



Nephrology Times

Practical News, Trends, and Analysis

May 2025

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What Is Diallytrauma?



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Acute kidney injury (AKI) is common, affecting nearly one-fifth of all hospitalized patients and two-thirds of critically ill patients. In an insightful report in *Kidney360* in 2023, **Erin Barreto, PharmD, PhD**, and colleagues from the AKINow Recovery workgroup¹ cite some of the key gaps in care that seem commonplace and preventable in managing AKI, including issues of transition of care, patient education, collaborative care delivery, inconsistent evaluation of kidney health after discharge, and lack of best practices in selecting post-AKI medications. In their report, the authors concluded that “proactive attention to developing, testing, and implementing evidence-based practices in the identified areas is needed to improve the health outcomes of AKI survivors, the care quality they receive, and the healthcare experience encountered by themselves, their loved ones, and their clinician team.”

Following this report, a more recent concept called *diallytrauma* has emerged. Originally, diallytrauma referred to harmful adverse events associated with continuous renal replacement therapy or dialysis. The recent publication in the *Journal of the American Society of Nephrology* titled “ASN Kidney Health Guidance on the Outpatient Management With Dialysis-Requiring Acute Kidney Injury”² has broadened the term to include the potentially harmful effects of dialysis in patients with AKI who transition from an inpatient to an outpatient setting.

Preventing diallytrauma is a priority for the approximately 12,000 patients with AKI requiring dialysis (AKI-D) who transition from inpatient to outpatient settings in the United States. At least in some proportion of these patients, preventing diallytrauma might allow their kidneys to recover and for them to discontinue dialysis.

In the American Society of Nephrology (ASN) guidance, **Anitha Vijayan, MD**, and colleagues² offer several sensible recommendations, albeit some based more on common sense and opinion than strong evidence. These are summarized in the **TABLE**.

The ASN guidance correctly emphasizes the overarching importance of minimizing intradia-

TABLE | Practice Points to Consider for Prevention of Diallytrauma

Optimize dialysis and ultrafiltration to minimize hypotension.
Monitor kidney function to detect recovery (measure predialysis creatinine and urine output at least weekly).
Prescribe thrice-weekly dialysis with a target single pool Kt/V (clearance multiplied by time divided by volume) of 1.2 to 1.4.
For patients with iron deficiency, consider IV iron but avoid maintenance iron protocols.
Reserve ESAs for patients receiving dialysis for >30 days.
Due to the risk of hypophosphatemia, avoid phosphate binders.
Initiate treatment of patients with secondary hyperparathyroidism if dialysis is needed for >30 days.
Support patients with transition-of-care services.

lytic hypotension (IDH). (The review on IDH by **Andrew Davenport, MD, MB BChir**, is worth reading.³) Preventing IDH begins with knowing the patient. In terms of transition of care from an inpatient to an outpatient setting, the emphasis on a warm handoff is on point. A warm handoff needs to be rich in terms of information and advice provided to the receiving dialysis team from their inpatient colleagues about how to manage the patient.

During the handoff, specific questions about how to prevent IDH are critical. Has the patient's dry weight been established? How well has the patient tolerated volume removal while undergoing dialysis? Is there underlying cardiac pathophysiology at play (eg, diastolic dysfunction)? Has the prescription been customized (eg, cooling the dialysate, using albumin, using a sequential strategy [an initial period of hypotension followed by solute clearance during dialysis])? Patients can be susceptible to IDH for a variety of reasons including incorrect estimation of dry weight, diastolic dysfunction, presence of anemia, slow recovery from the vasoactive effects of sepsis syndrome, hypoalbuminemia, and so on.

Another point covered by the ASN guidance is the issue of monitoring the patient for recovering kidney function. Sometimes it's simply an issue of asking the patient whether they have started passing urine, and if so, how much. Then it is worth measuring predialysis creatinine and documenting urine output. The phrase *good urine* is often used in practice. Early on, the urine output

may be robust, but clearance is suboptimal.

The practice points related to withholding erythropoiesis-stimulating agents (ESAs), iron, and phosphate binders are also important to consider, although the level of evidence to support recommendations is quite limited. In my own practice, I have often started the patient on regular ESA therapy during dialysis (after repleting their iron) while they are an inpatient. Anemia may increase the risk of IDH. Besides, allowing the patient's hemoglobin to drift down increases the risk of the patient requiring a blood transfusion, thereby sensitizing a patient who may otherwise be a good candidate for transplant. With regard to metabolic bone disease treatments, the value of withholding phosphate binders or vitamin D3 seems largely opinion based, and I have tended to manage this among inpatients by starting both a phosphate binder and vitamin D3 if they are needed.

In summary, the term *diallytrauma* used in the new recovery from AKI-D context is a useful addition to the dialysis team's lexicon. It fundamentally relies on the Oslerian idea of “record, tabulate, communicate.” ●

REFERENCES

1. Barreto EF, et al. *Kidney360*. 2024;5(1):124-132. doi:10.34067/KID.000000000000309
2. Vijayan A, et al. *J Am Soc Nephrol*. 2025;36(5):926-939. doi:10.1681/ASN.0000000646
3. Davenport A. *Kidney Int Rep*. 2022;8(3):405-418. doi:10.1016/j.ekir.2022.10.031

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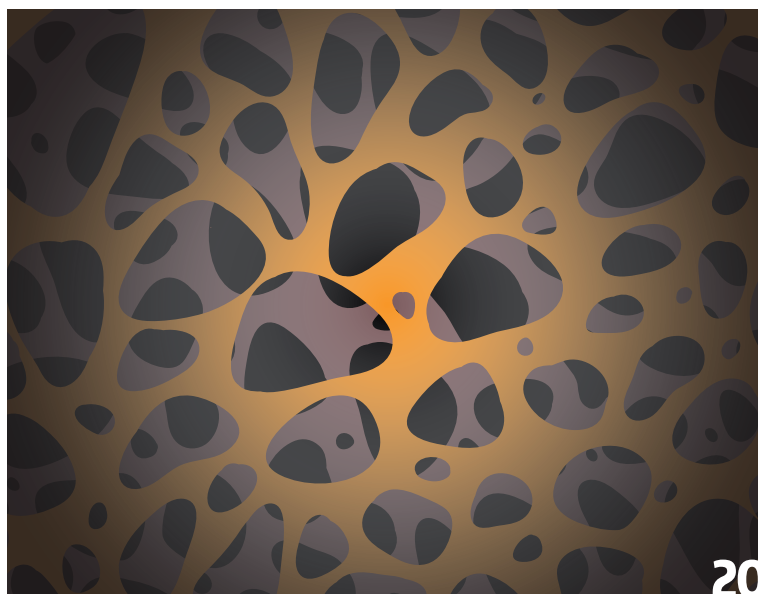
NATIONAL KIDNEY FOUNDATION SPRING CLINICAL MEETINGS

Nephrologists, fellows, and residents with a special interest in kidney disease, general internists, pharmacists, physician assistants, nurse practitioners and nurses, technicians, social workers, and renal and clinical dietitians all attended the 2025 NKF Spring Clinical Meetings (SCM25) in Boston, Massachusetts, to learn about developments in all areas of nephrology practice and network with colleagues. Presenters reported the latest insights into chronic kidney disease care, and participants were informed about new and evolving concepts related to kidney disease.



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Conference Coverage

Boston, Massachusetts | April 10-13, 2025

Nephrologists, fellows, and residents with a special interest in kidney disease, general internists, pharmacists, physician assistants, nurse practitioners and nurses, technicians, social workers, and renal and clinical dietitians all attended the 2025 NKF Spring Clinical Meetings (SCM25) in Boston, Massachusetts, to learn about developments in all areas of nephrology practice and network with colleagues. Presenters reported the latest insights into chronic kidney disease care, and participants were informed about new and evolving concepts related to kidney disease.

NATIONAL KIDNEY FOUNDATION SPRING CLINICAL MEETINGS



Kidney Stone Incidence With Chlorthalidone Versus Hydrochlorothiazide

Results from a secondary analysis of the Diuretic Comparison Project were presented at SCM25. The analysis examined whether patients with hypertension who were randomized to chlorthalidone (CTD) had fewer kidney stones compared with patients who received hydrochlorothiazide (HCTZ). Both drugs are longer-acting diuretics.

The study included 13,523 adults aged 65 years and older with systolic BP 120 mm Hg or higher who were receiving HCTZ. Of those patients, 1,164 had a history of kidney stones, and 12,359 had no history of kidney stones. Participants were randomized to either continue HCTZ treatment or switch to CTD. The primary study outcome was the development of a kidney stone (as defined by *International Classification of Diseases* codes).

During a mean follow-up period of 4.2 years, no significant difference was observed between the twogroups regarding kidney stone formation. In the CTD group, 4.9% of patients had a new kidney stone, compared with 5.2% in the HCTZ group (hazard ratio [HR], 0.94; 95% CI, 0.82-1.08; $P=0.43$).

However, a significant interaction was observed dependent on participants' baseline history of kidney stones ($P=0.005$). Adjusted analysis revealed that participants without a history of kidney stones who received CTD experienced a nonsignificant reduction in the risk of stones (HR, 0.81; 95% CI, 0.65-1.01; $P=0.05$). Those without a history of stones who received HCTZ had a significantly increased risk of stones (HR, 1.25; 95% CI, 1.01-1.53; $P=0.037$).

Participants in the CTD group were more likely to experience hypokalemia compared with those in the HCTZ group regardless of their baseline kidney stone status (respectively, 10.2% vs 8.3% with no history; 13.8% vs 11.5% with a history). "Hypokalemia may have influenced stone formation," the authors wrote.

In summary, CTD and HCTZ had a similar effect on kidney stone formation among patients without a history of stones, but patients treated with CTD had a higher incidence of stones than those treated with HCTZ when they had a history of stones, indicating a strong interaction between baseline history of kidney stones and treatment assignment.

Source: National Kidney Foundation Spring Clinical Meetings 2025. Abstract #LB-01.

Effect of Dosing Equation for Carboplatin on Related Adverse Events

The cancer drug carboplatin is known to cause adverse events (AEs). Excess dosing of carboplatin may occur because the Calvert equation for dosing usually uses Cockcroft-Gault creatinine clearance (CG), and this may lead to an overestimation of measured glomerular filtration rate (GFR).

A prospective study presented at SCM25 compared carboplatin dosing using Chronic Kidney Disease Epidemiology Collaboration creatinine and cystatin C (eGFR-CR-CYS) and evaluated the association between excess dosing and AEs.

Study participants comprised 292 adults with cancer (lung, $n=106$ [36%]; gynecologic, $n=94$ [32%]; intestinal, $n=35$ [12%]; breast, $n=31$ [11%]) who began receiving carboplatin between 2023 and 2025 and whose creatinine and cystatin C were measured before the first dose. Mean (\pm SD) participant age was 66 ± 11.7 years, and 193 participants (66%) were women.

The researchers compared the dose administered based on CG with the dose calculated using eGFR-CR-CYS. They defined an *excess dose* of carboplatin as a dose more than 15% higher than the dose calculated using eGFR-CR-CYS and *underdosed* as a dose less than 15% lower than the dose calculated using eGFR-CR-CYS. They used a Fine-Gray model to determine the association between excess dose and cytopenia, acute kidney injury (AKI), and hospitalizations and a Cox model to determine mortality.

Calculating dosing with eGFR-CR-CYS resulted in clinically significant dose adjustments for 76 study participants (26%). Of those, 35 (12%) received an excess dose and 41 (14%) were underdosed. Receiving an excess dose was associated with a higher risk of anemia, thrombocytopenia, AKI of grade 3 or higher, and death within 90 days.

The results highlight the discrepancies between dosing calculations made using CG and eGFR-CR-CYS. Using the latter might help identify patients for whom a dose reduction could result in fewer AEs.

Source: National Kidney Foundation Spring Clinical Meetings 2025. Abstract #LB-02.

Conference Coverage

Boston, Massachusetts | April 10-13, 2025

Association of Serum Creatine/Cystatin C Ratio and Adverse Events With Platinum Therapies

A prospective cohort study presented at SCM25 explored the association between serum creatinine (Scr)/cystatin C (CYS) ratio and AEs associated with the platinum-based cancer therapies cisplatin and carboplatin. These AEs included cytopenia, AKI, hospitalization, and mortality within 90 days of initiating the therapy.

The cohort comprised 441 adults with cancer who started treatment with cisplatin or carboplatin between 2023 and 2025 at a cancer center in Boston, Massachusetts. Mean (\pm SD) patient age was 65 \pm 12 years and 201 (45.6%) were men. Patients' Scr and CYS levels were measured before the first dose was given.

To evaluate the association of a Scr/CYS ratio less than 0.7 with the development of AEs grade 2 or higher or grade 3 or higher (according to the National Cancer Institute's Common Terminology Criteria for Adverse Events), the researchers used a Fine-Gray subdistribution hazard model that was adjusted for age, sex, Charlson comorbidity index, and cancer stage. In addition, they used a Kaplan-Meier curve to assess 90-day survival.

One hundred twenty-five participants (28.5%) had a Scr/CYS ratio less than 0.7, which was independently associated with AEs and hospitalization. This included grade 2 or higher and grade 3 or higher anemia and thrombocytopenia, grade 3 or higher AKI, all-cause hospitalizations, and hospitalizations for AEs within 90 days. In addition, patients with a Scr/CYS ratio less than 0.7 had a 6.61-fold higher risk of death within 90 days [95% CI, 2.27-19.20].

Given the prevalence of Scr/CYS ratios less than 0.7 and their association with AEs, the authors suggested that studies should examine whether platinum dose reductions might benefit patients in this category.

Source: National Kidney Foundation Spring Clinical Meetings 2025. Abstract #LB-04.

60-Month Results for Lumasiran in PH1

Primary hyperoxaluria type 1 (PH1) is a genetic disease that results in oxalate overproduction, which can lead to urolithiasis, nephrocalcinosis, and systemic oxalosis. The ILLUMINATE-B trial (NCT03905694) examined the efficacy and safety of lumasiran, a liver-directed RNA interference therapeutic approved for the treatment of PH1 in infants and toddlers. Final 60-month results were presented at SCM25.

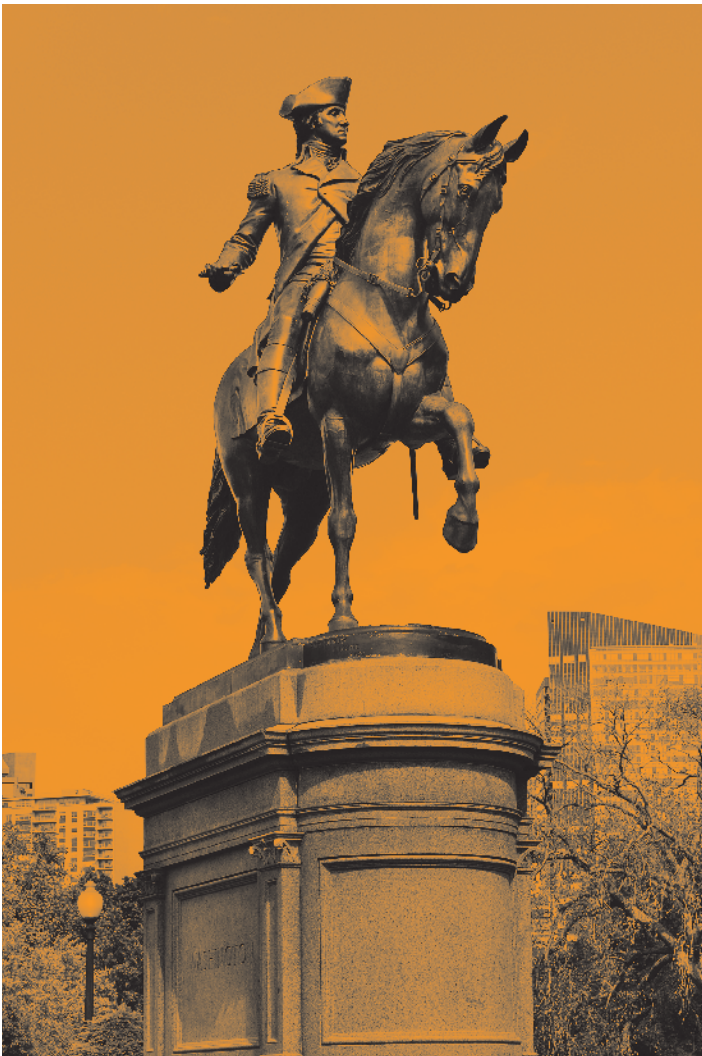
ILLUMINATE-B is a phase 3, open-label, single-arm study. Enrolled patients were younger than 6 years of age with eGFR greater than 45 mL/min/1.73 m² (age 12 months or older) or normal serum creatinine (age < 12 months) and urinary oxalate to creatinine ratio (UOx:Cr) greater than the upper limit of normal. Participants received lumasiran subcutaneously, based on weight. All 18 enrolled patients completed the 6-month primary analysis, began the 54-month extension, and completed the study at 60 months.

At 60 months, the mean reduction in spot UOx:Cr from baseline was 74%. At 1 or more post-baseline visits, 100% of participants had a spot UOx:Cr at or less than the upper limit of normal. The mean reduction in plasma oxalate at month 60 was 25%, and the annual rate of change (slope) in mean eGFR was 0.26 (SD 0.8) mL/min/1.73 m².

Of the 14 participants who had nephrocalcinosis at baseline, 12 (86%) had an improvement in grade at 60 months and none had a worsened grade. The four participants who did not have nephrocalcinosis at baseline did not have it at month 60. The prevalence of kidney stones was 0.11 per person-year [95% CI, 0.06-0.21]. Three patients (17%) experienced mild, temporary injection site reactions.

The ILLUMINATE-B findings were positive overall. The results demonstrated that lumasiran reduced UOx and plasma oxalate and sustained those reductions over 60 months. In addition, eGFRs were stable, kidney stone rates were low, nephrocalcinosis grade improved in most patients, and the drug's safety profile was satisfactory.

Source: National Kidney Foundation Spring Clinical Meetings 2025. Abstract #LB-05.



Kidney Function and Apixaban

Although patients with diminished kidney function are often prescribed the anticoagulant apixaban, a lower dose is recommended for those aged 80 years and older, weighing 60 kg or more, or with serum creatinine measuring 1.5 mg/dL or higher.

Research presented at SCM25 clarified the association between kidney function and apixaban pharmacokinetics, pharmacodynamics, and hemorrhage among the patients treated with the drug. The study followed up 1,697 patients treated with apixaban for up to 2 years. Forty percent of participants were Black and 48% were women. Of the full cohort, 34.1% had an estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73 m², broken down as follows: 15.9% with eGFR 45 to 59.9 mL/min/1.73 m², 9.0% with eGFR 30 to 44.9 mL/min/1.73 m², and 9.1% with eGFR less than 30 mL/min/1.73 m². Seventy of the 155 patients with eGFR less than 30 mL/min/1.73 m² were receiving dialysis.

The overall hemorrhage rate was 10.8 per 100 person-years [95% CI, 9.5-12.2]. The risk of hemorrhage did not vary by age and was 10.9 per 100 person-years for participants younger than 80 years and 10.1 per 100 person-years for those aged 80 or older. However, hemorrhage risk was higher among participants who weighed 60 kg or less compared with those weighing more than 60 kg (19.8 vs 10.5 per 100 person-years). The risk was also higher for those with lower eGFRs.

A 12-hour subgroup pharmacokinetic-pharmacodynamic analysis included 89 participants; 45% were Black and 45% were women. Eighteen subgroup patients had an eGFR of 60 mL/min/1.73 m² or greater; 18 had an eGFR of 45 to 59.9 mL/min/1.73 m²; 22 had an eGFR of 30 to 44.9 mL/min/1.73 m²; 10 had an eGFR less than 30 mL/min/1.73 m² (without dialysis); and 19 were receiving dialysis. The patients with eGFR less than 30 mL/min/1.73 m² (without dialysis) demonstrated greater systemic exposure to apixaban and corresponding anti-Xa activity.

In summary, the researchers found that impaired kidney function was the primary predictor of hemorrhage among patients treated with apixaban after accounting for clinical predictors. The findings suggest that kidney function should factor into risk prediction rules for hemorrhage and that a lower apixaban dose is appropriate for patients with eGFR below 30 mL/min/1.73 m² regardless of whether they are receiving dialysis.

Source: National Kidney Foundation Spring Clinical Meetings 2025. Abstract #LB-03.

Effect of KidneyIntelX DKD Risk Predictions on SGLT2i Prescription Rates

Researchers assessed prescription rates of sodium-glucose cotransporter 2 inhibitors (SGLT2i) among patients whose diabetic kidney disease (DKD) risk was predicted by a KidneyIntelX test versus untested patients. They presented their findings at SCM25.

KidneyIntelX is an FDA-approved test that assesses the risk of DKD progression using biomarkers and clinical variables. The test ranks patients as being at low, moderate, or high risk for a 40% decline in eGFR or kidney failure over 5 years.

The study's test arm (NCT04802395) comprised 3,546 patients who received a KidneyIntelX test result between March 2021 and December 2022. Their DKD risk according to KidneyIntelX testing was 50.5% low, 39.9% moderate, and 9.6% high. The median baseline urine albumin-to-creatinine ratio (UACR) was 54.0 mg/g, and the median baseline eGFR was 63.3 mL/min/1.73 m².

The control arm consisted of 933 patients with matching intended use criteria (eGFR 30-59 mL/min/1.73 m² or eGFR ≥60 mL/min/1.73 m² and UACR >30 mg/g). The control arm had baseline encounters in the same period as the test arm but did not receive a KidneyIntelX test until 2 years later. The median baseline UACR for the control group was 65.0 mg/g, and the median baseline eGFR was 59.0 mL/min/1.73 m².

The researchers compared SGLT2i initiation rates between the two arms within 1 year of the baseline encounter, overall and across risk levels. Patients with KidneyIntelX test results had approximately 60% higher use of SGLT2i versus those in the control arm (30.8% vs 19.2%; *P*<0.05).

In the test group, the increase in SGLT2i use was proportional to the risk level predicted by KidneyIntelX: low, 12.3%; moderate, 46.4%; high, 58.2% (*P*<0.001 for moderate and high vs low risk). No such proportionality of SGLT2i use to future predicted risk levels was observed in the control group. "Risk assessment for DKD progression with KidneyIntelX resulted in increased and targeted use of SGLT2i by risk level for kidney health protection," the authors concluded.

Source: National Kidney Foundation Spring Clinical Meetings 2025. Abstract #LB-06.

Comparison of Sparsentan and Irbesartan in FSGS

The DUPLEX trial (NCT03493685) determined that the dual endothelin angiotensin receptor antagonist sparsentan resulted in sustained proteinuria reduction among patients with focal segmental glomerulosclerosis (FSGS). Researchers sought further insights by comparing the effects of sparsentan and irbesartan on proteinuria remission and assessed how achieving complete or partial remission affected progression to kidney failure. Results were presented at SCM25.

Patients with FSGS received sparsentan 800 mg/d (n=184) or irbesartan 300 mg/d (n=187) during the phase 3, 108-week trial. The study end points included proteinuria partial remission (urine protein-to-creatinine ratio [UPCR] ≤1.5 g/g and >40% reduction from baseline) or complete remission (UPCR <0.3 g/g). To examine the effects of remission on progression to kidney failure (eGFR <15 mL/min/1.73 m² or kidney replacement therapy), the researchers conducted post hoc analyses using pooled data on sparsentan and irbesartan.

Patients receiving sparsentan achieved partial and complete remission of proteinuria earlier and more often than those receiving irbesartan. Furthermore, achieving remission led to a notable reduction in progression to kidney failure, regardless of which therapy patients received.

In addition, sparsentan was found to be safe and well tolerated. The safety and efficacy results support the use of sparsentan in FSGS.

Funding for the study was provided by Travele Therapeutics, Inc.

Source: National Kidney Foundation Spring Clinical Meetings 2025. Abstract #LB-07.



Awards and Honors

Healthcare professionals who have made significant contributions to the field of kidney disease were honored at the National Kidney Foundation (NKF) 2025 Spring Clinical Meetings.



Bradley A. Warady, MD
Dr. Warady is the McLaughlin Family Endowed Chair in Nephrology and a professor of pediatrics at the University of Missouri-Kansas City School of Medicine and serves as the director of the nephrology division and director of dialysis and transplantation at Children's Mercy Kansas City. He focuses on pediatric chronic kidney disease (CKD) and end-stage renal disease, with an academic emphasis on collaborative research.



Sankar Dass Navaneethan, MD, MS, MPH
received the Garabed Eknoyan Award for exceptional contributions to key NKF initiatives. Dr. Navaneethan is the Garabed Eknoyan, MD, Endowed Professor of Medicine, associate chief of nephrology, and co-lead of the Resources Module of the Consortium for Translational and Precision Health at Baylor College of Medicine and chief of the renal section at Michael E. DeBakey VA Medical Center. His interests include clinical trials in diabetic kidney disease, obesity and intentional weight loss in CKD, cardiovascular disease in kidney disease, health services research, and systematic reviews in nephrology.



Jayme Locke, MD, MPH, FACS, FAST
received the Excellence in Kidney Transplantation Award. Dr. Locke is an abdominal transplant surgeon specializing in innovative strategies for the transplantation of incompatible organs, disparities in access to and outcomes after transplantation and living donation, transplantation of HIV-infected patients with end-stage renal disease, and xenotransplantation. She is the Arnold G. Diethelm, MD, Endowed Chair in Transplantation Surgery, a tenured professor of surgery, and director for the Division of Transplantation at the University of Alabama at Birmingham Heersink School of Medicine.



Jeffrey Perl, MD, SM, FRCP (C)
received the J. Michael Lazarus Distinguished Award, a lectureship recognizing those whose research has yielded novel insights related to renal replacement therapy. Dr. Perl is a staff nephrologist at St. Michael's Hospital in Toronto and an associate professor of medicine at the University of Toronto. His clinical practice, research, and teaching focus on enhancing universal access to and improving clinical outcomes in home dialysis. He is editor-in-chief of *Peritoneal Dialysis International*.



Kathleen Liu, MD, PhD, MAS
was recognized with the Shaul G. Massry Distinguished Lecture, named to honor Dr. Massry's scientific achievements and his contributions to the kidney healthcare community and to the NKF. Dr. Liu is a professor of medicine and anesthesia in the divisions of nephrology and critical care medicine and the medical director of the medical intensive care unit and the apheresis/hemodialysis unit at the University of California, San Francisco. Her research focus is acute kidney injury and acute respiratory distress syndrome, with an emphasis on biomarkers and clinical trials.



Dinushika Mohottige, MD, MPH
received the Medical Advisory Board Distinguished Service Award, recognizing educational activities and community service in promoting the mission of the NKF on a local level. Dr. Mohottige is an assistant professor at the Institute for Health Equity Research at the Icahn School of Medicine at Mount Sinai and the Barbara T. Murphy Division of Nephrology and provides nephrology care at the James J. Peters VA in the Bronx. Her research focuses on the impact of sociostructural factors and racialized medicine on kidney health and kidney transplantation.



Roger Rodby, MD, FACP, FASN
won the 2025 Donald W. Seldin Award for excellence in clinical nephrology. Dr. Rodby is a professor of medicine in the Division of Nephrology at Rush University Medical Center. His research has focused on lupus nephritis and diabetic nephropathy through the Collaborative Study Group. A proponent of internet-based education, Dr. Rodby is active on social media, is a participant in the *Channel Your Enthusiasm* podcast, and is a community leader of the American Society of Nephrology's online "Open Community."



Brandon Kistler, PhD, RD
The Joel D. Kopple Award, honoring an individual who has made significant contributions to the field of renal nutrition, went to **Brandon Kistler, PhD, RD**. Dr. Kistler is a registered dietitian, assistant professor in the Department of Nutrition Science, and codirector of the Clinical and Translational Nutrition Research Lab at Purdue University. His research focuses on utilizing lifestyle, primarily diet and exercise, to improve the quality of life and outcomes for people with CKD.



Jennifer Kortyna, MSN, RN, CNN
The Carol Mattix Award, named for a home dialysis training nurse who worked tirelessly to improve patients' lives, was given to **Jennifer Kortyna, MSN, RN, CNN**. A nephrology nurse at UW Health in Madison, Wisconsin, she helped launch an urgent peritoneal dialysis program and create educational classes focused on this treatment option. She is a clinical educator and clinical nurse specialist and has served as president, president-elect, and treasurer of the local chapter of the American Nephrology Nurses Association.



Patrick Gee, PhD, JLC
The Celeste Lee Award, the highest honor given by the NKF to a distinguished patient with kidney disease and named for a longtime advocate of patient-centered care, went to **Patrick Gee, PhD, JLC**. Dr. Gee is a healthcare consultant, professional patient activist, and founder of IAdvocate, Inc., a nonprofit organization that promotes health and wellness in underserved communities. He has a background in criminal justice and holds a doctorate in justice, law, and criminology. ●

Print-only Content



Chlorthalidone Not Superior to Hydrochlorothiazide for Kidney Outcomes

By Charlotte Robinson

Among the population with chronic kidney disease (CKD), 92% also have hypertension. Both CKD and hypertension increase the risk of cardiovascular disease and kidney disease progression. In addition, hypertension is a leading cause of kidney failure requiring treatment. Thiazide diuretics have been shown to improve cardiovascular outcomes, but evidence is limited regarding their effect on the progression of kidney disease or the development of end-stage kidney disease.

To better understand the effects of thiazide diuretics on kidney outcomes, **Areef Ishani, MD**, and colleagues conducted a prespecified secondary analysis of data from the Diuretic Comparison Project (DCP), a randomized clinical trial comparing chlorthalidone and hydrochlorothiazide for the treatment of hypertension. Their results were published in *JAMA Network Open* [doi:10.1001/jamanetworkopen.2024.49576].

The DCP was a multicenter, two-arm, comparative-effectiveness, embedded, pragmatic, open-label trial; it randomized 13,523 participants to continue hydrochlorothiazide or switch to chlorthalidone. DCP was conducted between June 1, 2016, and June 1, 2022, through 72 Veterans Affairs healthcare systems across the United States.

The study included veterans aged 65 years and older with hypertension who were taking hydrochlorothiazide. In addition, participants had a history of hypertension with a most recent clinic systolic BP (SBP) of 120 mm Hg or higher, plus an active hydrochlorothiazide prescription of 25 or 50 mg/d.

The secondary analysis extended follow-up to December 31, 2023. Patients who were randomized and had a baseline and one or more follow-up creatinine measures were included in this intention-to-treat analysis. Patients and physicians were aware of the treatment assignment.

The main DCP analysis found no difference between chlorthalidone with hydrochlorothiazide groups for major adverse cardiovascular events and noncancer death. Adverse kidney events were a prespecified secondary outcome in the DCP protocol. Evaluation of treatment effects on risks of exploratory kidney outcomes and adverse events, such as hypokalemia (potassium <3.1 mEq/dL) and acute kidney injury requiring hospitalization, were also included in the secondary analysis.

The secondary analysis sought to determine whether chlorthalidone was superior to hydrochlorothiazide at preventing adverse kidney outcomes. The researchers reported patient characteristics as mean (SD) or

median (IQR) for continuous variables with nongaussian distribution by the Shapiro-Wilk test. Discrete and categorical variables were presented as a percentage. The overall changes in SBP and potassium levels with mean (SD) were presented graphically.

The authors studied treatment effects on risks for hypokalemia and acute kidney injury requiring hospitalization, as well as the proportion of participants with incident CKD, using the Fisher exact test. They used the Mann-Whitney U test to evaluate group differences on the overall change in mean estimated glomerular filtration rate (eGFR) slope. A Cox proportional hazards regression model was used to estimate hazard ratios (HRs) for the kidney outcomes. Baseline factors were adjusted to further refine analyses. Covariates were chosen based on study protocol description and clinical relevance. Cox proportional hazards regression was used to assess potential interactions between treatment assignments and the prespecified subgroups.

The primary kidney outcome was CKD progression, defined as doubling of serum creatinine level from baseline, a terminal eGFR less than 15 mL/min, or dialysis initiation. Other exploratory kidney outcomes evaluated included: (1) an alternative composite measure of a 40% reduction in eGFR (a terminal eGFR <15 mL/min or dialysis initiation); (2) incidence of new CKD (eGFR <60 mL/min) among patients who did not have CKD at baseline; and (3) assessment of the change in annual eGFR slope (estimated as the absolute change between baseline and last eGFR taken during the study divided by duration of the two measurements and multiplied by 365.25 days).

The secondary analysis included 12,265 participants (90.7%) with a baseline and one or more follow-up creatinine measurements. Median (IQR) age was 71 (69-75) years. Of the participants, 3.2% were female, 96.8% were male, 15.0% were Black, 77.6% were White, 2.3% were other race, and 5.1% were unknown race. The mean (SD) study duration was 3.9 (1.3) years.

Of those participants, 6,118 were randomized to receive chlorthalidone, and 6,147 received hydrochlorothiazide. Regarding the primary kidney outcome, chlorthalidone was not superior to hydrochlorothiazide in the incidence of doubling of serum creatinine level, an eGFR less than 15 mL/min, or dialysis initiation by treatment group (369 of 6,118 [6.0%] vs 396 of 6,147 [6.4%]; HR, 0.94; 95% CI, 0.81-1.08; $P=0.37$).

The findings were similar for a 40% decrease in eGFR, an eGFR less than 15 mL/min/1.73 m², or dialy-

sis initiation by treatment group (778 [12.7%] in the chlorthalidone group vs 818 [13.3%] in the hydrochlorothiazide group; HR, 0.96; 95% CI, 0.87-1.06; $P=0.39$).

Incident CKD developed in 1,900 of 9,038 (21.0%) participants without CKD at baseline. It did not differ by randomized groups (961 of 4,520 [21.3%] in the chlorthalidone group vs 939 of 4,518 [20.8%] in the hydrochlorothiazide group; $P=0.59$). Results did not change when adjusted for baseline characteristics.

The overall mean slope of eGFR progression was -1.0 mL/min/1.73 m² annually. There was no mean (SD) difference between groups (-1.0 [7.9] in the chlorthalidone group vs -1.1 [8.9] in the hydrochlorothiazide group; $P=0.18$).

Within subgroups defined by baseline CKD status, race, sex, the presence or absence of diabetes, myocardial infarction or stroke at baseline, or baseline mean SBP, chlorthalidone was not superior to hydrochlorothiazide. The incidence of acute kidney injury requiring hospitalization did not differ between groups. Participants in the chlorthalidone group had a higher risk of hypokalemia and of hospitalization for hypokalemia compared with participants receiving hydrochlorothiazide, particularly those without CKD at baseline.

The researchers recognize some limitations to their study. The trial design likely limited adverse effects associated with thiazide diuretics and led to a greater incidence of self-reported adverse events and switches back to hydrochlorothiazide among participants who switched to chlorthalidone. After randomization, all follow-up was carried out by the primary care physician, and there were no laboratory evaluations subject to protocols. Some dialysis events may have been missed due to dialysis initiation being identified through claims data. Finally, most participants (95%) started out taking lower doses of hydrochlorothiazide (25 mg/d) or chlorthalidone (12.5 mg/d), so effects of 50 mg or 25 mg doses, respectively, could have been missed.

The authors concluded, "Overall results from this secondary analysis of the DCP demonstrate that chlorthalidone was not superior to hydrochlorothiazide for kidney outcomes at the doses observed. There was a greater tendency for a higher incidence of hypokalemia in those randomized to chlorthalidone compared with hydrochlorothiazide even in those with CKD, although the incidence and difference between the groups were small." Considering the findings, they advise that clinicians should feel confident using either drug to treat hypertension. ●

Associations Between Social Determinants of Health and CKM Stages

By Victoria Socha

The interplay among obesity, diabetes, chronic kidney disease (CKD), and cardiovascular disease has recently been defined by the American Heart Association (AHA) as cardiovascular-kidney-metabolic (CKM) syndrome. The AHA established a staging framework for CKM ranging from stage 0 to 4. Results of recent studies have shown that between 2011 and 2020, approximately 90% of adults in the United States met the criteria for CKM stage 1 or higher. Furthermore, 15% of US adults met the criteria for CKM stage 3 or 4. There are significant differences in prevalence based on sex and age, with men more likely to have advanced CKM stages than women and advanced CKM stages being more common in adults aged 65 years and older than in those aged 20 to 44 years.

Social determinants of health (SDOH) are indicators of health equity. SDOH include risk factors such as income, education, employment, housing, food insecurity, and access to affordable health services. Ruixin Zhu, PhD, and colleagues conducted a cross-sectional study to examine whether the prevalence of CKM stages varies by SDOH among US adults. Results were reported in *JAMA Network Open* [doi:10.1001/jamanetworkopen.2024.45309].

The researchers used data from the National Health and Nutrition Examination Survey (1999-2018). A nationally representative sample of adults aged 30 to 79 years was identified through multistage probability sampling. The study exposure of interest was CKM stages 0 to 5 reflecting progressive pathophysiology. Advanced CKM was defined as stage 3 or 4. CKM stages were defined based on risk factors for metabolic syndrome, cardiovascular disease, and CKD.

The primary outcome of interest was the age-standardized prevalence of CKM stages and advanced CKM stages across SDOH, including education (high school graduate or higher vs less than high school), marital status (married or living with a partner vs not), family income to poverty ratio ($\geq 300\%$ vs $\leq 300\%$), food security (full security vs marginal, low, or very low security), health insurance (private vs government or no insurance), employment, home ownership (own home vs rent home or other arrangement), and access to healthcare (at least one regular healthcare facility vs none or emergency department [ED]).

Data from 29,722 participants were analyzed. Weighted mean age was 50.8 years; 49.3% were female, and 50.7% were male. Regarding race and ethnicity, 7.5% self-reported as Mexican American,

12.3% as non-Hispanic Black, 70.9% as non-Hispanic White, and 9.3% as other race and ethnicity. Those with advanced CKM stages were more likely to be older, male, smokers, nondrinkers, and physically inactive and to have unfavorable SDOH.

Among the total cohort, the age-standardized prevalence of CKM stages 0, 1, 2, 3, and 4 was 13.6% (95% CI, 13.0%–14.3%), 29.9% (95% CI, 29.1%–30.7%), 43.7% (95% CI, 42.9%–44.5%), 4.7% (95% CI, 4.4%–5.0%), and 8.1% (95% CI, 7.6%–8.5%), respectively. There were significant differences in the prevalence of CKM stages across age groups, sexes, and SDOH.

There was a higher prevalence of advanced CKM stages among participants with two or more cumulative unfavorable SDOH compared with participants with fewer than two unfavorable SDOH.

Compared with participants with a higher education level, the relative risk ratios (RRRs) for CKM stages 2, 3, and 4 were significantly higher among those with a lower education level, at 1.38 (95% CI, 1.18–1.61), 1.44 (95% CI, 1.12–1.85), and 1.97 (95% CI, 1.63–2.38), respectively. Trends were similar in family income to poverty ratio, food insecurity versus full food security, unemployment versus employment, and home nonownership versus ownership. Conversely, RRRs for advanced CKM were lower for participants with no regular healthcare or only ED access compared with participants with access to at least one regular healthcare facility (stage 3: 0.61 [95% CI, 0.40–0.94]; stage 4: 0.32 [95% CI, 0.23–0.46]).

Participants who were unmarried or not living with a partner had a higher prevalence of advanced CKM compared with their married counterparts (age-standardized prevalence, 14.2% [95% CI, 13.5%–15.0%] vs 12.2% [95% CI, 11.7%–12.8%]). There was also a higher prevalence of advanced CKM observed

among those who had a family income to poverty ratio lower than 300% (16.1% [95% CI, 15.4%–6.8%] vs 10.1% [95% CI, 9.5%–10.7%]); those who had food insecurity (18.3% [95% CI, 17.1%–19.6%] vs 11.7% [95% CI, 11.2%–12.2%]); those who had government insurance or lacked health insurance (16.5% [95% CI, 15.7%–17.4%] vs 11.0% [95% CI, 10.5%–11.6%]); those who were unemployed (18.8% [95% CI, 17.7%–20.1%] vs 11.4% [95% CI, 11.0%–11.9%]); those who had a lower education level (17.3% [95% CI, 16.4%–18.3%] vs 11.8% [95% CI, 11.3%–12.4%]); and those who lived in a rented home (16.1% [95% CI, 15.2%–16.9%] vs 11.9% [95% CI, 11.4%–12.4%]).

There was a higher prevalence of advanced CKM stages among participants with two or more cumulative unfavorable SDOH compared with participants who had fewer than two unfavorable SDOH (adjusted prevalence ratio, 1.36; 95% CI, 1.26–1.46). Conversely, participants with no regular healthcare or those who used EDs were less likely to have advanced stages of CKM than participants with access to at least one regular healthcare facility (7.6% [95% CI, 6.6–8.7%] vs 13.2% [95% CI, 12.7%–13.7%]). Except for education level, the results remained robust in the sensitivity analyses. Decision trees revealed that the key SDOH having an influence on CMK stage risk were employment status, health insurance, and family income to poverty ratio.

Among female participants, the likelihood of advanced CKM stages increased for those living in a rented home or not living with a partner. The increased likelihood of advanced CKM stages was not seen in men living in a rented home or those not living with a partner.

There were some limitations to the study findings cited by the authors, including the cross-sectional design, which limited the ability to establish a causal relationship between SDOH and CKM stages; the lack of some data related to cardiovascular disease; not assessing other SDOH such as social cohesion, structural racism, and neighborhood and community environments; and limiting the cohort to adults aged 30 to 79 years and excluding those with extreme values of cardiovascular risk factors.

In conclusion, the researchers said, “In this cross-sectional study, disparities in the prevalence of CKM stages by SDOH, particularly family income, food security, and employment, with notable sex differences, were observed in US adults. These findings highlight the need to address inequities in CKM syndrome through targeted interventions. ●



Urinary Sediment mRNA As a Biomarker for IgAN

By Charlotte Robinson

IgA nephropathy (IgAN) is the most common primary glomerulonephritis and a leading cause of chronic kidney disease (CKD). Renal biopsy is the leading method for diagnosing and predicting the progression of IgAN, but urinary biomarkers need to be identified to provide a less invasive and more reliable alternative.

The quantification of mRNA expression in urinary sediment has emerged as a reliable biomarker for various diseases. However, not many studies have examined the clinical relevance of urinary mRNA levels in patients with IgAN. Dr. Jin Sug Kim and colleagues addressed this gap with a recent study, the results of which appeared in *BMC Nephrology* [doi:10.1186/s12882-024-03696-7].

Using the public Gene Expression Omnibus (GEO) repository and a literature review, the researchers identified the differential expression of mRNAs in renal tissue between patients with IgAN and healthy study participants and selected IgAN disease-specific mRNA candidates. They measured urinary expression levels of the mRNAs in patients with IgAN and compared them with those in control participants using quantitative, real-time polymerase chain reaction. In addition, they examined the relationship between urinary mRNA levels and the clinicopathologic parameters of patients with IgAN and analyzed the predictive value of each mRNA for CKD progression.

Two hundred participants with biopsy-proven IgAN from two hospitals in South Korea were enrolled in the study between September 2010 and September 2019. The disease control group with non-IgAN nephropathy included six participants with lupus nephritis, 16 with minimal change disease (MCD), 17 with crescentic glomerulonephritis, and nine with membranous nephropathy (MN). An additional 76 individuals who did not have kidney disease were enrolled as healthy control participants.

The mean age of the IgAN group was 42.4 years, 49.5% were male, and they had significantly higher serum albumin levels than participants in the control group. Participants with crescentic glomerulonephritis had significantly decreased renal function compared with that of participants with IgAN and other disease controls. Participants who had MN and MCD excreted significantly more urinary proteins than those with IgAN. The prevalence of diabetes and hypertension did not differ significantly between the groups.

Baseline variables including age, sex, BMI, and prevalence of hypertension and diabetes were recorded, and blood samples were collected to measure serum albumin, IgA, and creatinine. Urine

samples were collected to measure urinary protein excretion and the presence of hematuria at the time of renal biopsy.

Urinary protein excretion was calculated as the spot urine protein to creatinine ratio (PCR). The estimated glomerular filtration rate (eGFR) was used to measure renal function, calculated using the Chronic Kidney Disease Epidemiology Collaboration equation. The pathologic IgAN findings were described using the Oxford classification system.

The participants with IgAN received angiotensin receptor blockers or angiotensin-converting enzyme inhibitors alone or in combination with immunosuppressants. Those patients visited the outpatient clinic every 1 to 2 months to have their renal function assessed. The clinical outcome was CKD progression (>50% reduction in the eGFR from the value determined at the time of renal biopsy or progression to end-stage renal disease).

The results imply that urinary mRNA expression signatures could provide useful biomarkers of IgAN and allow the differentiation of proteinuria resulting from active inflammation and chronic changes.

Researchers measured the levels of urinary candidate mRNAs in urine samples from participants in the IgAN, disease control, and healthy control groups. They found that urinary expression of *CCL2*, *CD14*, *DNMT1*, *FKBP5*, *Nephrin*, and *IL-6* was significantly upregulated in the participants with IgAN compared with the healthy control participants.

Levels of *C3* ($r=0.207$; $P=0.005$) and *Podocin* ($r=0.162$; $P=0.044$) were significantly positively correlated with eGFR, whereas levels of *FLOT1* ($r=-0.206$; $P=0.004$) were significantly negatively correlated with IgAN. Other urinary mRNAs did not demonstrate a significant correlation with renal function.

C3, *FLOT1*, and *TfR* levels were significantly correlated with urinary protein excretion. Urine PCR demonstrated a negative correlation with urinary mRNA levels of *C3* ($r=-0.200$; $P=0.007$) and *TfR* ($r=-0.184$; $P=0.013$), whereas the correlation of *FLOT1* with urinary mRNA levels was positive ($r=0.173$; $P=0.017$).

In patients with mesangial hypercellularity, urinary mRNA levels of *CCL2* ($P=0.028$), *DNMT1*

($P=0.049$), and *Podocin* ($P=0.001$) were significantly decreased. In patients with endocapillary hypercellularity, urinary mRNA levels of *Podocin* ($P=0.035$) and *PODXL* ($P=0.003$) were significantly elevated. In patients with tubular atrophy/interstitial fibrosis, urinary mRNA levels of *IL-6* were significantly elevated ($P=0.040$). No mRNAs demonstrated a significant correlation with segmental glomerulosclerosis or cellular or fibrocellular crescents.

During follow-up, 26 (13.0%) participants with IgAN experienced disease progression (>50% reduction in eGFR or progression to end-stage renal disease). Multivariate analysis revealed that eGFR (hazard ratio [HR], 0.937; 95% CI, 0.904-0.973; $P=0.001$), urine PCR (HR, 1.357; 95% CI, 1.019-1.808; $P=0.037$), and urinary mRNA levels of *FLOT1* (HR, 3.706; 95% CI, 1.373-10.005; $P=0.010$) were independently associated with CKD progression among participants with IgAN.

The authors acknowledge the limitations of their study. The mRNAs might reflect other conditions in addition to IgAN because the researchers selected candidates using GEO datasets based on comparisons of IgAN and healthy control participants. The researchers were unable to investigate the monitoring function of mRNAs due to the study design. Lastly, because of the small number of study participants, the authors could not pinpoint the clinical significance of mRNA in disease controls.

In summary, the results imply that urinary mRNA expression signatures could provide useful biomarkers of IgAN and allow the differentiation of proteinuria resulting from active inflammation and chronic changes. The authors assert, “This distinction is crucial for clinical applications, as it enables more precise monitoring of disease activity and progression. By identifying the underlying cause of proteinuria, clinicians can more effectively tailor treatment strategies. The ability to noninvasively assess active inflammation versus chronic damage through urinary mRNA analysis provides a significant advantage in the management of IgAN.” ●

Incidence of AKI Among Patients Treated for In-Hospital Severe Hypertension

By Victoria Socha

Ten percent of patients admitted to the hospital for reasons other than hypertension develop severe hypertension (sHTN) following admission. Standard treatment for patients with sHTN is administration of IV antihypertensives. However, IV antihypertensive treatment has been associated with end-stage organ injury, including acute kidney injury (AKI). Results of a previous study suggested that compared with no treatment, treatment for patients with sHTN with IV antihypertensives was associated with an 18% greater risk of AKI at the population level.

Hospitalized patients who develop AKI are at increased risk for adverse outcomes, including prolonged hospital stay, persistent loss of kidney function, and death. **Lama Ghazi, MD, PhD**, and colleagues conducted a study to examine whether there is heterogeneity in the effect of the use of IV antihypertensives on the incidence of AKI in patients who develop in-hospital sHTN. Results were reported online in the *American Journal of Kidney Diseases* [doi:10.1053/j.ajkd.2024.09.011].

The study population included patients without kidney failure who developed sHTN. The study exposure was treatment with IV antihypertensives within 3 hours of BP elevation. The primary outcome of interest was time to development of AKI.

The researchers captured the association between the time to develop AKI and predictors utilizing an accelerated failure time Bayesian Additive Regression Trees (AFT-BART) model. A counterfactual outcome framework was used to estimate individual treatment effects for each participant. Those estimates were used to identify patient characteristics associated with treatment effect heterogeneity in response to IV antihypertensives and to explore potential subgroups of patients who may or may not benefit from the treatment.

Eligible participants were adult patients who were admitted to one of five large hospitals in the New England Health System between 2016 and 2020. Excluded were patients admitted for a hypertensive emergency; those with sHTN on admission or in the emergency department (ED); those with no measurement of BP; those admitted to an intensive care unit, maternity ward, or research unit; those with length of stay less than 2 days or more than 30 days; those who received vasopressors 0 to 6 hours prior to developing sHTN; those with missing covariate data; and those with end-stage kidney disease, renal failure, or on dialysis.

In-hospital sHTN was defined as the first documentation of systolic BP (SBP) higher than 180 mm Hg or diastolic BP (DBP) higher than 110 mm Hg reported at least 1 hour following hospital admission. Blood pressure measurements recorded in the ED were excluded.

Patients in the group receiving IV antihypertensive treatment within 3 hours of development of sHTN were treated with hydralazine, labetalol, metoprolol, or nicardipine (treatment group). The untreated patients did not receive IV or oral antihypertensives (control group).

Analysis results demonstrated that most patients would have been harmed by treatment with IV antihypertensives with the exception of a small subgroup of patients.

The analyses included 28 preselected covariates. The preselected covariates were age, sex, race, surgical ward, vital signs, and Elixhauser comorbidity index score. The 2021 Chronic Kidney Disease Epidemiology Collaboration creatinine equation that measures estimated glomerular filtration rate (eGFR) without race was used to determine eGFR, considered as a continuous variable.

AKI was ascertained at 3 hours following development of sHTN, continuing until the end of the follow-up period (30 days after hospital admission). The Kidney Disease: Improving Global Outcomes criteria were used to define AKI. AKI was diagnosed if a patient's serum creatinine increased by 0.3 mg/dL or more within 48 hours or if serum creatinine level was 1.5 times the lowest measured serum creatinine within the previous 7 days.

The cohort comprised 11,951 patients who developed sHTN during hospitalization. Of them, 741 were treated with IV antihypertensives within 3 hours of severe elevation in BP (treatment group); 18.2% (n=135) developed AKI. There were 11,210 patients in the control group. Of them, 12.7% (n=1422) developed AKI. The median time from development of sHTN to time of development of AKI was 57.7 hours; median time to AKI development from IV antihypertensive treatment was 59.1 hours.

Median age of the overall cohort was 72.5 years, 19.9% identified as Black, 42.9% were male, median Elixhauser score was 4, and 70% had a history of hypertension. Median SBP/DBP at admission was 154/82 mm Hg and at the time of sHTN was 185/91 mm Hg. Those in the treatment group were older, more likely to be admitted to the surgical ward, and had higher SBP and DBP at the time of admission and at development of sHTN.

The first stage of the statistical analysis used the AFT-BART models to estimate each patient's characteristics and treatment status. The second stage

implemented an exploratory fit-the-fit approach using classification and regression trees to clarify the key moderators for conditional average treatment effects.

Results showed that most patients would have been harmed by treatment with IV antihypertensives except a small subgroup of patients (n=317). Those patients were White, had SBP of 156 mm Hg or higher on admission, eGFR of 70.7 mL/min/1.73 m² or higher, and a serum bicarbonate level of less than 21.7 mmol/L.

Limitations of the study included use of observational data and causal inference methods, using a single data source limited to one healthcare system, and the inability to determine how BP was measured.

The researchers said of AFT-BART, "Overall, this innovative machine learning approach within the causal modeling framework allowed us to assess whether there are subpopulations that might benefit from IV antihypertensive treatment following sHTN development. We mainly observed that IV antihypertensive treatment is not beneficial following sHTN development. Our findings are exploratory, thus hypothesis-generating; we encourage more future studies with different data sources to assess for effect heterogeneity when identifying treatment options, if any are needed, for sHTN." ●



Transplantation of Kidneys With HIV-Positive Donors and Recipients

By Victoria Socha

In individuals with HIV and end-stage renal disease, kidney transplantation provides a significant survival benefit. The risk of death is higher and access to kidney transplantation is lower among persons with HIV who are dependent on dialysis.

Since 2016 and the implementation of the US HIV Organ Policy Equity Act, the use of kidneys from donors with HIV for transplantation to recipients with HIV for research purposes has been an increasingly utilized practice. (Effective November 27, 2024, the US Department of Health and Human Services removed the clinical research requirement for kidney and liver transplants involving donors and recipients with HIV.) However, data relative to the use of kidneys from donors with HIV are limited; existing small case studies did not include donors without HIV as controls.

At 1 year after transplant, the incidence of rejection was 13% in the HIV-donor group and 21% in the non-HIV group. The 3-year values were 21% and 24%, respectively.

Christine M. Durand, MD, and colleagues conducted a multicenter observational study that was larger than an earlier pilot study. The newer study was designed to examine the safety and noninferiority of kidney transplants from donors with HIV to recipients with HIV compared with kidney transplants from donors without HIV. The researchers also sought to assess the risks of HIV breakthrough infection, HIV superinfection, and posttransplant complications. Results were reported in *The New England Journal of Medicine* [2024;391(15):1390-1401].

The study was conducted at 26 centers in the United States. The primary outcome was a safety event, a composite of death from any cause, graft loss, serious adverse event, HIV breakthrough infection, persistent failure of HIV treatment, or opportunistic infection. The safety outcome was assessed for noninferiority (margin for the upper bound of the 95% CI, 3.00). Overall survival, survival without graft loss, rejection, infection, cancer, and HIV superinfection were assessed as secondary outcomes.

A total of 515 individuals with HIV consented to participate in the study. Of those, 408 were eligible for transplantation and were put on a waiting list. Of the 408 eligible individuals, 58 were withdrawn from the study, 209 received a kidney, and 141 remained on the waiting list. Two of the 209 recipients withdrew from the study on the day of transplantation. Nine received a kidney from a donor without HIV and were randomly assigned to limited observation. The final analysis group included 198 participants who had received a kidney from a deceased donor; 99 received a kidney from a donor with HIV and 99 received a kidney from a donor without HIV. The two groups were similar in recipient and transplant characteristics.

The study included 146 donors, 64 with HIV and 82 without HIV. Twenty-seven donors initially had

a false-positive HIV test result. The two groups were generally similar in characteristics. The exceptions were that donors with HIV were more often Black, had a lower median Kidney Donor Profile Index score, and were more often seropositive for hepatitis B and cytomegalovirus than the donors without HIV.

Median follow-up in the group of recipients of kidneys from donors with HIV was 2.2 years. Median follow-up in the group of recipients of kidneys from donors without HIV was 2.3 years. For the composite primary outcome, the adjusted hazard ratio in the group that received a kidney from a donor with HIV compared with the group whose donors did not have HIV was 1.00 (95% CI, 0.73–1.38), showing noninferiority.

The adjusted incidence ratio of opportunistic infections in the HIV-donor group compared with the non-HIV-donor group was 1.28 (95% CI, 0.51–3.18). At 1 year, overall survival was 94% in the HIV-donor group and 95% in the non-HIV-donor group. At 3 years, the corresponding

values were 85% and 87%, respectively. At 1 year, survival without graft loss was 93% in the HIV-donor group and 90% in the non-HIV donor group. The 3-year percentages were 84% and 81%, respectively.

At 1 year after transplant, the incidence of rejection was 13% in the HIV-donor group and 21% in the non-HIV group. The 3-year values were 21% and 24%, respectively. The incidence rate ratio (IRR) for rejection in the group whose donors had HIV as compared with the group whose donors did not have HIV was 0.63 (95% CI, 0.37–1.10).

Median estimated glomerular filtration rate (eGFR) at 1 year after transplant in the group that received a kidney from a donor with HIV was 49 mL/min/1.73 m² compared with a median eGFR of 48 mL/min/1.73 m² in the group that received a kidney from a donor without HIV. At 3 years, median eGFR in the HIV-donor group was 41 mL/min/1.73 m² and 48 mL/min/1.73 m² in the non-HIV-donor group.

There was no significant difference between the two groups in the incidence of serious adverse events, including infections, infections leading to hospitalizations, opportunistic infections, surgical or vascular complications, or cancer. There were 11 opportunistic infection events in the HIV-donor group and eight in the non-HIV-donor group. Cytomegalovirus and esophageal candidiasis were the two most common infections.

The incidence of HIV breakthrough infection was higher in the group that received a kidney from a donor with HIV compared with the group that received a kidney from a donor without HIV (IRR, 3.14; 95% CI, 1.02–9.63). Among the 58 recipients in the HIV-donor group with sequence data, there was one potential HIV superinfection.

The researchers cited some limitations to the study findings, including the inability to achieve true randomization of organs from donors with HIV and those without HIV due to Organ Procurement and Transplantation Network allocation constraints.

In summary, the authors said, “This multicenter, observational study showed that kidney transplantation from donors with HIV to recipients with HIV is noninferior to kidney transplantation from donors without HIV to recipients with HIV.” ●

Statin Therapy in Recipients of Kidney Allografts

By Victoria Socha

The leading cause of mortality among recipients of kidney allografts with a functioning graft is cardiovascular disease. One-third of hospitalizations among kidney allograft recipients are related to cardiovascular care, leading to high healthcare costs. Both traditional and nontraditional risk factors are associated with the high incidence of cardiovascular events among kidney allograft recipients, including comorbid hypertension, diabetes mellitus, and dyslipidemia, as well as factors specific to recipients such as oxidative stress, anemia, hyperhomocysteinemia, and effects of immunosuppression therapy.

Dyslipidemia is associated with the combined effects of factors that include posttransplant diabetes mellitus, obesity, impaired renal function, proteinuria, and glucocorticoid administration. At present, there are no established lipid targets for kidney allograft recipients. However, according to **Ioannis Bellos, MD**, and colleagues, a significant proportion of those patients may be undertreated, not reaching the proposed targets for the general population.

The researchers conducted a systematic review and meta-analysis designed to examine the efficacy and safety of the use of statins among kidney allograft recipients, with particular emphasis on the potential effects of statin therapy on the risk of cardiovascular events, mortality, and graft survival in that patient population. Results were reported in *BMC* [doi:10.1186/s12944-024-02276-w].

The researchers systematically searched Medline (via PubMed), Scopus, Web of Science, CENTRAL (Cochrane Central Register of Controlled Trials), Clinicaltrials.gov, and Google Scholar. All searches were conducted from inception to June 20, 2024. Eligible trials comprised randomized controlled trials and observational studies that evaluated the effects of statin administration after kidney transplant. The maximum likelihood method was used to fit random-effects models, and the certainty of evidence was appraised using the GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) approach.

The primary outcome of interest was the occurrence of major cardiovascular events (MACE). MACE were a composite that could include a combination of cardiovascular mortality, acute coronary syndrome, cerebrovascular accident, peripheral artery disease requiring revascularization, and congestive heart failure. Secondary efficacy end points were patient overall survival and kidney allograft survival. Safety end points included hepatotoxicity, rhabdomyolysis, creatine kinase elevation, posttransplant diabetes mellitus, cataract, venous thromboembolic events, hip fracture, and cancer.

The initial search located 1,952 electronic articles. After deduplication, 1,068 studies were screened for potential inclusion. After application of inclusion and exclusion criteria, the meta-analysis included 27 studies. Of those, 10 were randomized controlled trials and 17 were observational studies.

There was an association between the administration of statins and a significantly lower risk of major cardiovascular events.

Six studies examined the association between statin use and risk of MACE (one randomized controlled trial and five cohort studies). There was an association between the administration of statins and a significantly lower risk of MACE (relative risk [RR], 0.87; 95% CI, 0.67-0.96; 3,621 participants). There was no significant interaction with the type of calcineurin inhibitor, and the meta-analysis outcome was not significantly influenced by study sample size, location, design, or risk of bias. Results of meta-regression analysis did not reveal any significant effects of age, sex, BMI, estimated glomerular filtration rate (eGFR), history of cardiovascular disease, or diabetes.

Fifteen studies (six randomized controlled trials and nine cohort studies) examined the association between statin use and overall patient survival. There was an association between the administration of statins and a significantly lower risk of overall mortality (RR, 0.84; 95% CI, 0.74-0.94; 70,750 participants). There was no significant influence of calcineurin type, study sample size, location, design, or risk of bias. Results of meta-regression analysis suggested that the association was more pronounced in studies of participants of a younger age and high eGFR on average.

Nine studies assessed graft survival (five randomized controlled trials and four cohort studies). There was no statistically significant difference in the risk of graft loss between the group receiving a statin and the control group (RR, 0.72; 95% CI, 0.48-1.08; 10,255 participants). There were significant differences in the meta-analysis results depending on location and study design: there was an association between statin use and a significantly lower risk of graft loss in studies conducted in Asia and in observational studies.

The risk of liver toxicity was assessed in four randomized studies and two cohort studies. Results of pooled analysis of the study data suggested that there was an association between statin use and a significantly lower risk of liver injury (RR, 0.81; 95% CI, 0.70-0.93; 60,641 participants). The estimate remained statistically significant after the imputation of two potentially missing studies (new RR, 0.80; 95% CI, 0.70-0.93). There was no significant influence by calcineurin inhibitor type, study sample size, location, design, or risk of bias.

Four randomized controlled trials reported the safety end point of creatine kinase elevation. The risk was similar between participants treated with a statin and those not treated with a statin (RR, 0.97; 95% CI, 0.50-1.89). There was no difference in the outcome among participants treated with cyclosporine and tacrolimus, and the result was not significantly affected by sample size, location, design, or risk of bias.

Two studies assessed the potential link between statin use and rhabdomyolysis (one randomized controlled trial and one retrospective cohort study). There was a significantly greater risk of rhabdomyolysis associated with statin use (RR, 1.37; 95% CI, 1.10-1.70). There was no significant influence on the findings by study sample size, location, design, or risk of bias.

One retrospective cohort study evaluated the risk of cataract among kidney allograft recipients treated with a statin. There was an increased risk of cataract associated with statin use (RR, 1.22; 95% CI, 1.14-1.31).

There were no statistically significant differences between those receiving a statin and those not treated with a statin in the risk of posttransplant diabetes mellitus, hip fracture, venous thromboembolism, or cancer.

Limitations to the study findings cited by the authors included the limited availability of data regarding the potential differential statin effects among participants treated with cyclosporine or tacrolimus; only a few patients were treated with mammalian target of rapamycin (mTOR) inhibitors. In addition, the included studies did not consistently report statin dosing.

In summary, the researchers said, “Among kidney transplant recipients, statin therapy is associated with significant benefits in terms of cardiovascular event reduction and survival improvement. Statin administration is well-tolerated, being associated with minor increases in the risk of rhabdomyolysis and cataract. Further research in large scale is needed to establish the favorable cardiovascular effects of statins and determine the subpopulation of kidney transplant recipients that may be safety targeted for higher-intensity statin treatment.” ●



OSTEOPOROSIS **WITH LUPUS NEPHRITIS**

By Charlotte Robinson

Osteoporosis is a common and serious complication of the autoimmune disorder systemic lupus erythematosus (SLE). Women with SLE are at a higher risk for reduced bone mineral density (BMD) and have a high prevalence of osteoporosis and osteoporotic fractures. However, not enough is known about osteoporosis prevalence and risk factors in Chinese patients with lupus nephritis (LN), a severe manifestation of SLE.

To address this knowledge gap, **Dr. Yu Hong** and colleagues conducted a single-center, cross-sectional study of patients with renal biopsy-proven LN at Tongji Hospital in Wuhan, China, from May 2011 to June 2018. The patients' BMD was measured using dual x-ray absorptiometry at the lumbar spine, total hip, and femoral neck. Findings of the study appeared in *BMC Nephrology* [doi:10.1186/s12882-024-03882-7].

Information collected included age at enrollment, ethnicity, menstrual status, age at menopause, personal history of fractures, alcohol consumption, and smoking status. Laboratory investigations, such as measurements of serum creatinine, uric acid, urea nitrogen, and serum ionized calcium, were also collected, and weight, height, and BMI were measured.

In addition, information about disease duration, calcium supplements, anti-osteoporotic therapy, and corticosteroid use were noted, along with the maximum and current dosages. The Systemic Lupus Erythematosus Disease Activity Index was used to score disease activity. Disease damage was evaluated based on criteria established by the Systemic Lupus International Collaborative Clinics/American College of Rheumatology.

There were 130 participants enrolled in the study, of whom 128 (98.5%) were female and two were male. Mean age (\pm SD) was 46.2 ± 12.9 . Of the female participants, 61 were premenopausal and 67 were postmenopausal. Postmenopausal participants were older, had been diagnosed with LN at a later age, and had higher weight, lower height, higher BMI, higher blood urea nitrogen level, and more frequent bisphosphonate use than the premenopausal participants ($P < 0.05$).

To compare values between the premenopausal and postmenopausal groups, the researchers used statistical tests, including two-tailed *t* test, Mann-Whitney U test, Fisher exact test, χ^2 test with Yates correction, and χ^2 test, based on the distribution of the data and the type of variables. They used univariate logistic regression analysis to identify factors that might be associated with osteoporosis. Variables that showed statistical significance in the univariate analysis, plus age, were then incorporated into a multivariate logistic regression model to determine the independent predictors of osteoporosis.

When compared with premenopausal participants, those who were postmenopausal had significantly reduced BMD in the lumbar spine (L1-L4) (0.802 ± 0.165 vs 0.877 ± 0.151 g/cm², $P = 0.008$) and total hip (0.760 ± 0.143 vs 0.814 ± 0.125 g/cm², $P = 0.027$). Postmenopausal patients also had lower T scores at the lumbar spine (L1-L4) (-2.194 ± 1.434 vs -1.372 ± 1.403 , $P = 0.002$), femoral neck (-1.576 ± 1.240 vs -1.160 ± 1.052 , $P = 0.047$), and total hip (-1.491 ± 1.167 vs -1.079 ± 1.037 , $P = 0.041$). In addition, postmenopausal participants demonstrated a significantly higher prevalence of osteoporosis at the spine (L1-L4) (50.7% vs 19.7%, $P < 0.001$), femoral neck (29.9% vs 4.9%, $P < 0.001$), total hip (25.4% vs 6.6%, $P = 0.009$), and at least one measured site (55.2% vs 24.6%, $P < 0.001$).

Age at menopause, weight, height, and BMI might positively correlate with BMD in the lumbar spine, total hip, and/or femoral neck. Meanwhile, age, age at diagnosis of LN, and menopause duration might negatively correlate with BMD in the same regions. Multivariable linear regression analysis showed that BMI was positively associated with BMD. Disease duration and menopause duration were negatively associated with BMD of the lumbar spine, total hip, and femoral neck.

Univariate logistic regression analysis for osteoporosis showed that older age, older age at diagnosis of LN, younger age at menopause, lower weight, shorter height, and absence of bisphosphonates were potential risk factors among patients with LN. In premenopausal participants, shorter height was a potential risk factor for osteoporosis. Among postmenopausal participants, younger age at menopause, lower weight, shorter height, lower BMI, and absence of bisphosphonates might be risk factors for osteoporosis.

Multivariate logistic regression analysis showed that older age, lower weight, and absence of bisphosphonates were independently associated with an increased risk of osteoporosis among participants with LN. Shorter height was independently associated with an increased risk of osteoporosis among premenopausal participants. Younger age at menopause, lower weight, and absence of bisphosphonates were independently associated with an increased risk of osteoporosis among postmenopausal participants.

The authors acknowledge certain limitations of their study. By including patients with LN at various disease durations for BMD measurements, potential variability of results may have been introduced. Differences in treatments that patients received may have introduced confounding factors that could influence the association between risk factors and osteoporosis. Some factors that could be associated with osteoporosis, such as serum vitamin D levels, were not assessed and adjusted. Lastly, participants were diagnosed by means of renal biopsy, and most had good renal function, which may not be representative of all patients with LN.

In summary, the authors wrote, "Our findings indicate that patients with LN are at significant risk of developing osteoporosis, particularly in the lumbar spine and among postmenopausal individuals. The risk factors associated with osteoporosis that were identified may include older age, lower weight, and the absence of bisphosphonate treatment." ●

When compared with premenopausal participants, those who were postmenopausal had significantly reduced bone mineral density in the lumbar spine (L1-L4) and total hip.



FDA Grants Accelerated Approval to Atrasentan for IgAN

The FDA granted accelerated approval to atrasentan (Vanrafa), a selective endothelin-1 receptor type A antagonist, for reduction of proteinuria in primary IgA nephropathy (IgAN).

The approval was supported by data from a prespecified interim analysis of the phase 3 ALIGN study, which found that the drug achieved proteinuria reduction of 36.1% ($P < 0.0001$) versus placebo. Improvements were observed at week 6 and sustained through week 36. In addition, atrasentan demonstrated a favorable safety profile consistent with previously reported data.

Continued approval of atrasentan may be reliant upon additional forthcoming data from ALIGN. The study is assessing whether atrasentan slows disease progression as measured by a decline in estimated glomerular filtration rate (eGFR) at week 136. Those data are expected to be available in 2026.

Chinese Patient Living With Pig Kidney

Researchers in China announced that they performed a successful transplant of a gene-edited pig kidney into a female patient. The surgery took place in early March and the patient is doing well, **Dr. Lin Wang** of Xijing Hospital of the Fourth Military Medical University in Xi'an said in a press briefing about 3 weeks after the surgery.

The patient is one of only two people worldwide living with a pig kidney. The other is a New Hampshire man who had transplant surgery in January 2025 at Massachusetts General Hospital.

A Massachusetts man and a New Jersey woman who received pig kidneys in 2024 both died later. An Alabama woman who received one in November 2024 is still living but had the kidney removed in April 2025 when it stopped functioning.

In addition to the successful kidney xenotransplantation, the same Chinese researchers reported in *Nature* [doi:10.1038/s41586-025-08799-1] that a pig liver they transplanted into a brain-dead person survived for 10 days, with no early signs of rejection.

United Therapeutics and eGenesis received approval from the FDA in early 2025 to begin the first clinical trials of pig kidney transplants.

ASN Issues Guidance for AKI-D

The American Society of Nephrology (ASN) published "ASN Kidney Health Guidance on the Outpatient Management of Patients with Dialysis-Requiring Acute Kidney Injury" in the *Journal of the American Society of Nephrology* [doi:10.1681/ASN.0000000646].

Although hospital mortality rates have improved for patients with severe cases of acute kidney injury that require in-hospital hemodialysis (AKI-D), up to 30% of survivors need dialysis treatment after hospital discharge. Most patients with AKI-D are treated at outpatient facilities intended for providing long-term dialysis care to patients with end-stage renal disease. Protocols for patients receiving long-term dialysis are often used for patients with AKI-D, but the two groups have significant pathophysiologic differences.

The new guidance was developed by an ASN working group of kidney care experts to address the special needs of patients with AKI-D, who are at higher risk for permanent dialysis dependence, cardiovascular disease, rehospitalization, and death. The guidance emphasizes the importance of individualized dialysis care and coordination of care for these patients and includes recommendations for future research and policy priorities to further inform best practices to optimize outcomes.

KDIGO Issues New ADPKD Guideline

Kidney Disease: Improving Global Outcomes (KDIGO) for the first time published guidance on the evaluation, management, and treatment of autosomal dominant polycystic kidney disease (ADPKD). The guideline is available at kdigo.org.

The guideline was developed with patient partners, clinicians, and researchers worldwide and followed an explicit process of evidence review and appraisal, based on a rigorous, formal systematic literature review.

The guideline includes chapters covering: nomenclature, diagnosis, prognosis, and prevalence; kidney manifestations; chronic kidney disease management and progression, kidney failure, and kidney replacement therapy; therapies to delay the progression of kidney disease; polycystic liver disease; intracranial aneurysms and other extrarenal manifestations; lifestyle and psychosocial aspects; pregnancy and reproductive issues; pediatric issues; and approaches to the management of people with ADPKD.

ADPKD affects millions of people worldwide and is the most common cause of kidney replacement therapy. The evolving genetic and clinical landscape, including the approval of tolvaptan for the treatment of rapidly progressive ADPKD, makes the release of the guideline particularly timely.

Furosemide Approved to Treat Edema in CKD

The FDA approved a supplemental New Drug Application for furosemide (Furoscix), expanding the drug's indication to include treatment of edema in patients with chronic kidney disease (CKD).

Furosemide, a loop diuretic administered by subcutaneous infusion, was previously approved to treat edema in adults with chronic heart failure.

"We are excited to introduce Furoscix to nephrologists and are focused on providing treatment options to both heart failure and CKD patients experiencing acute fluid overload," said **John Tucker**, CEO of drug maker scPharmaceuticals Inc. ●

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ACUTE KIDNEY INJURY

Usefulness of UPCR Measurements During AKI

KI Reports. 2024;9(12):3455-3463.

Measurement of proteinuria using urine protein-to-creatinine ratio (UPCR) may lack accuracy during acute kidney injury (AKI) because reduced urine creatinine in the denominator may artificially inflate the ratio. To help address this concern, **Ian E. McCoy, MD**, and colleagues conducted a retrospective assessment examining whether the magnitude and direction of changes in UPCR during severe AKI episodes are associated with how serum creatinine levels change at the time of sample collection for UPCR estimation. The researchers repeated the analyses to compare UPCRs during hospitalization with those before hospitalization or after discharge, when available.

The study included 329 adults who were hospitalized with stage 2 or 3 AKI (defined as peak/nadir serum creatinine during hospitalization ≥ 2) at the University of California, San Francisco, from January 1, 2014, to December 31, 2022. All patients had multiple UPCR measurements during their hospitalizations for AKI.

UPCR values were similar regardless of whether serum creatinine was increasing or decreasing at the time of measurement (median difference, 0.06 g/g; interquartile range [IQR], -0.26 to 0.50 g/g). The difference in serum creatinine slopes during sample collection for UPCR estimation was not associated with the difference in UPCR values (UPCR 0.05 g/g higher per mg/dL/d serum creatinine slope; 95% CI, -0.36 to 0.47; $P=0.80$).

UPCR measurements taken during hospitalization showed positive and negative predictive values. This suggests that evaluating clinically relevant outpatient UPCR levels is useful. In conclusion, the authors wrote, "Despite nonsteady state serum creatinine at the time of collection, UPCRs measured during AKI hospitalizations may be more informative than previously believed and should not be wholly disregarded."

CHRONIC KIDNEY DISEASE

Association of Ankle-Brachial Index and CKD Progression With T2D and Elevated BMI

American Journal of Kidney Diseases. 2025;85(1):36-44.

Ankle-brachial index (ABI) is commonly used to screen for vascular complications in patients with diabetes. A post hoc analysis of the Look AHEAD (Action for Health in Diabetes) trial by **Mengyi Liu** and colleagues examined the relationship of longitudinal ABI data and chronic kidney disease (CKD) progression among patients with type 2 diabetes (T2D) and increased BMI.

A total of 3,631 patients from Look AHEAD were included in this analysis. All had a baseline estimated glomerular filtration rate (eGFR) greater than 60 mL/min/1.73 m². The study outcome was CKD progression (kidney failure requiring maintenance dialysis or the occurrence of an eGFR <60 mL/min/1.73 m² with a decrease of $\geq 30\%$ vs baseline at a follow-up visit).

The researchers calculated average ABI and average annual change in ABI based on annual ABI

measurements during the first 4 years of the study. They used restricted cubic spline and Cox proportional hazards models to estimate associations and to explore nonlinearity.

Over a median follow-up of 10.1 years, 1,051 participants experienced CKD progression. Chronic kidney disease progression had a reversed J-shaped relationship to average ABI (ABI <1.17: hazard ratio [HR] per 1 standard deviation [SD] decrement, 1.23; 95% CI, 1.06-1.42; ABI ≥ 1.17 : HR per 1 SD increment, 1.10; 95% CI, 1.00-1.22) and average annual change in ABI (change in ABI less than -0.007: HR per 1 SD decrement, 1.37; 95% CI, 1.12-1.66; change in ABI of at least -0.007: HR per 1 SD increment, 1.13; 95% CI, 1.03-1.24).

In summary, low and high-average ABI and decreasing and increasing average annual ABI were associated with an increased risk of CKD progression among patients with T2D and elevated BMI. Monitoring ABI and its changes may help with CKD risk stratification among patients who have T2D.



Combined Nutritional Supplementation/Exercise Training Intervention in CKD

Journal of Renal Nutrition. doi:10.1053/j.jrn.2024.11.009

A study by **Fan Zhang** and others investigated whether a combined intervention comprising nutritional supplementation and exercise training could help treat frailty and improve health outcomes in a population with CKD. The researchers assessed the effectiveness of nutritional supplementation combined with an exercise training intervention on frailty characteristics, physical function, and health-related quality of life in these patients.

Their study included data from the PubMed, Embase, Web of Science, and Scopus databases from inception to October 22, 2022; the search was updated in May 2023. Included studies were randomized controlled trials that compared nutritional supplementation combined with exercise training with usual care/single nutritional supplementation or exercise training to assess the effect on Fried-based frailty characteristics and physical function in patients with CKD.

Two authors chose the literature, extracted data, and assessed the risk of bias using the Cochrane risk

of bias tool 2. To analyze the outcome, the researchers used a random-effects model according to the Hartung-Knapp-Sidik-Jonkman method or a fixed-effects model with restricted maximum likelihood. They used the leave-one-out method for sensitivity analyses.

Seven articles, including nine trials and 324 patients, were included in the meta-analysis, which showed that nutritional supplementation combined with an exercise training intervention may improve frailty characteristics of patients receiving dialysis. These characteristics include walking speed (mean difference [MD], 0.09 m/s²; 95% CI, 0.02-0.16); physical functioning, such as cardiorespiratory fitness (standardized MD [SMD], 0.56; 95% CI, 0.20-0.93); and lower extremity mobility as measured by the Timed Up and Go test (MD, -1.11 seconds; 95% CI, -1.79 to -0.43). The effect of combined nutritional and exercise interventions on characteristics such as body weight (MD, 1.28 kg; 95% CI, -2.06 to 4.62), fatigue (SMD, 0.57; 95% CI -1.44 to 0.30), and health-related quality of life is unclear.

Although they acknowledged the heterogeneity of the included studies and the relatively small sample size as limitations of the study, the authors concluded that, "An intervention strategy of nutritional supplementation combined with exercise training may help improve frailty and physical functioning in CKD patients, particularly walking speed, cardiorespiratory fitness, and lower extremity mobility." Confirmatory studies with larger sample sizes and longer follow-up are needed.

Continuing Versus Stopping Metformin Use in Advanced CKD

American Journal of Kidney Diseases. 2025;85(2):196-204.

Current guidance advises against the use of metformin for individuals with advanced kidney disease. However, supporting evidence for this recommendation is lacking. **Emilie J. Lambourg, PharmD, PhD**, and colleagues conducted an observational cohort study to address this knowledge gap.

Their research included all adults in Scotland with T2D and incident stage 4 CKD (eGFR <30 mL/min/1.73 m²) who received metformin treatment between January 2010 and April 2019. The study compared outcomes for patients with T2D who continued metformin treatment with outcomes for patients who stopped treatment with metformin after developing stage 4 CKD. The primary study outcome was all-cause mortality, and secondary outcomes included major adverse cardiovascular events (MACE). The study followed a target trial emulation framework with a clone-censor-weight design and marginal structural models fit for sensitivity analyses.

A total of 4,278 patients with a T2D diagnosis before April 30, 2019, were identified as prevalent metformin users with incident stage 4 CKD. Within 6 months of reaching stage 4 CKD, 1,713 (40.1%) patients discontinued metformin use. Compared with those who continued using metformin, those who stopped had a lower 3-year survival (63.7%; 95% CI, 60.9%-66.6% vs 70.5%; 95% CI, 68.0%-73.0%; HR, 1.26; 95% CI, 1.10-1.44). However, the incidence of MACE was comparable between the two groups (HR, 1.05; 95% CI, 0.88-1.26). The



results regarding all-cause mortality (HR, 1.34; 95% CI, 1.08-1.67) and incidence of MACE (HR, 1.04; 95% CI, 0.81-1.33) were confirmed by marginal structural models.

Although they cited residual confounding as a limitation, the study's authors concluded that continuing metformin may be appropriate when a patient's eGFR falls below 30 mL/min/1.73 m².

Race, Changing eGFR Equations, and Risk of Stroke and Dementia

Kidney Medicine. doi:10.1016/j.xkme.2024.100961

A prospective, observational study by **Samuel R. Moen** and colleagues assessed and compared risk of incident stroke and dementia between previous equations for eGFR and new, race-free equations. The study included both African American and non-African American participants.

Baseline values from 6,814 participants in the Multi-Ethnic Study of Atherosclerosis cohort were collected between 2000 and 2002, and the participants were followed up through 2018. Of that cohort, 6,646 participants were included in this analysis.

Mean (SD) participant age was 62 (10) years; 53% were women, 39% were White, 27% were African American, 12% were Chinese American, and 22% were Hispanic/Latino. Median follow-up was 17 years, during which 349 (5.3%) participants had an incident stroke event, and 574 (8.6%) participants experienced incident dementia.

The researchers used Cox proportional regression adjusting for demographic, lifestyle, and clinical variables to estimate associations between different eGFR measures and risk of incident stroke and dementia. In the fully adjusted model, participants with an eGFR of less than 60 mL/min/1.73 m² had a significantly increased risk of dementia when compared with participants with an eGFR greater than 90 mL/min/1.73 m² (HR, 1.73; 95% CI, 1.21-2.45). However, a lower eGFR was not significantly associated with incident stroke (HR, 1.30; 95% CI, 0.75-2.24).

The new equations tended to reclassify African American participants to a lower eGFR group, while reclassifying non-African American participants to a higher eGFR group. However, the new and previous equations for calculating eGFR exhibited little difference regarding their association with incident stroke and dementia among both African American and non-African American participants.

In conclusion, the study demonstrated that both African American and non-African American patients with an eGFR less than 60 mL/min/1.73 m² have a higher risk of dementia than those with an eGFR greater than 90 mL/min/1.73 m². However, the risk of stroke was not greater among patients with lower eGFR.

Incidence of Tuberculosis With Kidney Failure

Journal of the American Society of Nephrology.

doi:10.1681/ASN.0000000621

CKD is associated with a higher risk for tuberculosis after infection with *Mycobacterium tuberculosis*. **Kimberly R. Schildknecht, MPH**, and colleagues produced an estimate of tuberculosis incidence and a description of the disease among the US population with kidney failure.

Their cross-sectional analysis began by identifying individuals in the US with a reported case of tuberculosis between 2010 and 2021. The researchers then stratified these patients by reported kidney failure status. The study's primary outcome was tuberculosis incidence among people with kidney failure. The researchers also compared the characteristics of patients with tuberculosis by reported kidney failure status.

The researchers identified 111,155 individuals who were diagnosed with tuberculosis between 2010 and 2021; 2,892 of them (3%) also had kidney failure. The incidence of tuberculosis was 26.1 to 45.4 per 100,000 patients with kidney failure and 2.1 to 3.5 per 100,000 patients without kidney failure annually. Patients who had both tuberculosis and kidney failure were nearly twice as likely to have a false-negative tuberculin skin test result as patients with tuberculosis only (39% vs 20%).

COVID-19

Kidney Function Decline After COVID-19 Infection

JAMA Network Open. doi:10.1001/jamanetworkopen.2024.50014

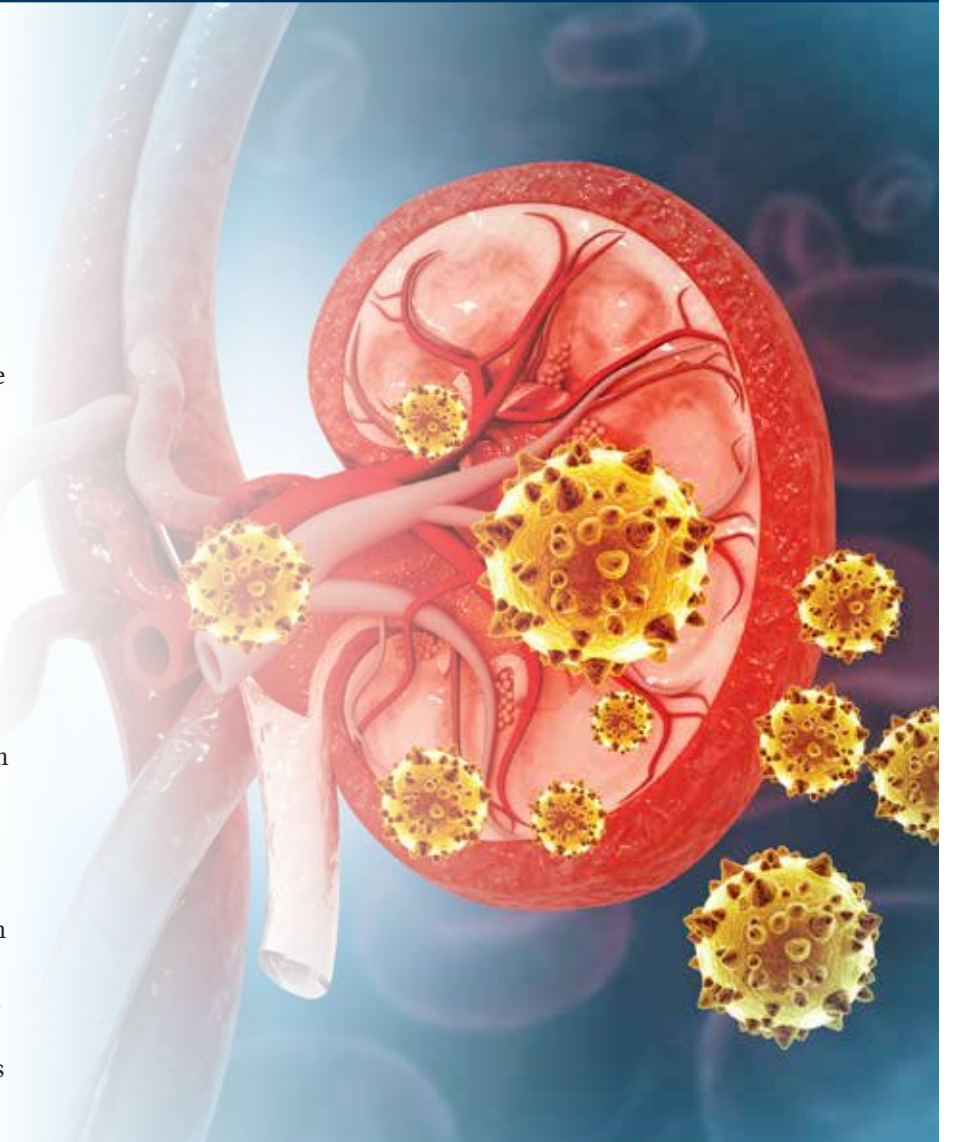
The association between COVID-19 and long-term kidney function is not well understood, although it is known that COVID-19 is associated with AKI. To address this gap, **Viyaasan Mahalingasivam, MPhil**, and colleagues conducted a cohort study examining whether kidney function decline hastened after COVID-19 infection compared with after other respiratory tract infections.

Their study used data from the Stockholm Creatinine Measurements Project in Stockholm, Sweden, between February 1, 2018, and January 1, 2022. Statistical analyses took place between June 2023 and October 2024. Participants comprised hospitalized and nonhospitalized adults with at least one eGFR measurement in the 2 years before receiving a positive COVID-19 test result or pneumonia diagnosis. Outcomes included mean annual change in eGFR after COVID-19 and after pneumonia, which was calculated using a linear regression model.

A total of 134,565 patients were included in the COVID-19 cohort. Their median (IQR) age was 51 (37-64) years and 74,819 (55.6%) were women. The pneumonia cohort comprised 35,987 patients; their median (IQR) age was 71 (56-81) years and 19,359 (53.8%) were women. Median (IQR) baseline eGFR was 94 (79-107) mL/min/1.73 m² for the COVID-19 group and 79 (61-92) mL/min/1.73 m² for the pneumonia group.

Both COVID-19 and pneumonia infections were associated with annual decline in eGFR, after adjusting for covariates. The decline was greater after COVID-19 infection (3.4%; 95% CI, 3.2%-3.5%) than after pneumonia infection (2.3%; 95% CI, 2.1%-2.5%). The decline in kidney function was more severe among patients who were hospitalized for COVID-19 (5.4%; 95% CI, 5.2%-5.6%). However, hospitalization did not demonstrate a similar effect among patients hospitalized for pneumonia.

In summary, the study demonstrated an association between COVID-19 and an acceleration in kidney function decline compared with pneumonia. The decline was particularly severe after hospitalization, suggesting that patients hospitalized for COVID-19 should be monitored closely for kidney function. This will help ensure early diagnosis and optimal management of CKD to prevent complications and further decline in kidney function.



Of the patients with kidney failure, 924 (32%) had only extrapulmonary tuberculosis. Nearly 40% of patients with kidney failure died; 286 were diagnosed with tuberculosis after death, and 792 died during treatment.

In summary, the incidence of tuberculosis among US individuals with kidney failure between 2010 and 2021 was ten times the incidence among individuals without kidney failure.

DIALYSIS

Effects of US Reimbursement Policy Change for Calcimimetics

Clinical Journal of the American Society of Nephrology. 2025;20(2):218-228.

Angelo Karaboyas, PhD, and colleagues investigated the effects of a US reimbursement policy change that moved calcimimetic drugs from the transitional drug add-on payment adjustment (TDAPA) to an increased bundled payment.

Calcimimetics, including IV etelcalcetide and oral cinacalcet, are often used by patients undergoing hemodialysis to help prevent complications from elevated parathyroid hormone (PTH) levels. The policy change, which went into effect in January 2021, added \$10.09 per hemodialysis session to cover the expense of calcimimetics, regardless of whether patients also receive etelcalcetide.

The study included 713 patients enrolled in the United States Dialysis Outcomes and Practice Patterns Study who received in-center hemodialysis and discontinued etelcalcetide during the TDAPA transition period from December 2020 to April 2021. The researchers used a self-matched longitudinal design and linear regression adjusted for confounders to examine changes in mean PTH, calcium, and phosphorus levels within patients in the 6 months before and after etelcalcetide discontinuation.

Among patients in the United States Dialysis Outcomes and Practice Patterns Study, etelcalcetide use declined by 58%, from 12% to 5% from July 2020 to 2021. Of those who discontinued etelcalcetide, 73% switched to cinacalcet within 6 months.

Mean PTH levels increased by 107 pg/mL (95% CI, 80-133) when the 6 months before discontinuation were compared with the 6 months after discontinuation. Also, the prevalence of PTH .600 pg/mL increased by 15% (95% CI, 11%-19%), from 28% to 43% overall; the prevalence increased from 26% to 49% among Black patients. Mean serum calcium levels increased by 0.42 mg/dL, and mean phosphorus levels increased by 0.16 mg/dL.

In summary, the study revealed that the use of etelcalcetide substantially decreased after the reimbursement policy change, and most patients switched to cinacalcet. Subsequently, PTH levels increased quickly, and the increase was sustained. This increase was especially noticeable among Black patients, suggesting potential disparities and effects on clinical outcomes.

The authors noted that, “Despite the spirit of the policy change, the flat per-treatment increased payment may have inadvertently created a financial incentive to restrict patient access to a more effective therapy and potentially stifle drug innovation.”

Altered Mental Status and Falls When Gabapentinoid and Other Psychoactive Medications Are Coprescribed to Patients Receiving Dialysis

American Journal of Kidney Diseases. 2025;85(2):215-225.

A group of researchers including **Rasheeda K. Hall, MD**, conducted an observational cohort study to determine whether coprescription of gabapentinoids and other psychoactive potentially inappropriate medications (PPIMs) is associated with altered mental status (AMS) and falls among patients with kidney disease. The study also considered whether such associations are modified by frailty.

The cohort comprised adults in the US Renal Data System receiving dialysis and having an active gabapentinoid prescription but no other PPIM prescriptions in the prior 6 months. The primary exposure was PPIM coprescribing, defined as prescription of a gabapentinoid medication and at least one other PPIM. The study outcome was acute-care visits for AMS and injurious falls.

The researchers used Prentice-Williams-Petersen Gap Time models to estimate the association between coprescription of PPIMs and each of the two outcomes, with adjustment for demographics, comorbidities, and frailty (as determined by a validated frailty index [FI]). Each of the models used tested for interaction between PPIM coprescribing and frailty.

PPIM coprescribing was found to be associated with an increased risk of both AMS (HR, 1.66; 95% CI, 1.44-1.92) and falls (HR, 1.55; 95% CI, 1.36-1.77). Frailty significantly altered the effect coprescribing PPIMs had on the risk of AMS (*P* interaction=0.01) but did not demonstrate such an alteration with fall risk.

Among those with low frailty (FI=0.15), the HR for AMS with PPIM coprescribing was 2.14 (95% CI, 1.69-2.71). For those with severe frailty (FI=0.34), the HR for AMS with PPIM coprescribing was 1.64 (95% CI, 1.42-1.89). Patients who were coprescribed PPIMs and also had severe frailty (FI=0.34) had a higher risk for both AMS (HR, 3.22; 95% CI, 2.55-4.06) and falls (HR, 2.77; 95% CI, 2.27-3.38) compared with patients without frailty or PPIM coprescribing.

The authors concluded that, “Compared with gabapentinoid prescriptions alone, PPIM coprescribing was associated with an increased risk of AMS and falls. Clinicians should consider these risks when coprescribing PPIMs to patients receiving dialysis.”



GERIATRICS

Association of Multimorbidity and Kidney Function Decline in Older Age

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Although chronic conditions have been linked with a decline in kidney function, the role of multimorbidity (defined as the presence of two or more conditions) in this decline, as well as patterns of multimorbidity, remain unclear. **Giorgi Beridze MD, MMSc**, attempted to address this gap with an analysis of 3,094 patients from the Swedish National Study on Aging and Care in Kungsholmen. The mean age of participants was 73.9 years, 87% had multimorbidity, and they were followed up for 15 years.

Latent class analysis was used to identify multimorbidity patterns. The researchers used joint models and Cox regression models, respectively, to examine the associations between multimorbidity and subsequent absolute and relative ($\geq 25\%$ decline from baseline) changes in eGFR (measured using the creatinine-based Berlin Initiative Study equation).

An independent dose-response relationship was observed between the number of chronic conditions and absolute (β , -0.05 ; 95% CI, -0.07 to -0.03) and relative (HR, 1.23; 95% CI, 1.17-1.29) declines in eGFR. The researchers identified five patterns of multimorbidity: (1) the *unspecific, low burden* pattern demonstrated the lowest morbidity burden and was used as the reference category; (2) the *unspecific, high burden* pattern demonstrated accelerated absolute (β , -0.15 ; 95% CI, -0.26 to -0.05) and relative (HR, 1.45; 95% CI, 1.09-1.92) declines; (3) the *cardiometabolic* pattern also showed accelerated absolute (β , -0.77 ; 95% CI, -0.98 to -0.55) and relative (HR, 3.45; 95% CI, 2.27-5.23) declines; (4) the *cognitive and sensory* pattern showed accelerated relative decline (HR, 1.53; 95% CI, 1.02-2.31); and (5) the *psychiatric and respiratory* pattern demonstrated no associations.

In summary, multimorbidity showed a strong association with an accelerated kidney function decline in individuals of older age, and those with a cardiometabolic multimorbidity had a particularly increased risk. “Increased monitoring and timely interventions may preserve kidney function and reduce cardiovascular risks in individuals presenting with conditions that are characteristic of high-risk multimorbidity patterns,” the authors wrote. ●



Sarah Tolson

Phosphate Binders and Payment Pitfalls

Insights for Dialysis Administrators



As someone who has had the privilege of participating in national forums with stakeholders across the renal industry—particularly those overseeing the financial operations of dialysis programs—I’ve seen firsthand how reimbursement challenges can quickly rise to the top of everyone’s agenda. Lately, there’s one topic that has dominated these discussions: phosphate binders.

Although these medications are critical in managing hyperphosphatemia in patients receiving dialysis, their reimbursement—especially under the Transitional Drug Add-on Payment Adjustment (TDAPA)—has proven to be anything but straightforward. The variability in how different payers approach reimbursement has placed added strain on dialysis providers trying to do right by their patients and remain financially viable.

MEDICARE ADVANTAGE PLANS: A MOVING TARGET

One of the most perplexing trends we’ve observed relates to Medicare Advantage (MA) plans. Under certain circumstances, these plans are intended to mirror the reimbursement methodologies of traditional Medicare, yet we’re seeing significant inconsistencies. Some MA plans are reimbursing claims for phosphate binders well above Medicare rates, and others are paying far less.

To bring clarity to this process, my organization has turned to the Centers for Medicare and Medicaid Services End Stage Renal Disease Prospective Payment System (CMS ERRD PPS) Web Pricer, a tool designed to estimate the reimbursement Medicare would issue if it were the primary payer. By comparing Web Pricer data with actual payments received from MA plans, we’ve uncovered widespread misalignment. Although overpayment may seem like a windfall, it often leads to painful refund requests down the line. Chronic underpayment, on the other hand, can quietly erode a program’s financial health.

Our recommendation? Dialysis programs should actively review MA plan payments against Medicare benchmarks and engage those payers when discrepancies arise. Proactive communication and documen-

tation can help correct course early, avoiding costly retroactive adjustments or protracted disputes.

CONTRACTING CONCERNS: UNDERPAYMENT BY DESIGN?

In many cases, MA plans are reimbursing at rates outlined in contracts with dialysis providers. The catch? These contracted rates are, on average, significantly lower than what traditional Medicare would pay.

This presents a serious concern. If your organization is receiving less than the Medicare-allowed amount for dialysis services from an MA plan, it may be time to revisit that agreement. There is anecdotal evidence that renegotiation is not only possible but can also include retroactive adjustments. I’ve heard of successful efforts to amend contracts and backdate new rates to January 1, 2025, ensuring that all medications covered under TDAPA—including phosphate binders—are reimbursed fairly from the outset.

When renegotiating, consider including language that allows for flexibility in the event of future changes by Medicare. Building in triggers for renegotiation or inclusion of newly reimbursed services can safeguard your program against the shifting tides of policy.

VA: A SURPRISING STANDOUT

Interestingly, amidst the reimbursement confusion, the US Department of Veterans Affairs (VA) has emerged as a model of consistency.

Unlike many private MA plans, the VA has been pricing and reimbursing phosphate binder claims at exactly the rates Medicare would have paid. This consistency not only simplifies billing but also ensures reliable reimbursement—something every dialysis provider can appreciate.

BINDERS IN THE BUNDLE: A BARRIER TO ACCESS?

Despite the well-intentioned move to shift phosphate binder provision into dialysis facilities to improve access, the current reality is quite the opposite. Nationwide, dialysis programs are experiencing delays in receiving these medications, leaving patients in limbo.

This irony should not be lost on policymakers. A mandate intended to streamline access has, in practice, complicated the supply chain and introduced new barriers. Providers must now make case-by-case decisions about the best way to ensure patients receive their medications, all while navigating a patchwork of payer rules and logistic challenges.

FINAL THOUGHTS

Phosphate binders are not just a line item on a spreadsheet. They’re essential medications that directly impact patient outcomes. Ensuring fair, timely, and consistent reimbursement is not only a financial imperative but a clinical one.

As we continue to share insights and experiences across the industry, it’s clear that collaboration—between providers, payers, and regulators—is essential. Whether it’s leveraging tools such as the ESRD Web Pricer, renegotiating contracts with MA plans, or pushing for flexibility in payer policies, every step we take helps secure a stronger, more equitable system for our patients and our programs. ●

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.

figure1

Where Clinicians Come to Collaborate

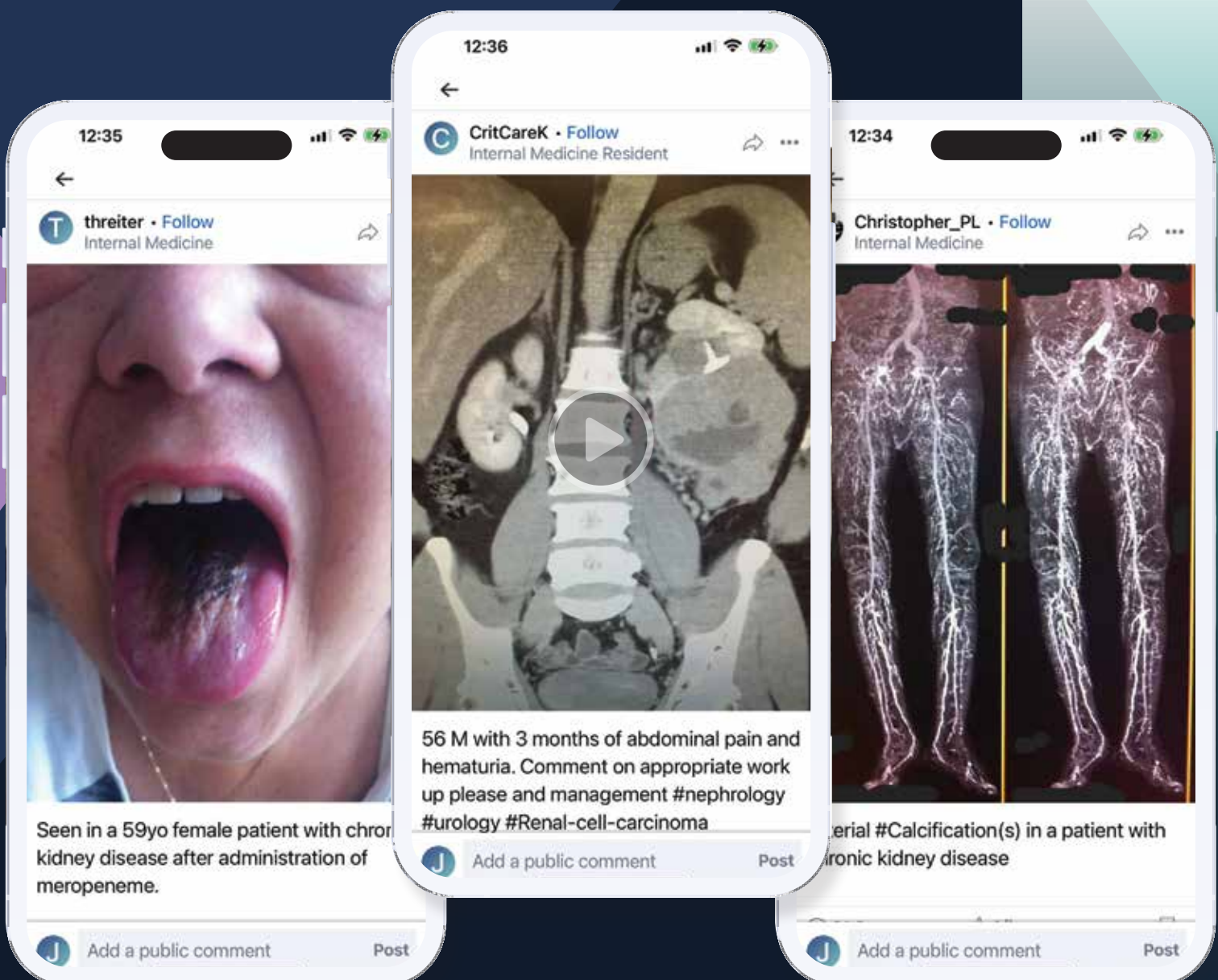


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