney diseases from

108 UK renal care facilities. The median age at diagnosis for the entire RaDaR cohort was 40.6 years (interquartile range [IQR] 23.7-57.1). However, the median age varied by rare disease group. Follow-up was calculated as the time from the date of diagnosis until the data extraction date (July 25, 2022) or until death, whichever came first; median follow-up from diagnosis was 9.6 years (IQR 5.9-16.7).

The exposure being investigated was a diagnosis of rare kidney disease. Primary outcomes included cumulative incidence of mortality and kidney failure in patients with rare kidney diseases, which was calculated and compared with that of unselected patients with CKD.

Kidney failure was defined as the need for chronic KRT (dialysis or transplantation), or an estimated glomerular filtration rate (eGFR) of less than 15 mL/min per 1.73 m² for 4 weeks or more. Secondary outcomes included median age at kidney failure, median age at death, and time from start of dialysis to death. Another secondary outcome was time from diagnosis to eGFR thresholds, which allowed for calculation of time from the last eGFR of 75 mL/min per 1.73 m² or more to the first eGFR of less than 30 mL/min per 1.73 m² (the therapeutic trial window, an estimate of time from diagnosis that patients would have sufficient renal function to participate in a standard therapeutic trial).

The participants with rare kidney diseases differed significantly from individuals with CKD regarding both kidney failure and mortality. Those with rare kidney diseases had higher five-year rates of kidney failure (28% vs 1%; *P*<.0001), although there was significant heterogeneity in age at kidney failure among rare disease groups. For example, patients with cystinosis often reached kidney failure as children (median age at kidney failure 15.4 years; IQR 11.6-19.9), while those with vasculitis, *HNF1B* mutations, thin basement membrane nephropathy, monoclonal gammopathy of renal significance, and membranous nephropathy usually reached kidney failure at ≥65 years. Sensitivity analyses for age at kidney failure and time from diagnosis with death as a competing risk had similar findings.

> The participants with rare kidney diseases differed significantly from individuals with CKD regarding both kidney failure and mortality.

Survival was higher among those with rare kidney diseases versus those with CKD stages 3-5 (standardized mortality ratio 0.42; 95% CI, 0.32-0.52; *P*<.0001). Survival on dialysis was also longer for those with rare kidney diseases. Therefore, patients with rare kidney diseases represent a disproportionate number of those receiving KRT.

The median age at kidney failure, median age at death, time from start of dialysis to death, time from diagnosis to eGFR thresholds, and therapeutic trial window varied significantly among rare kidney diseases. Median age at death was either not evaluable due to too few events or >75 years for all rare disease groups. The exception was cystinosis, with a median age at death of 56.4 years.

Notably, disease progression was faster among those with rare kidney diseases than unselected patients with CKD. In patients younger than 65 years, the kidney failure risk equation did not accurately predict disease trajectory.

The heterogeneous outcomes among rare kidney diseases highlight the need for precise diagnosis, which helps to inform treatment decisions and may provide important prognostic information.

The authors acknowledge limitations of the study: The UK focus of the data may not be more broadly generalizable. Recruitment criteria for certain rare disease groups may favor the ascertainment of patients with more severe disease. Data for age at death are limited by length of follow-up and survivor bias. Comparisons of intervals between diagnosis and kidney failure among different diseases may not always be meaningful, as different rare diseases occur at different ages. Biases may be present in some estimates due to the absence of healthy or unselected CKD control groups.

"In unselected cohorts with chronic kidney disease, death before kidney failure is a common adverse outcome, whereas among patients with rare kidney diseases, survival is higher and kidney failure much more common," the authors summarized. "This finding means that, although strategies to address cardiovascular risk and other causes of death are very important in the large number of individuals with [CKD] in the population, a substantial proportion of kidney failure is attributable to individually rare kidney diseases in which cardiovascular risk reduction will not prevent kidney failure. Patients with rare kidney diseases should therefore be distinguished from those with more common causes of [CKD, emphasizing] the importance of early specialist referral and diagnosis, and the need for rare kidney disease-specific treatments aimed at delaying progression to kidney failure." ■

TAKEAWAY POINTS

- People with rare kidney diseases comprise 5%-10% of those with CKD but make up more than 25% of patients receiving KRT.
- This study evaluated 27,285 UK patients with rare kidney diseases for incidence of mortality and kidney failure compared with nonparticipants with CKD.
- Patients with rare kidney diseases differ from the general CKD population and are overrepresented among patients requiring KRT. Addressing their unmet therapeutic needs could be beneficial for long-term KRT demand.

Post-AKI Mortality, Readmission With Blood Pressure, Time From Discharge

More than one-fourth of patients discharged from the hospital after AKI will die within the next year, with cardiovascular disease (CVD) being the leading cause. Among patients in the Veterans Health Administration (VHA) system, the prevalence of cardiovascular risk factors and existing CVD are higher than in the general population. Blood pressure control is critical for patients who have experienced AKI, yet optimal blood pressure targets and timing of blood pressure control for this population are not defined.

Data on the association of blood pressure with post-AKI outcomes and the degree to which time from discharge is associated with risks and benefits is lacking. Researchers led by **Benjamin R. Griffin, MD,** wanted to determine the associations of systolic blood pressure (SBP) with mortality and hospital readmission, as well as whether time from hospital discharge affects these associations among those post-AKI. Their findings were published in *JAMA Network Open* [doi:10.1001/jamanetworkopen.2024.10824].

The retrospective cohort study was conducted between January 2013 and December 2018 and included 80,960 adults with AKI during hospitalization in VHA hospitals. Data analysis took place from May 2022 to February 2024.

The study excluded patients with ≤1 year of data within the health system prior to admission, severe or end-stage liver disease, stage 4-5 chronic kidney disease, end-stage kidney disease, metastatic cancer, or no blood pressure values within 30 days of discharge. Of the total participants, 77,965 (96.3%) were male, 2,995 (3.7%) were female, and 57,242 (70.7%) were aged 65 years or older.

Rates of diabetes were high and included 16,060 patients (20.0%). In addition, 22,516 patients (28.1%) had congestive heart failure and 27,682 (34.2%) had chronic lung disease. One-year mortality occurred in 12,876 patients (15.9%).

SBP was treated as time-dependent and was categorized as <120 mmHg, 120-129 mmHg, 130-139 mmHg, 140-149 mmHg, 150-159 mmHg, and ≥160 mmHg. Time spent in each SBP category was gathered and represented in 30-day increments. The study's primary outcomes were the time to mortality and the time to all-cause hospital readmission.

The researchers adjusted Cox proportional hazards regression for demographics, comorbidities, and lab values. To assess associations over time, they calculated hazard ratios (HRs) at 60, 90, 120, 180, 270, and 365 days after discharge.

TAKEAWAY POINTS

- This retrospective cohort study examined patients with AKI to determine associations of SBP with mortality and hospital readmissions following AKI, and whether time from discharge impacts these associations.
- Patients with SBP 130-139 mmHg had the most favorable risk level for mortality and readmission over time. Those with higher blood pressures were generally at lower risk for mortality and readmission at first but were at higher risk later postdischarge.
- There were substantial differences in the associations of SBP with readmission and mortality based on time from discharge. The findings may inform the timing and treatment of blood pressure post-AKI.

> Patients with SBP 130-139 mmHg had the most favorable risk level for mortality and hospital readmission and the lowest mortality risk.

Timing relative to hospital discharge significantly affected associations of SBP with both mortality and hospital readmission rates. There were clear, time-dependent mediations on associations in all groups. Patients with SBP 130-139 mmHg had the most favorable risk level for mortality and hospital readmission and the lowest mortality risk at most time points.

The SBP 130-139 mmHg group had a statistically significant increase in mortality risk compared to patients with SBP of ≥160 mmHg at 60 days (adjusted HR [aHR], 1.20; 99% CI, 1.00-1.44). No association with mortality was observed at 90, 120, and 180 days, but there was a statistically significant decrease in mortality risk by 270 days (aHR, 0.72; 99% CI, 0.59-0.90) that endured at 365 days (aHR, 0.58; 99% CI, 0.45-0.76).

Patients with SBP ≥160 mmHg had the lowest projected mortality at 60 days but the highest projected mortality of all groups except those with SBP <120 mmHg at 365 days. Patients with SBP 120-129 mmHg had a significantly higher risk of mortality than patients with SBP ≥160 mmHg through the first 180 days, but there were no statistical differences between those groups at 270 or 365 days. Patients with SBP <120 mmHg had the highest risk of mortality at each time point, including at 60 (aHR, 2.20; 99% CI, 1.85-2.62) and 365 days (aHR, 1.82; 99% CI, 1.47-2.25).

Patients with SBP 130-139 mmHg had the lowest risk of readmission at most time points and a significantly lower risk of readmission by 180 days. This was also the only group without a statistically higher risk for readmission at 60 days compared to patients with SBP ≥160 mmHg. Patients with SBP ≥160 mmHg or greater had the lowest projected readmission rate at first, but the highest rate at every time point after approximately six months.

The study's limitations include possible residual confounding, ascertainment bias, and bias related to the level of medical care. There is also inadequate data to determine whether medication regimens were adjusted in this population to achieve blood pressure goals and limited generalizability due to participants being largely male.

"In this retrospective cohort study of patients post-AKI there were substantial variations in the associations of SBP with mortality based on time from discharge," the authors summarized. "Risks of mortality and readmission relative to elevated blood pressure were highest in the immediate postdischarge period, with a shift toward lower mortality and readmission at later time points. Veterans with SBP between 130 and 139 mmHg had the most favorable risk level over time of any group. These findings may have important implications for the timing and targets for blood pressure control used in post-AKI care." ■

Hyperglycemic Crises Concurrent With Newly Diagnosed Diabetes and Risk of CKD

Life-threatening hyperglycemic crises (HC) associated with diabetes, including diabetic ketoacidosis (DKA) and hyperglycemic hyperosmolar state (HHS), are commonly seen in patients with preexisting diabetes. According to researchers, up to 20% of cases of those complications are seen in patients with newly diagnosed diabetes. Patients with HC are at an increased risk of subsequent morbidity and mortality compared to those without HC.

There are few data available on the risk of chronic complications among patients experiencing HC at the initial presentation of type 2 diabetes. **Chun-Ta Huang, MD,** and colleagues in Taiwan conducted a study to assess the risk of developing chronic kidney disease in patients experiencing HC at the time of type 2 diabetes diagnosis. The study was designed to test the hypothesis that there is an association between HC occurring at the time of diabetes diagnosis and a higher risk of developing CKD. Results of the study were reported online in *Scientific Reports* [doi:10.1038/s41598-024-67678-3].

The study utilized the Taiwan National Health Insurance Research Database (NHIRD) to identify newly diagnosed cases of type 2 diabetes between 2006 and 2015. Exclusion criteria were diagnosis with diabetes or use of glucose-lowering drugs prior to the study period, age less than 20 years, history of kidney disease (including benign or malignant neoplasms of the kidney, CKD of any cause, glomerulonephritis, nephrotic syndrome, urolithiasis, and congenital renal anomalies), or deceased at baseline.

The primary outcome of interest was the combined incidence of CKD or diabetic kidney disease (DKD) or both. CKD was defined as GFR <60 mL/min/1.73 m^2 and/or markers of kidney damage that persist for more than 3 months. DKD was defined as cases with CKD presumed to be caused by diabetes.

The HC cohort included individuals with concurrent HC at the time of their type 2 diabetes diagnosis. A control cohort (non-HC) of the same sample size frequency matched by diagnosis year and propensity score was drawn from the NHIRD. Multivariable logistic regression for each person at baseline was used to calculate propensity scores. Variables included sex, age, type of residence, enrollment category, monthly income, comorbidities (hypertension, heart failure, coronary artery disease, ischemic stroke, transient ischemic attack, peripheral arterial disease, hyperlipidemia, obesity, and malignancy), and use of angiotensin-converting enzyme inhibitors (ACEis) or angiotensin II receptor blockers (ARBs).

Each cohort included 13,242 participants. The mean age was approximately 54 years and 62% were male. The HC cohort had lower income and higher prevalence of malignancy compared to the control cohort (6.24% vs 2.99%, respectively). The HC cohort had lower prevalence of hypertension and hyperlipidemia compared to controls (32.7% vs 37.5% and 13.2% vs 20.7%, respectively). The proportions of patients who received ACEis or ARBs were similar in the two groups.

The HC cohort comprised three subcohorts: patients with DKA, those with HHS, and those with combined DKA and HHS. In the overall HC cohort, 55.1% had DKA, 39.2% had HHS, and 5.7% had combined DKA-HHS. During a median follow-up of 4.97 years in the HC cohort, there were 4,106 (31%) events observed, compared to 2,735 (20.7%) events during a median of 7.15 years of follow-up in the control cohort, corresponding to incidence rates of 56.47 and 29.48 per 1,000 person-years, respectively. The cumulative incidence was higher in patients with HHS and combined DKA-HHS than in those with DKA in the HC cohort.

The cumulative incidence of CKD and DKD was significantly higher in the HC cohort than in the control cohort. In the HC cohort, the cumulative incidence was greater in those with HHS and combined DKA-HHS than in those with DKA. The adjusted HRs (aHRs) among the HC subcohorts ranged from 1.69 (95% CI, 1.59-1.79) for DKA to 2.47 (95% CI, 2.33-2.63) for HHS and 2.60 (95% CI, 2.29-2.95) for combined DKA-HHS. The HRs were attenuated but retained statistical significance in the main HC cohort and its subcohorts in subdistribution hazard models.

The researchers performed separate subgroup analysis in individuals 40 years or older (HC group, n=10,266 and control group, n=10,419), including 5,104 individuals with DKA and 4,591 with HHS in the HC cohort. The results were similar to those in the primary analysis, with a comparable increase in the HR between the HC and control cohorts. There was also a stepwise escalation in the aHR among the HC subcohorts from 1.62 (95% CI, 1.51-1.72) for DKA to 2.33 (95% CI, 2.19-2.49) for HHS, and 2.59 (95% CI, 2.25-2.98) for combined DKA-HHS.

Results of the nested-case control analysis demonstrated that the risk of developing CKD or DKD was significantly higher for patients with a history of hyperlipidemia (adjusted OR [aOR], 1.22; 95% CI, 1.15-1.30), acute kidney injury (aOR, 1.33; 95% CI, 1.18-1.50), DKA (aOR, 1.56; 95% CI, 1.47-1.66), and HHS (aOR, 1.75; 95% CI, 1.64-1.86). The risk was also higher for those who received treatment with ACEis or ARBs compared to those who did not receive those agents (aOR, 1.93; 95% CI, 1.75-2.13 for those treated for ≤90 days and aOR, 1.69; 95% CI, 1.57-1.82 for those treated for ≥90 days).

Limitations to the study cited by the authors included relying solely on claims data that might have created the possibility of misclassification of diseases, the inability to adjust for covariates not included in the NHIRD (laboratory tests, blood pressure, waist circumference, body mass index, and lifestyle), and the possibility that the findings are limited to populations with similar characteristics.

In summary, the researchers said, "Patients who experience HC upon type 2 diabetes diagnosis have a higher risk of developing CKD compared with those without HC at diagnosis. As type 2 diabetes and end-stage renal disease are highly prevalent in Taiwan, proactive preventive measures are imperative to mitigate risks in this vulnerable population. These interventions should include early introduction of ACEis or ARBs and sodium glucose cotransporter-2 inhibitors, stringent control of diabetes and the reduction of other risk factors, and educational programs for continuous diabetes self-care management. Furthermore, health care authorities should reinforce government-subsidized diabetes screening programs, especially for the underprivileged to facilitate early recognition of undiagnosed diabetes and prevent HC Incidents." ■

TAKEAWAY POINTS

- Data on long-term kidney outcomes among patients with hyperglycemic crisis as their initial type 2 diabetes presentation are limited.
- Researchers examined the risk of CKD development in patients with concurrent hyperglycemic crisis at diagnosis.
- The combined incidence of CKD and DKD was twofold higher in the HC cohort than in the control group. Medical attention and customized interventions are needed to reduce this risk.

Using Genetic Testing to Identify Risk of Morbidities in Kidney Transplant Recipients

Compared with dialysis, treating end-stage renal disease (ESRD) with kidney transplantation is associated with significant improvements in survival and quality of life. However, recipients of kidney transplants may experience complications and face increased risk of morbidity and mortality, despite the use of modern immunosuppression regimens and improved surgical techniques.

Complications experienced by kidney transplant recipients include cardiovascular diseases, diabetes, infections, malignancies, and venous thromboembolism. The leading cause of mortality in kidney transplant recipients is cardiometabolic disorders. Previous studies have indicated that 15% of deaths at 10 years following transplantation result from cardiovascular events. Nonfatal cardiovascular events are also associated with future allograft failure and increased mortality. The second most common cause of mortality in this patient population is infection. Kidney transplant recipients are at risk of serious infections due to the need for lifelong immunosuppression. Malignant neoplasm is third among causes of death in kidney transplant recipients, and venous thromboembolism is fourth.

There are multifactorial causes associated with these complications; however, they may be caused by monogenic forms of disease in a subset of patients. Identification of monogenic conditions that predispose patients to kidney disease and to complications following kidney transplant may enable clinicians to initiate personalized management plans for those at risk, beginning during the perioperative period.

Becky M. Ma and colleagues conducted a clinical investigation to develop a transplant morbidity gene panel to assess its diagnostic yield and identify its potential impact on clinical care in the kidney transplantation space. Results were reported in *Kidney International* [2024;106(1):115-125].

Kidney transplant recipients followed at Columbia University Irving Medical Center, New York, in a biobanking study were recruited from October 2007 to January 2023 (n=1,590). Genomic DNA samples were isolated, from samples gathered from patients per standard protocol. The diagnostic yield of actionable variants was calculated on counts of individuals with variants classified as pathogenic or likely pathogenic.

The transplant morbidity panel developed by the researchers consisted of 355 genes. The majority of the panel represented genes associated with cardiovascular events and with diseases associated with increased risk of cardiovascular events (hypercholesterolemia or diabetes; 198 genes, 56%). Genes associated with malignant neoplasm, adult-onset immunodeficiency, and thrombophilia were also included (105 genes, 30%; 39 genes, 11%; and 13 genes, 4%, respectively). Ninety-seven (27%) genes in the panel were associated with Mendelian kidney and genitourinary disorders, and 67 (19%) genes were also part of the American College of Medical Genetics and Genomics-recommended genes for secondary findings.

Study participants received their first kidney transplant between May 1970 and October 2022. Most (98.3%) of the patients were ≥18 years of age. Mean age at the time of first kidney transplant was 43.6 years, 60.3% were male, and 25.3% self-identified as non-White, 26.8% as Hispanic, and 46.2% as White. Causes of ESRD were glomerulopathy (38.7%), diabetic kidney disease (16.7%), congenital/cystic kidney disease (13.7%), hypertensive nephropathy (10.9%), tubulointerstitial disease (2.6%), other (6.8%), and chronic kidney disease (CKD) of unknown origin (10.6%). Of the total cohort, 1,010 individuals had been included in a previous study investigating the diagnostic utility of exome sequencing in patients with CKD, and 69 of those 1,010 (6.8%) had a known monogenic cause of CKD.

Results of the analysis of the morbidity gene panel identified 155 variants associated with 56 monogenic disorders in 144 of the 1,590 (9.1%) study participants. In the cardiovascular category, the diagnostic yield was 5.1% (81/1,590). In the malignant neoplasm category, the yield was 2.1% (34/1,590); in the immunodeficiency category, the yield was 1.8% (29/1,590); and in the thrombophilia category, the yield was 0.2% (3/1,590). Eight of the 1,590 (0.8%) participants had dual genetic diagnoses; three of those had genetic diagnosis under two different disease categories.

More than half of the study participants had diagnostic variants in one of nine genes (listed in descending order): *TNFRSF13B, TTR, BRACA2, KCNQ1, PLIN1, HFE, HNF1A, TSC1,* and *MYBPC3*. Most of the monogenetic disorders were of autosomal dominant inheritance, and 145 of the 155 had been previously reported.

Among the participants with genetic disorders, identification of the disorders and risk factors could allow clinicians to create specific risk factor targets in nine of the 144 individuals with monogenetic disorders (6.3%), schedule intensive surveillance in 140 individuals (97.2%), use preventive measures in 19 individuals (13.2%), prescribe disease-specific therapy in 92 individuals (63.9%), refer 130 individuals to a specialist (90.3%), and revise immunosuppressive regimens in 82 individuals (56.9%).

Analysis of the Mendelian kidney and genitourinary disorders gene panel revealed 170 diagnostic variants associated with 37 monogenic disorders in 158 individuals, for a diagnostic yield of 9.9%.

In citing limitations to the study findings, the researchers mentioned not including mitochondrial disease in the gene panel, not examining the cost-effectiveness and long-term benefits of incorporating the transplant morbidity gene panel as part of the pretransplant workup, and the lack of guidelines specific to the transplant population to address cohort-specific risks and needs.

In summary, the authors said, "Our findings illustrate the clinical utility of the morbidity gene panel in kidney transplantation and should be applicable to any solid organ transplantation. By integrating genetic testing early in transplant evaluation, a management plan can be individually tailored, aiming to reduce complications. ... Studies to longitudinally evaluate the impact of both monogenetic and polygenetic risk on transplant treatment decisions, allograft survival, overall morbidity, and mortality are needed. ... Incorporating genetic diagnostics for transplant morbidities would enable personalized management in pre- and post-transplant care." ■

TAKEAWAY POINTS

- Cardiovascular disease, infection, malignancy, and thromboembolism are leading causes of mortality in kidney transplant recipients (KTRs). Prospectively identifying such conditions could boost personalized management.
- This study examined the potential of using panel-based exome sequencing in identifying monogenic causes of major post-transplant complications. The transplant morbidity panel found a high diagnostic rate (9.1%) in KTRs.
- The findings suggest that incorporating genetic diagnostics into transplant evaluation would allow for personalized management to help improve prognosis for KTRs.

Kidney Transplant Outcomes With Organs From Toxoplasma–Positive Donors

In light of the shortage of organ donors and the considerable number of patients on the waiting list for kidney transplant, a systematic review of organ acceptance practices may yield new insight into donors previously considered unsuitable. Recent examples of additions to acceptable donor profiles include kidneys from donors following cardiac arrest, as well as donors who have experienced acute kidney injury.

Toxoplasma, an intracellular protozoan parasite commonly found in humans and animals, is associated with mild and self-limited illness in immunocompetent individuals. Based on historical data indicating high mortality, particularly in recipients of heart transplant, kidney transplantation with kidneys from toxoplasma-positive donors (TPD) has been considered risky and been discouraged. In 2017, the Organ Procurement and Transplantation Network (OPTN) mandated the screening of all deceased organ donors for toxoplasma. Guidelines and final decisions regarding the use of kidneys from TPD were left to individual transplantation centers.

Lavjay Butani, MD, and **Daniel Tancredi, PhD,** conducted a retrospective cohort analysis comparing outcomes in recipients of TPD kidney transplantation with those who received kidneys from toxoplasma-negative donors. Results were reported online in *Transplant International* [doi:10.3389/ti.2024.13203].

The study cohort included patients in the OPTN database who received their first deceased donor kidney-only transplant between February 28, 2018, and June 30, 2022. Pearson Chi-squared or Fisher exact tests were used to compare categorical variables in donor and recipient demographics and peritransplant characteristics among the study cohort stratified by toxoplasma IgG antibody status (positive or negative). The Kruskal Wallis test was used to compare continuous variables.

Survival analyses were used to identify the primary outcome measure of time to graft failure or death. Secondary outcomes were infection as cause of death, infection as cause of graft failure, and a composite of infection as the cause of either death or graft failure, compared with all other known causes of death.

The study population included 51,422 patients. Of those, 95.7% were adults, 59.9% were male, 34.6% self-identified as non-Hispanic White, and 34.4% self-identified as Black. The most prevalent cause of chronic kidney disease (CKD) was glomerular disease (77.3%). Anoxia was the leading cause of donor death (51.7%), followed by head trauma (29.4%). The majority of recipients were poorly matched for human leukocyte antigens (HLA; 76.8% had ≥3 HLA mismatches). Ninety percent of patients had received dialysis prior to transplantation. Of the overall cohort, 8.4% (n=4,317) of the transplants were from TPD. At one year post-transplant, the rates of delayed graft function and acute rejection were 28.5% and 4.9%, respectively.

The two cohorts were similar in most demographic and peritransplant characteristics. There was a disproportionately higher percentage of deaths in the TPD group attributed to stroke/cerebrovascular accident compared with the toxoplasma-negative group (21.6% vs 14.5%), a difference that may be explained by the known association between toxoplasma and stroke. Adult recipients were more likely to have received a TPD kidney compared with pediatric recipients (8.5% vs 5.3%; $P<.0001$). Men were more likely to have received a TPD kidney compared to women (8.7% vs 8.0%; $P=.005$). The two groups were similar in race/ethnicity and causes of CKD.

Multivariate regression analyses revealed some independent predictors of graft failure, including recipient sex (males had higher risk of failure), recipient age (the oldest three recipient age groups had the highest risk of failure compared to the youngest group), recipient ethnicity (the risk was lower among White and Hispanic recipients compared to Black recipients), receipt of pretransplant dialysis, pretransplant serum hypoalbuminemia, increasing donor age, five or more HLA mismatches, and cold ischemia time. Donor toxoplasma antibody status was not a significant predictor of graft failure.

The crude mortality rate among patients receiving kidneys from toxoplasma-negative donors was 4.93 deaths per 100 years of follow-up (95% CI, 4.76-5.09). The crude mortality rate among recipients of kidneys from TPD was 5.64 deaths per 100 years of follow-up (95% CI, 5.06-6.23). The unadjusted rate ratio was 1.14 (95% CI, 1.02-1.27; $P=.02$). Following adjustment using the same covariates used to model graft loss, the adjusted rate ratio was 1.02 (95% CI, 0.91-1.24; $P=.73$). There were no statistically significant differences between the two groups in any of the secondary outcome measures.

The researchers cited some limitations to the study findings, including restriction of analyses to recipients of deceased donor kidney transplants only and the use of antimicrobial prophylaxis in the post-transplant period. Also cited was the possibility of selection bias due to differences in transplant center policies related to selectively opting for transplant TPD organs in seropositive recipients who are at lower risk of post-transplant toxoplasmosis.

In conclusion, the authors said, "Our data confirm that transplants from TPD occur in all geographic regions of the United States and are associated with comparable graft failure rates. We do strongly advocate for ongoing donor testing for toxoplasma, testing of transplant recipients for toxoplasma, universal [trimethoprim-sulfamethoxazole] prophylaxis if either the donor or recipient is positive, and close monitoring of patients, especially after discontinuation of prophylaxis, as late-onset toxoplasma may occur.

"Based on our data, we suggest that transplant centers reevaluate their current policy on the acceptance of TDP organs in light of the recent data, and not discard such organs without considering the pros and cons of doing so, for each individual potential transplant recipient. Even if all of our recipients were toxoplasma seropositive (which is unlikely), we believe that this study adds to the literature and would be of practical value and benefit in that at least in the recipient cohort that is seropositive for toxoplasma, the use of TPD organs should not be a cause for concern." ■

TAKEAWAY POINTS

- Kidney transplantation with kidneys from toxoplasma-positive donors (TPD) is considered risky, but decisions about the use of such kidneys are left to individual transplantation centers.
- Researchers compared outcomes in recipients of TPD kidney transplantation with those who received kidneys from toxoplasma-negative donors. The study population included 51,422 patients; 8.4% (n=4,317) of transplants were from TPD.
- Donor toxoplasma antibody status was not a significant predictor of graft failure, suggesting that transplant centers should reevaluate their current policy on the acceptance of TDP organs.

Promising Data on JuxtaFlow Renal Assist Device

The medical device company Roivios shared clinical data from the BIPASS-AKI Feasibility Study of the JuxtaFlow Renal Assist Device (RAD) at the Society of Thoracic Surgeons Perioperative Care Conference. The findings were presented by **Evelio Rodriguez, MD,** chief of cardiothoracic surgery at Ascension Saint Thomas Hospital in Nashville, Tennessee, at a poster session.

The study supported the potential of JuxtaFlow RAD to enhance kidney function after cardiac surgery with cardiopulmonary bypass, a critical advancement for patients with existing kidney impairment. Patients with CKD undergoing cardiac surgery have incidence rates of acute kidney injury (AKI) up to 50% or more.

Only two of 10 patients treated with the RAD experienced a postoperative AKI, and one case was the result of a protocol deviation. The RAD was found to be safe, with no cases of gross hematuria and no adverse events linked to the device's active energy.

The study marks the first use of the JuxtaFlow RAD in a surgical setting.

Partnership to Enhance Diagnostic Capabilities for AKI

Beckman Coulter Diagnostics Inc. and SphingoTec GmbH have entered a partnership to bring an assay for SphingoTec's kidney function biomarker, Proenkephalin 119-159 (penKid), to Beckman Coulter's test menu for use on the Access Family of Immunoassay Analyzers.

Under the agreement, Beckman Coulter will develop and validate a fully automated diagnostic test for penKid, leveraging SphingoTec's IVD-certified assay. The move is expected to greatly enhance diagnostic capabilities for AKI by leveraging Beckman Coulter's global installed base of instruments.

PenKid is a real-time biomarker in plasma designed to address gaps in the standard diagnostic practices for AKI, particularly in critical care environments. The partnership will facilitate the high-throughput availability of penKid assays in central laboratories, supporting critical care physicians with the ability for timely and precise kidney health assessment.

Pig Kidney Survives Transatlantic Flight

For the first time, a pig kidney preserved at subzero temperatures was successfully transported across the Atlantic Ocean several times. X-Therma's XT-ViVo organ preservation solution and TimeSeal transportation device were used to extend organ storage and preservation times, showing the potential of the products to make long-distance organ transportation possible.

Led by **Gerald Brandacher, MD,** a surgical and research team at the Johns Hopkins University School of Medicine in Baltimore, Maryland, removed a kidney from a pig and transported it on a commercial aircraft to the Medical University of Innsbruck in Austria, where it was assessed on a clinical-grade machine perfusion device and demonstrated viability and functionality.

The team repeated the process five times over 12 months with preservation times ranging from 48 to 72 hours. In addition, they performed a life-supporting transplant in a pig, with the kidney maintaining normal function for 200 days post-transplant after 72 hours ice-free subzero preservation.

Extending organ preservation time could lead to more transplants and more lives saved. The current standard time for kidney preservation is 24 hours.

KidneyVault Portable Renal Perfusion System Gets FDA 510(k) Clearance

Paragonix Technologies has received US Food and Drug Administration 510(k) clearance for its donor kidney preservation system, KidneyVault. This is the company's first perfusion device.

In hypothermic machine perfusion, a machine continuously pumps a specialized solution through an organ to help preserve it for transplantation. Although this method has demonstrated benefits for kidney transplantation, a portable, user-friendly perfusion device did not previously exist. KidneyVault offers a state-of-the-art preservation device that integrates perfusion techniques with advanced digital monitoring and transport capabilities to streamline the process from donation to recipient and ensure donor organs arrive in optimal condition.

ASN President Seeks to Redefine the Standard of Care

In her opening address at the American Society of Nephrology (ASN) Kidney Week, ASN President **Deidra C. Crews, MD,** called on health care providers and advocates to address social disparities among patients with kidney disease and "redefine the standard of care."

Crews pointed out several ways in which the ASN is leading the way in this effort, including collaborating with federal agencies to increase funding and improve policy, working with global entities (such as the European Renal Association and the International Society of Nephrology) to increase kidney care awareness, partnering with specialty groups to enhance education and training, and leading clinical trials of interventions addressing the effects of structural racism and other inequities and their impact on disparities in kidney health.


Deidra C. Crews, MD

In 2021, the ASN, along with the National Kidney Foundation, led a review of the use of race in eGFR calculations that ultimately led to the adoption of a race-free measure. The previous calculation is believed to have resulted in the underestimation of kidney disease severity for many Black patients, and negatively affected their candidacy and wait time for transplant. ■

ACUTE KIDNEY INJURY

Association of AKI With Dementia

Neurology. doi:10.1212/WNL.0000000000209751

Building on previous research suggesting that AKI leads to changes in the brain, **Hong Xu, PhD,** and colleagues examined the association between AKI and subsequent dementia risk. Their study centered on 305,122 patients aged 65 years and older in Stockholm, Sweden, from 2006 to 2019, none of whom had a dementia diagnosis. The median age was 75±8 years, and 56.6% were women. Median follow-up was 12.3 years (IQR, 8.7-13.3).

The study exposure was an AKI episode, and the outcome was all-cause dementia and specific types of dementia. Cox proportional hazard regression was used to study the associations between dementia and AKI, the severity of AKI, AKI recurrence, and setting (community-acquired vs hospital-acquired AKI).

In total, 79,888 patients (26%) had at least one AKI episode. There were 47,938 (16%) incident cases of dementia. The rate of dementia after AKI was 37.0 per 1,000 person-years (95% CI, 36.2-37.8), while the rate observed prior to AKI was 17.3 per 1,000 person-years (95% CI, 17.2-17.5).

After multivariable adjustment, AKI was associated with a 49% higher rate of subsequent dementia (adjusted HR, 1.49; 95% CI, 1.45-1.53). This pattern was consistent among different types of dementia. Hazard ratios were 1.88 (95% CI, 1.53-2.32) for dementia with Lewy bodies and Parkinson disease with dementia, 1.47 (95% CI, 1.38-1.56) for vascular dementia, and 1.31 (95% CI, 1.25-1.38) for Alzheimer dementia. The associations with dementia risk were stronger in more severe AKI and in hospital-acquired AKI compared to community-acquired AKI.

In summary, patients who experienced an AKI had a greater risk of being diagnosed with dementia after the AKI incident.

CARDIOVASCULAR-KIDNEY- METABOLIC HEALTH

Effects of SGLT2i on Renal Outcomes Across Cardiovascular-Kidney-Metabolic Conditions

Journal of the American Society of Nephrology. doi:10.1681/ASN.0000000000000491

The effects of sodium-glucose cotransporter-2 inhibitors (SGLT2i) on renal outcomes in patients with different combinations of chronic kidney disease, heart failure, and type 2 diabetes have not been quantified. To address this gap, **Tariq Jamal Siddiqi, MD,** and colleagues queried the PubMed and Scopus databases through December 2023 for primary and secondary analyses of placebo-controlled trials of SGLT2i in such patients.

The study outcomes were a composite kidney endpoint (combination of eGFR <15 mL/min/1.73 m^2, continuous doubling of serum creatinine, variable percentage change in eGFR, and need for kidney replacement therapy), rate of eGFR slope decline, and albuminuria progression. Hazard ratios and mean differences with 95% confidence intervals were extracted, and the results were pooled using a random-effect model through Review Manager.

Analysis of 11 trials and 80,928 patients found that SGLT2i reduced the risk of the composite kidney endpoint by 41% (HR, 0.59; 95% CI, 0.42-0.83) in heart failure with reduced ejection fraction, 36% (HR, 0.64; 95% CI, 0.55-0.73) in CKD, and 38% (HR, 0.62; 95% CI, 0.56-0.69) in type 2 diabetes compared to the placebo. SGLT2i was similarly beneficial in combinations of the three comorbidities and in patients without heart failure, CKD, or type 2 diabetes at baseline.

SGLT2i also reduced the risk of sustained doubling of serum creatinine by 36% (HR, 0.64; 95% CI, 0.56-0.72) and slowed the rate of eGFR slope decline in the overall population. A consistent positive effect on renal outcomes was observed in most subpopulations with available data.

In conclusion, SGLT2i improved renal outcomes in patients with heart failure, CKD, and type 2 diabetes. The benefits were consistent among patients with different combinations of these comorbidities.

CHRONIC KIDNEY DISEASE

Urine Acid/Base Score for Predicting CKD Progression

Journal of the American Society of Nephrology. doi:10.1681/ASN.0000000000000447

Acid/base status in CKD is currently determined using plasma measures, but acidosis may be present before it is observable in plasma. Low urine NH4+ excretion has been proposed as a marker for subclinical acidosis, but low NH4+ excretion could be due to a low capacity or low demand for acid excretion.

Samuel Levi Svendsen and colleagues proposed that a urine acid/base score accounting for both the demand and capacity for acid excretion would better predict CKD progression. They examined 24-hour urine collections from three clinical studies of CKD stage 3-4 patients, divided into a development cohort (n=82), a variation cohort (n=58), and a validation cohort (n=73).

Urinary pH and NH4+ were used to determine a urine acid/base score. Subclinical acidosis was defined as an acid/base score below the lower limit of the 95% prediction interval of healthy controls. Primary outcomes were the change in measured GFR after 18 months and CKD progression (≥50% decline in eGFR, initiation of long-term dialysis, or kidney transplantation) during a follow-up period of up to 10 years.

Subclinical acidosis was common among the development (n=54), variation (n=40), and validation cohorts (n=48), with 67% prevalence across all three. Subclinical acidosis was associated with an 18% (95% CI, 2-32) greater decrease in measured GFR after 18 months and with a higher risk of CKD progression during a median follow-up of 6 years. Adjusted HRs were 9.88 (95% CI, 1.27-76.7) for the development cohort and 11.1 (95% CI, 2.88-42.5) for the validation cohort.

The urine acid/base score using urinary pH and NH4+ had a higher predictive value for CKD progression than NH4+ excretion alone. Subclinical acidosis was associated with a higher risk of CKD progression in patients with CKD stages 3-4.

Association Between Smoking Timing and CKD Risk

American Journal of Kidney Diseases. doi:10.1053/j.ajkd.2024.04.011

Smoking is a risk factor for CKD, but the relationship between the timing of a patient's first cigarette of the day and CKD is mostly unstudied. In an observational cohort study, **Rui Tang, MPH,** and colleagues examined this relationship and potential interactions of smoking timing with other CKD risk factors.

Their study included 32,776 patients in the UK Biobank database free of prevalent CKD who had complete data on the time from waking to the first cigarette. Using Cox proportional hazards regression, the researchers studied the associations between the timing of a patient's first cigarette and the risk of CKD. They also assessed potential interactions of smoking timing with risk factors related to CKD risk on both multiplicative and additive scales.

There were 940 incident cases of CKD during a median follow-up period of 12 years, and shorter periods between waking and the first cigarette were associated with a higher risk of incident CKD (*P*=.01).

The adjusted HR associated with smoking timing was 1.28 (95% CI, 0.92-1.80) for 61-120 minutes, 1.48 (95% CI, 1.11-1.96) for 30-60 minutes, 1.36 (95% CI, 1.01-1.88) for 5-15 minutes, and 1.70 (95% CI, 1.22-2.37) for less than 5 minutes, respectively, compared to greater than 120 minutes. In addition, there was a significant additive interaction (*P*=.01) and multiplicative interaction (*P*=.004) between the timing of smoking and a healthy diet score.

The findings demonstrated a significant association between earlier smoking times and a higher CKD risk. The magnitude of the association was greater when combined with an unhealthy diet.

END-STAGE RENAL DISEASE

Post-Nephrectomy ESRD Among Patients With Severe CKD

Journal of Urology. 2024 Oct;212(4):550-559

The American Urological Association recommends nephron sparing in patients with preexisting CKD, but few studies have examined long-term kidney function in patients with preoperative severe CKD who have extirpative renal surgery.

Abhinav Khanna, MD, MPH, and colleagues compared the hazard of progression to ESRD after partial nephrectomy (PN) and radical nephrectomy (RN) among patients with preoperative severe CKD. Their study included 186 patients with stage 4 CKD who underwent PN or RN between 1970 and 2018. They utilized a multivariable Fine-Gray subdistribution hazard model to assess associations with progression to ESRD while accounting for competing risk of death.

Seventy-one (38%) patients underwent PN, while 115 (62%) had RN for renal neoplasms. Median follow-up was 6.9 years (IQR, 3.8-14.1). Multivariable analyses adjusting for competing risk of death found that the subdistribution HR (SHR) for older age at surgery (SHR for five-year increase, 0.81; 95% CI, 0.73-0.91; *P*<.001) and a higher preoperative eGFR (SHR for five-unit increase, 0.63; 95% CI, 0.47-0.84; *P*=.002) was associated with a lower hazard of progression to ESRD. PN and RN demonstrated no significant difference in the hazard of ESRD (SHR, 0.82; 95% CI, 0.50-1.33; *P*=.4).

In summary, a higher preoperative eGFR was associated with a lower hazard of progression to ESRD after nephrectomy for renal neoplasms. There was no significant difference between PN and RN surgeries regarding the overall hazard for developing ESRD.

Abstract Roundup

HYPERTENSION

Kidney Outcomes After ARNI Versus ACEI/ARB for mHTN-Related TMA

JAMA Network Open. doi:10.1001/jamanetworkopen.2024.32862

Jianbo Li, MD, and colleagues conducted a single-center cohort study to evaluate kidney outcomes of angiotensin receptor-neprilysin inhibitor (ARNI) compared to angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) treatment for patients with thrombotic microangiopathy (TMA) related to malignant hypertension (mHTN).

The study included 217 patients in China diagnosed with mHTN-associated TMA by kidney biopsy from January 2008 to June 2023. Their mean (SD) age was 35.9 (8.8) years, and 188 (86.6%) were men. Follow-up extended through the conclusion of the study period.

The primary outcome was a composite of kidney recovery (a 50% decrease in serum creatinine level, decrease in serum creatinine levels to the reference range, or kidney survival free from dialysis for more than one month). The secondary outcome was a 15% increase in eGFR relative to baseline. The tertiary outcome was kidney survival free from dialysis. The researchers used propensity score matching and Cox proportional hazards regression analysis to assess the association between ARNI (specifically, sacubitril/valsartan) or ACEI/ARB therapy and kidney recovery outcomes.

Sixty-six (30.4%) patients received sacubitril/valsartan and 151 (69.6%) received ACEI/ARBs at baseline. The ARNI treatment was associated with a shorter time to the primary outcome compared to ACEI/ARB treatment (20/63 [31.7%] vs 38/117 [32.5%]; adjusted HR [aHR], 1.85; 95% CI, 1.05-3.23).

ARNI was also independently associated with a shorter time to a 15% increase in eGFR (15/46 [32.6%] vs 46/83 [55.4%]; aHR, 2.13; 95% CI, 1.09-4.17) and kidney survival free from dialysis (11 of 23 [47.8%] vs 16 of 57 [28.1%]; aHR, 2.63; 95% CI, 1.15-5.88) compared to ACEI/ARB treatment. The differences were also significant in the propensity score matching comparison.

Compared to ACEI/ARB treatment, sacubitril/valsartan treatment was associated with possible kidney function benefits in patients with mHTN-associated TMA and could be a better therapeutic approach regarding kidney recovery.

KIDNEY REPLACEMENT THERAPY

Dialysis Versus Medical Management for Older Adults With Kidney Failure

Annals of Internal Medicine. 2024 Sep;177(9):1233-1243

To compare the survival and home time of older adults initiating dialysis within 30 days to those receiving continued medical management, **Maria E. Montez-Rath, PhD,** and colleagues conducted an observational cohort study using target trial emulation.

The study utilized data from the US Department of Veterans Affairs from 2010 to 2018 and included 20,440 adults aged 65 years or older with chronic kidney failure and an eGFR below 12 mL/min/1.73 m^2 who were not referred for transplant. The mean age was 77.9 (SD, 8.8) years.

The median time to dialysis initiation was 8.0 days in the dialysis group and 3.0 years in the continuing medical management group. Over three

years, the dialysis group survived 770 days, and the medical management group survived 761 days, a difference of 9.3 days (95% CI, -17.4 to 30.1 days).

Compared to the continuing medical management group, the group initiating dialysis spent 13.6 fewer days at home (95% CI, 7.7 to 20.5). The dialysis group had 77.6 days longer survival (95% CI, 62.8 to 91.1) and 14.7 fewer days at home (95% CI, 11.2 to 16.5).

In conclusion, older adults who were not referred for transplant and began dialysis when their eGFR fell below 12 mL/min/1.73 m^2 had limited gains in life expectancy and spent less time at home.

Vitamin D and Metabolic Bone Disease in Children on Prolonged CKRT

BMC Nephrology. 2024 Aug 19;25(1):265

Complications from prolonged continuous kidney replacement therapy (CKRT) have not been well described. Therefore, **Peace Dorothy Imani, MD,** and colleagues sought to study and document findings on vitamin D and metabolic bone disease in children requiring continued CKRT. Their single-center, prospective, observational study included 37 patients receiving CKRT with regional citrate anticoagulation for 28 days or longer. The study exposure was the duration of CKRT, and the outcomes were 25-hydroxy vitamin D and osteopenia and/or fractures.

Print-only Content

Vitamin D deficiency was observed in 17.2% of patients, while vitamin D insufficiency occurred in 69.0%. Age and ethnicity were not related to vitamin D deficiency or insufficiency, nor were time on CKRT or parathyroid hormone levels predictive of vitamin D levels. There was radiographic evidence of osteopenia and/or fractures in 29.7% of patients. After adjustment for age and time on CKRT, patients with chronic liver disease were more likely to experience osteopenia and/or fractures compared to patients with other primary diagnoses (OR, 3.99; 95% CI, 1.58-2.91; *P*=.003).

In conclusion, vitamin D deficiency and insufficiency, osteopenia, and fractures were common among children receiving extended CKRT. The risk for metabolic bone disease may be higher among patients with chronic liver disease. Patients on CKRT may require higher doses of vitamin D to maintain normal levels.

Adult Outcomes After Childhood KRT

Nephrology Dialysis Transplantation. doi:10.1093/ndt/gfae189

Little research has focused on young adults who began kidney replacement therapy (KRT) during childhood. However, this complex population should interest nephrologists as they will transition to adult renal centers as they move into adulthood. Therefore, **Iris R. Montez de Sousa** and colleagues wanted to describe the characteristics, treatment history, graft survival, and patient survival of these patients, and to report their five-year prognosis and expected remaining lifespan.

The researchers utilized data from the European Renal Association Registry on patients who reached age 18 from 2008 to 2019. The data included 2,944 patients from 21 countries. Patient characteristics and treatment trajectories were assessed before and after patients reached 18 years. Kaplan-Meier and Cox proportional hazards regression were used to conduct patient and graft survival analyses.

The unadjusted five-year patient survival rate was 96.9% (95% CI, 96.2-97.5). The percentage of adult survivors starting KRT at age 0-4 years and having preemptive kidney transplantation increased. There was a higher risk of death among patients on dialysis compared to transplant recipients (adjusted HR, 5.44; 95% CI, 3.34-8.86).

Between ages 18 and 23 years, 34% of dialysis patients continued the treatment, while about 21% of the transplant recipients lost their transplants. The life expectancy of transplant recipients and dialysis patients at age 18 years was 17 and 40 years shorter, respectively, compared to that of the general population.

In summary, although life expectancy was shorter for kidney transplant recipients at age 18 compared to the general population, those with a functioning kidney graft at age 18 fared better than patients on dialysis. Unfortunately, however, about one-fifth of grafts failed between ages 18 and 23 years, and one-third of patients remained on dialysis. ■

Sarah Tolson

Surviving the Shift: How Dialysis Centers Can Tackle Medicare Advantage Hurdles

Dialysis programs across the nation this year have been increasingly aware of the new challenges they face due to the increasing proliferation of Medicare Advantage (MA) plans and their impact on patients with end-stage renal disease (ESRD). As dialysis programs adapt, understanding Medicare and MA plans and educating patients on how these plans affect access to care is essential for financial sustainability and quality patient care.

ENROLLMENT CHALLENGES

Traditional Medicare open enrollment runs from October 15 to December 7, allowing coverage adjustments for the next year. In contrast, MA plans, which bundle hospital, physician, and pharmacy coverage, may include extra benefits like dental, vision, and rebates for prescriptions, groceries, and transportation. These perks make MA plans attractive, but patients may not understand their limitations.

MA plans have a separate open enrollment period from January 1 to March 31, offering flexibility to change plans. Certain patients can switch MA plans more often, but each change resets their out-of-pocket maximum, creating a financial burden. Some MA plans provide minimal out-of-pocket costs for in-network care but offer no out-of-network coverage, which can be problematic if the patient's dialysis center, nephrologist, or hospital is out of network.

CHALLENGES IN MEDICARE ADVANTAGE BILLING FOR ESRD CARE

Despite the benefits to patients, MA plans pose billing and reimbursement challenges for dialysis programs. Unlike the traditional standardized billing rules of Medicare, MA plans often lack transparency, with each plan employing different policies and requirements. This inconsistency necessitates constant monitoring and adjustments to billing systems, increasing administrative burden.

Other billing issues include rigid treatment frequency, timely filing, and authorization rules, which often fail to accommodate holiday schedules or partial weeks, and a lack of support for comprehensive claims that include both treatments and necessary medications.

The introduction of new payment models, such as the Transitional Drug Add-On Payment Adjustment, has been implemented slowly among MA plans, resulting in further reimbursement barriers for dialysis programs.

REIMBURSEMENT DIFFERENCES BETWEEN TRADITIONAL MEDICARE AND MEDICARE ADVANTAGE

A critical issue for dialysis programs is the difference in reimbursement between traditional Medicare and MA plans. While both payers cover ESRD treatments, MA plans often yield lower revenue due to maximum out-of-pocket costs and no bad debt reimbursement. For example, a typical dialysis patient under traditional Medicare could generate annual revenue ranging from $38,896 to $42,278 based on a base rate of $271.02 and 156 treatments, depending on secondary insurance. Under an MA plan, the same patient may only bring in $33,729, leading to a $5,000 shortfall per patient.

This discrepancy can have a significant impact on dialysis programs, particularly those with a high proliferation of patients with Medicare Advantage. With 54% of patients enrolled in MA plans, a typical center could see a significant annual revenue shortfall compared to revenue from traditional Medicare patients. These financial realities underscore the need for providers to carefully monitor MA contract terms and manage their patient mix strategically. It is worth mentioning that, based on the MA rate books (www.cms.gov/medicare/payment/medicare-advantage-rates-statistics/ratebooks-supporting-data), MA plans are receiving a significant monthly capitation amount from CMS to administer benefits, explaining the aggressive marketing to ESRD patients.

STRATEGIES TO NAVIGATE MEDICARE ADVANTAGE EXPANSION

Given the expanding MA market and its challenges, dialysis programs must adopt proactive strategies to manage their patient care and financial stability. Effective approaches include:

- **Contract Monitoring:** Regularly review and negotiate MA contracts to ensure fair reimbursement and clarity in billing requirements.
- **Payment and Claims Monitoring:** Implement systems to track payments and quickly identify discrepancies.
- **Patient Education:** Inform patients about their coverage options and potential out-of-pocket costs. Monthly insurance verification can help avoid disruptions in care, and clear internal communication about medication pricing and protocols is essential.

While these plans can offer comprehensive coverage for patients, the variability in billing and reimbursement requires careful management. By staying informed, maintaining strong contract negotiation practices, and educating patients, providers can navigate the expanding MA landscape effectively and ensure high-quality care for patients with ESRD. ■

Sarah Tolson is the director of operations for Sceptre Management Solutions, Inc., a company specializing in billing for outpatient ESRD dialysis programs, nephrology practices, and interventional nephrology. Your questions are welcome, and she can be reached at stolson@sceptremanagement.com, 801.775.8010, or via Sceptre's website, www.sceptremanagement.com.