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New ASN Guidance Helps Nephrologists Navigate CKM Care for People With Kidney Diseases

By Bridget M. Kuehn

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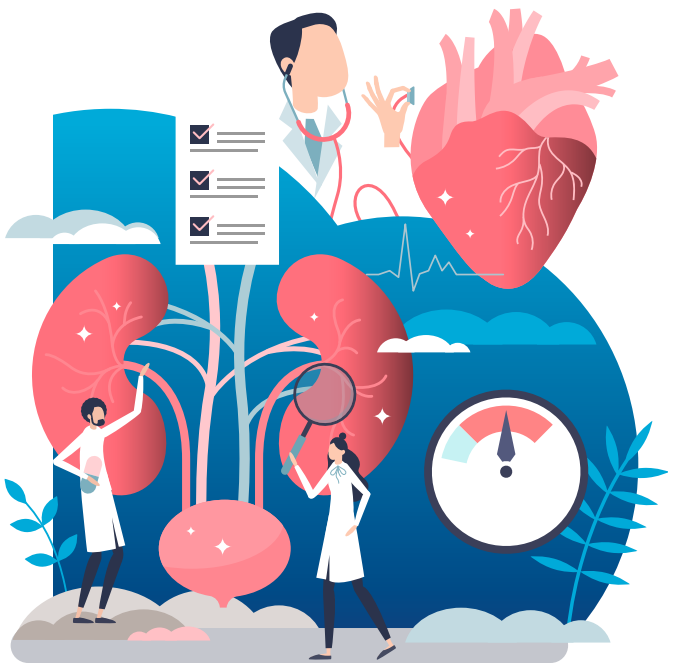

ASN's latest Kidney Health Guidance (KHG) provides expert guidance for nephrologists and other clinicians on managing integrated cardiovascular-kidney-metabolic (CKM) care for people living with chronic kidney disease (CKD).

Growing recognition of the interconnected nature of cardiovascular, kidney, and metabolic diseases has led to an increasing consensus across specialties about the need to address these conditions simultaneously. To develop detailed guidance for treating CKM syndrome in people with various stages or types of kidney diseases, ASN convened the multidisciplinary ASN Kidney Health Guidance Workgroup on the Cardiovascular-Kidney-Metabolic Syndrome in early 2026. The workgroup published the guidance and an accompanying KHG Executive Summary in *JASN* on September 2, 2026 (1). This ASN KHG complements the American Heart Association's (AHA's) 2023 Scientific Statement outlining the case for integrated CKM care (2) and more recently, the 2026 joint guideline for preventing, detecting, evaluating, and managing CKM syndrome, published by AHA, the American College of Cardiology, the American Diabetes Association, and ASN (3).

"There is a need to better highlight how the CKM framework applies specifically to patients with [CKD] cared for by nephrologists or nephrology colleagues," said Nisha Bansal, MD, MAS, FASN, cochair of the ASN Kidney Health Guidance Workgroup on the Cardiovascular-Kidney-Metabolic Syndrome and professor of medicine in the Division of Nephrology at the University of Washington, Seattle. The guidance also identifies gaps in the research on CKM care for these populations and identifies systemic barriers to effective CKM care in people with kidney diseases.

Predicting heart risks

The guidance emphasizes the importance of monitoring kidney, metabolic, and heart risks over time in individuals living with kidney diseases. It recommends monitoring the estimated glomerular filtration rate (eGFR) and albuminuria as markers of kidney and heart risks, alongside traditional heart and metabolic risk factors such as blood

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Telehealth Continues to Prove Its Value for Kidney Care

By Karen Blum

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When Sharica Brookins, MD, FASN, was pregnant and working for a group practice in Georgia, she saw patients both in her main office and as medical director of a rural dialysis center an hour outside of town. Then, unexpectedly, she delivered her daughter early.

Brookins later discovered that her rural patients' appointments were canceled when none of her partners were available to go to see them on short notice, and some patients lacked transportation to reach the main office for appointments. When she returned to work after maternity leave, patients expressed their concern about not getting care, and she noticed some downturns in their lab work since they were not being closely monitored.

While looking for a solution that would allow her to see rural patients and be closer to home for her child, Brookins began researching telehealth. In 2018, she opened Remote Renal Care, a 100% telehealth solo practice. Today, she sees patients virtually across Georgia and South Carolina, as well as parts of Florida.

Her patient mix includes just about everyone outside of those in dialysis care (which requires some in-person visits), from transplant recipients to people with chronic kidney disease (CKD), and polycystic kidney disease. If

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pressure, lipid levels, hemoglobin A_{1c}, waist circumference, and body mass index. It also highlights circumstances in which advanced testing, including liver function tests, coronary artery calcification, or high-sensitivity troponin testing, may be appropriate additions.

The guidance suggests using tools like the Kidney Failure Risk Equation, CKD-PC [CKD-Prognosis Consortium], and AHA's PREVENT ASCVD [Predicting Risk of Cardiovascular Disease Events Atherosclerotic Cardiovascular Disease] or PREVENT HF [Heart Failure] to simultaneously assess kidney and heart risks. "Heart disease is the number one cause of death for our patients with kidney disease," said the KHG CKM Workgroup Cochair Alexander Chang, MD, MS, professor in the Department of Nephrology at Geisinger College of Health Sciences in Danville, PA. "We need to move beyond assessing kidney risk alone and incorporate cardiovascular risk assessment into routine nephrology care to maximize cardiovascular health."

It also highlights overlap between the Kidney Disease: Improving Global Outcomes (KDIGO) kidney disease risk stratification framework on which nephrologists already rely and CKM staging frameworks. KDIGO guidelines link CKD severity with eGFR and albuminuria, and CKM staging starts with early cardiovascular, metabolic, and kidney risk factors, with CKD occurring in the later stages of the CKM staging framework, explained Bansal. "Patients who have more advanced CKD [as designated by KDIGO guidelines] are further along the CKM staging risk score," Bansal noted.

CKM care

Lifestyle modifications, including a healthy diet emphasizing plant-based foods, weight management, quitting smoking, and physical activity, are cornerstones of CKM care. Newer therapies, such as sodium-glucose cotransporter-2 (SGLT2) inhibitors, glucagon-like peptide-1 (GLP-1) agonists, and nonsteroidal mineralocorticoid receptor antagonists (nsMRAs), which target shared mechanisms of CKM syndrome, have also become pillars of care alongside established therapies like renin-angiotensin system (RAS) inhibitors and lipid-lowering drugs.

"RAS inhibition and SGLT2 inhibitors are foundational therapies that we should try to get as many of our patients on as soon as possible," Bansal said. "If they are tolerated and there's the ability to add additional medications from a patient acceptance and tolerability perspective, we should consider other therapies including nsMRAs as well as GLP-1s as appropriate."

Bansal also noted that patient care should be individualized. For some patients, that may mean starting a treatment with a low dose of all four therapies; for others, who are more cautious about adverse effects, it may mean adding one medication at a time. People with CKD, type 2 diabetes, poor glycemic control, or a urine albumin-to-creatinine ratio (UACR) over 100 mg/g may benefit from adding a GLP-1, according to the guidance. nsMRAs may be an appropriate add-on for people with CKD, diabetes, and a UACR more than 30 mg/g and in some cases, for people with CKD without diabetes. Statins were also suggested for most people with stage 3 to 5 CKD who are not on dialysis.

Patients' insurance coverage and the affordability of medication combos must also be considered, noted Chang. He explained that there is a need to improve the affordability of newer medications for people with kidney diseases. In the meantime, he added that clinicians can work with patient-assistance programs and with pharmacists and other members of the care team to facilitate prior authorization or access to discount programs.

The guidance also acknowledges that questions remain about how and when to deploy these medications across different patient populations with kidney diseases. "Not all patients [with kidney diseases] are the same," explained Bansal. "There are variations by age, the type of kidney disease, as well as whether they have received a kidney transplant."

Yet most of the evidence and guidance to date on CKM care focuses on diagnosing and treating people with early- to moderate-stage CKD and concomitant type 2 diabetes, Bansal noted. Chang explained that there are limited data on the use of some of these therapies in subpopulations of patients, including kidney allograft recipients, patients with glomerular nephritis, or those with genetic forms of kidney disease, who may have been excluded from initial trials for CKM therapies. There are also gaps in the evidence on how to treat individuals with more advanced CKD, particularly those on dialysis, Bansal noted. "[Patients on dialysis] are different," she said. "The risk of side effects is different, tolerability will be different, dosing will be different. We cannot just extrapolate from patients without kidney disease or earlier stages of kidney disease."

Age and hormonal transitions, such as pregnancy, adolescence, and menopause, may also influence patients' cardiac risks and care needs. Chang noted the importance of long-term follow-up care for women with a history of preeclampsia, given high risk of future cardiovascular and kidney disease. But he noted that this may require collaborative approaches among disciplines because many of these women may be seen only by an obstetrician-gynecologist or primary care clinician. Advanced age may also factor into clinical decision-making, but Chang emphasized the need to consider each patient and their condition and the risks and benefits of therapies rather than making a "knee-jerk" decision based on age alone.

"We should be evaluating cardiovascular risk across all of those different conditions too because patients could benefit from CKM therapies," Chang said. "In situations [in which data are] limited, treatment decisions need to be individualized with careful discussion of potential benefits and risks."

Closing gaps

Other patient populations that could benefit from additional research include pediatric patients, patients with glomerular diseases, and patients with Alport syndrome, Chang said. Bansal said she hopes that by identifying some of the knowledge gaps for CKM care in specific patient populations, KHG will also help promote research to fill them.

Additionally, the guidance highlights the need for interdisciplinary research on CKM care and implementation research on the best models for care delivery. The guidance acknowledges that the current specialty-siloed health care system creates barriers to optimal multidisciplinary care for people with CKM syndrome. "Patients are asked to navigate a fragmented health care system that is built around specialties, rather than patients who often have interconnected [CKM] conditions," Chang said.

Bansal suggested more efficient use of electronic health records to facilitate multidisciplinary coordination and comprehensive testing for CKM syndrome. Electronic health records may also facilitate patient education and more seamless communication between care teams and patients, she said. She noted that support is also needed to help primary care clinicians and advanced practice practitioners who may be taking the lead on CKD and CKM care in areas with few care specialists. The committee included an advanced practice nurse and a private practice physician who provided perspectives on the unique demands of different practice settings. Bansal noted that many of these systemic changes will take time to implement and will require a commitment from health care institutions and policymakers in addition to clinicians.

Chang urged fellow nephrologists to engage with health system leaders to develop more effective models of CKM care and to partner with advocacy and policy groups to advance system-level changes. He noted that growing recognition of the importance of CKM care and kidney health across specialties and the rising cost of dialysis are broadening support for the necessary changes. "The more we can do to advance the conversation and let others know how important this is to their community, the better," he said. ■

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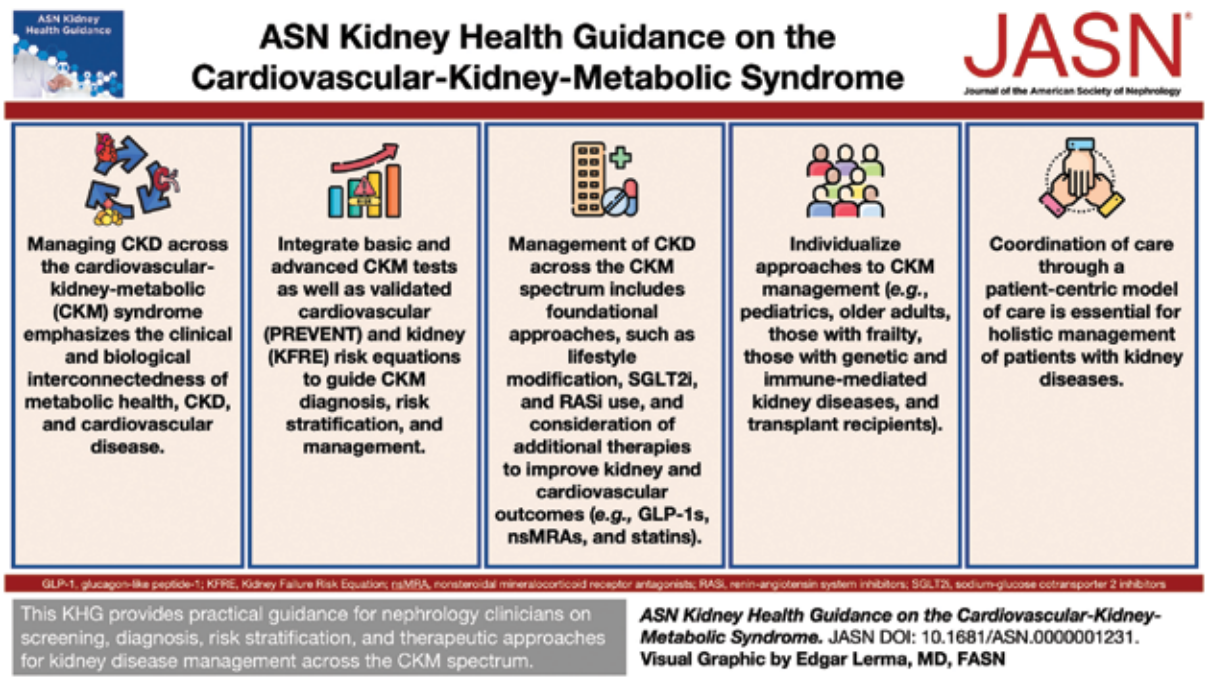

ASN Kidney Health Guidance on the Cardiovascular-Kidney-Metabolic Syndrome. JASN DOI: 10.1681/ASN.0000001231. **Visual Graphic by Edgar Lerma, MD, FASN**

Telehealth Continues to Prove Its Value for Kidney Care

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Brookins needs lab work or imaging, she refers patients to laboratories or rural hospitals in their communities for testing. Patients interested in remote monitoring can receive an electronic scale or blood pressure cuff through their insurer, or they send their own measurements to her office. Between Brookins' dedicated half-hour visits with patients, she communicates via the patient portal, email, and text.

"We're able to do genetic testing. We're able to manage any and every kidney disease," she said. "The beauty to nephrology versus other specialties is we function so much off of just urine and blood. As long as I have that, then there's a lot I can analyze and come up with the plan for the patient."

While Brookins may not be seeing the same volume of patients remotely as she did in person, she feels that she has a more personable relationship. "I think for that reason, I don't have an issue with no-shows, and that means I'm able to follow their kidneys very closely," she says.

Telemedicine capabilities for people living with kidney diseases and other health concerns have expanded since the COVID-19 pandemic and are likely to continue evolving, said Rebecca Schmidt, DO, FACP, FASN, professor and assistant dean of outreach and community engagement at West Virginia University School of Medicine in Morgantown. Many residents of rural America live in a health professional shortage area, she said, and telemedicine is proving a viable avenue for delivering specialty care to these medically underserved communities.

"The pandemic really taught us that we could do this, and we could do it effectively, not just for patients with CKD and transplants but also for patients who require dialysis for kidney failure," she said. "I think more and more it will be a large part of what we are doing."

"I think all aspects of kidney care can be done by telemedicine," said Susie Lew, MD, FASN, a professor of medicine at The George Washington University School of Medicine in Washington, DC, who manages three nephrology clinics, one of which is all telemedicine-based. "We talk about lifestyle changes, dietary changes. It's all about conversation, and it's face to face."

Telehealth can also allow for access to specialists for rare and genetic kidney diseases, noted Eric Wallace, MD, FASN, chief medical information and digital officer at The University of Alabama at Birmingham (UAB) and a member of ASN's Policy and Advocacy Committee. One of his areas of expertise is Fabry disease, a condition that affects 1 in 40,000 people. Not every physician is knowledgeable in that rare disease's management. "Now a patient can see me, even if they couldn't drive to see me," he said.

There are other advantages, too. If Wallace sees a patient with fluid overload, it is relatively difficult to arrange for unexpected in-center dialysis treatment because there may not be an available chair. But with remote patient monitoring for those on home dialysis, he can simply call and tell them to undergo an extra treatment.

Per federal regulations, individuals on home peritoneal dialysis are required to come to the office once a month, Wallace said. However, this typically ends up being twice a month: Once to see the nurse and obtain lab samples and another to see the doctor. "Then you realize that most patients with CKD, [including kidney failure], have a cardiologist, an endocrinologist, and others, and so they get just swamped with doctors' appointments, and that reduces quality of life," he said. He follows up with patients via telehealth after their lab samples are obtained to save them an in-person appointment.

In rural areas of the state, Wallace said, a person on dialysis with high potassium might go to a local emergency department that does not have nephrology care. The emergency department would give the patient a laxative and put them in an ambulance for a 2-hour ride to UAB, where on arrival, they would still have to wait until a space was available, meanwhile keeping the ambulance away from the county where it could be needed. Thanks to a partnership between UAB and a dialysis company, now when a patient presents to a rural hospital with hyperkalemia, the doctors participate in a telehealth consult with a nephrologist who reviews the patient's condition. The nephrologist can place an order for dialysis and have a technician come to the hospital with a home hemodialysis machine and dialyze the patient, after which, the patient usually can go home. "People want to prove that telehealth is as good as in-person care," he said, "but in this case, it is 100% better."

Care via telehealth brings varied advantages for different age groups, Lew noted. It allows pediatric patients to remain in school and their parents to be able to work. It also enables other caregivers, like grandparents or a babysitter, to participate in the visit to gain care instructions. Older teenagers leaving town for college can maintain a relationship with their existing nephrologist. For working adults, there are generally fewer delays than sitting in a waiting room. And for older adults with mobility issues, doctors can have someone visit the home to draw blood or ask them to obtain a specific test next time they go to a lab.

"It's about saving time, it's about transportation, and it's about getting an appointment time," she said. "If you want to get an appointment with me as a new patient, it's 3 months down the road. But in my telemedicine [clinic], I actually have space because not everybody signs up for it."

For families, the cost of gas; wear and tear on a vehicle; and interruption of work, school, and social calendars can be burdensome. "I think [telemedicine] may actually help lower the threshold to contact us as physicians when they know they're not going to be obliged to have to drive in and see us," said James Sloand, MD, FACP, FASN, a clinical professor of medicine at The George Washington University School of Medicine and Health Sciences. "This can allow for earlier management of medical issues that arise."

There are still some limitations to telemedicine, such as undergoing a physical, lung, or cardiac examination and collecting specimens. "If somebody's got some pulmonary issues, respiratory complaints, that can be harder to assess," Sloand noted. And for people with kidney failure, who are choosing between hemodialysis and peritoneal dialysis, he said, "Certainly, there's a lot they can learn remotely about it, but I think there's a lot to be said about coming into a dialysis unit, seeing, feeling, touching, and discussing things with some of the other patients that are actually on dialysis." If they elect to undergo home dialysis, "that training would be difficult but not impossible to do remotely," he said. Connectivity in some remote areas that could benefit from telemedicine also can be an issue, noted Schmidt.

But telemedicine will likely be increasingly helpful for patients both in rural and urban areas, experts said. Brookins mentioned that more practices are operating a hybrid model, offering both in-person and telehealth services. Some of her newer colleagues will call the patient in the event of a no-show and try to convert them to telehealth so they still get in a visit.

The next level of convenience is the ability to obtain lab samples in the home, Wallace said. Some companies are working on capillary action tests for blood that can be sent to a clinical laboratory to measure creatinine. Urine studies can also be sent from the home. "The more diagnostics I have at the home, the more care I can deliver over telehealth," he said. Wallace noted that more interoperability between medical records' systems also could help.

As older nephrologists are retiring, and fewer young doctors enter the field, which could increase the existing shortage of nephrologists, Lew said, "I think some of the older doctors who may want to continue to practice could do telemedicine. They don't have to travel, and the hours are much more flexible. I think there's a win-win for everybody." ■

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A Targeted Trial of Hyponatremia: From Avoiding Overcorrection to Accepting Undercorrection

By Michael L. Moritz and Juan Carlos Ayus

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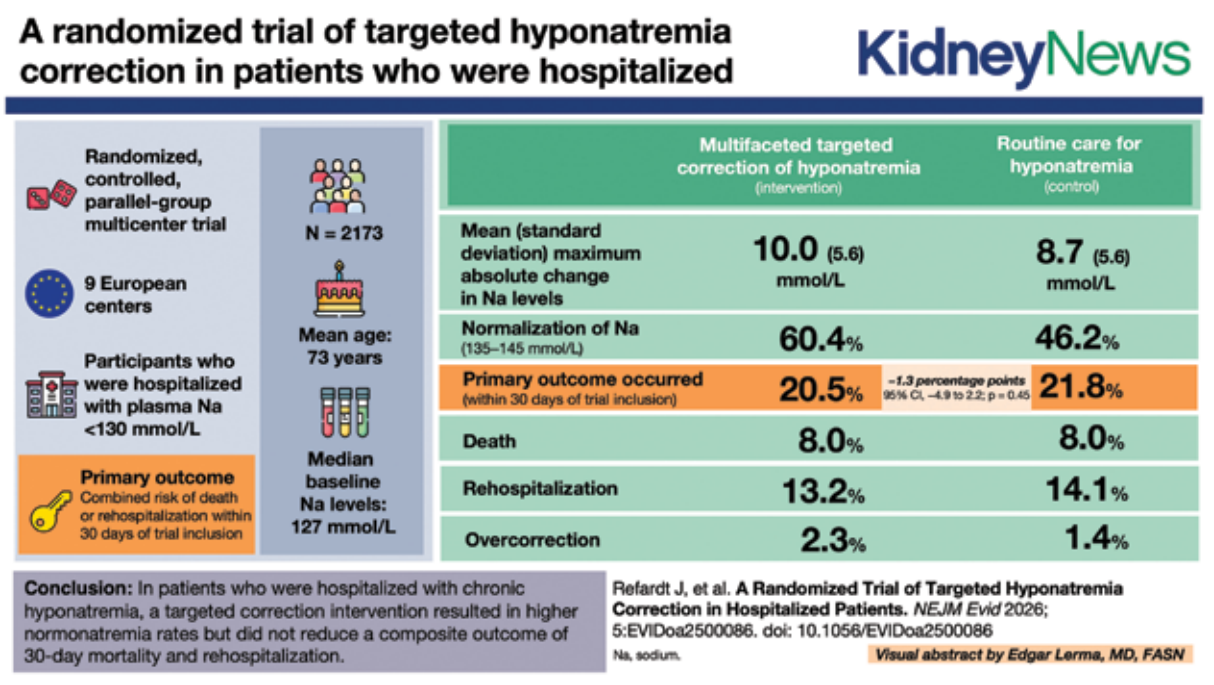
Hyponatremia is the most common electrolyte abnormality and an independent predictor of mortality (1). What has been unclear is whether hyponatremia is simply a marker of severity of illness and whether correction of hyponatremia can improve patient outcome. To address these questions, a prospective randomized controlled multicenter clinical trial was conducted between 2018 and 2024 to assess whether targeting hyponatremia correction decreased death or rehospitalization within 30 days (2). The intervention arm was designed to align with the 2013 US (3) and 2014 European (4) hyponatremia guidelines. Targeted therapy occurred if the sodium increase was less than 2 mEq/L per day. The primary therapies were fluid restriction (40%), isotonic fluids (25%), and urea (15%), with only 4% receiving vaptans and 3% sodium chloride not being a treatment option. The median plasma sodium was 127 mEq/L in both groups, with the mean maximum sodium increase in the targeted group of 10.0 mEq/L over a median of 6 days, nominally better compared with 8.7 mEq/L in controls. Normonatremia was achieved in only 60% of patients compared with 46% in controls. Targeted correction did not reduce 30-day mortality or rehospitalization, as both groups underwent similarly slow correction, with minimal separation from usual care. This trial compared two slow strategies with little difference in achieved sodium correction, not intensive versus standard therapy. An accompanying editorial concluded that current management of hyponatremia is "good enough" (5).

Importantly, the study demonstrated that patients who achieved normonatremia by discharge, irrespective of study group, had better outcomes, with reduced odds of death or rehospitalization (odds ratio, 0.74; 95% confidence interval [CI], 0.60–0.91). Accumulated evidence following the initiation of this study in 2018 suggests that insufficient correction may itself be harmful. A 2025 systematic review and meta-analysis that included 11,811 patients with severe hyponatremia found that rapid correction (≥8–10 mEq/L in 24 hours) was associated with 32% lower in-hospital and 45% lower 30-day mortality without a statistically significant increase in osmotic demyelination syndrome (ODS) (6). A 2026 large cohort study of 13,988 patients with severe hyponatremia found that faster correction (>12 versus <8 mEq/L per 24 hours) was associated with decreased 90-day mortality (absolute reduction, 8.1%; 95% CI, −10% to −6.2%), irrespective of the severity of illness, and no signal of excess ODS (7).

The longstanding rationale for slow correction has been preventing ODS. We must ask whether an intense focus on avoiding this rare neurologic complication has promoted systematic undercorrection that increases mortality. The question is no longer whether to treat hyponatremia but how to correct it. A major barrier is reluctance to use hypertonic saline, typically reserved for severe symptomatic cases with many acute care restrictions (8). Hypertonic saline is the most effective treatment for hyponatremia and can be given safely through a peripheral intravenous catheter in an acute care setting if it is dosed and monitored carefully (9). The targeted trial demonstrates that conventional therapies are largely ineffective (2). Greater use of hypertonic saline will likely be necessary to achieve more meaningful corrections of hyponatremia, and further studies with higher targets will be necessary. ■



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Green Dialysis: From Environmental Awareness to Action

By Jennifer Schoonmaker and Prakash Gudsoorkar

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Climate change is no longer a distant environmental concern for nephrologists. Rising temperatures, extreme weather events, water insecurity, and worsening air pollution are already reshaping the epidemiology of kidney diseases. Heat-related acute kidney injury, chronic kidney disease of multifactorial origin, and climate-associated disruptions in access to care are increasingly recognized worldwide. Yet nephrology occupies a paradoxical position: Kidney care is both a victim of climate change and a contributor to it.

Hemodialysis and peritoneal dialysis consume vast quantities of water and energy while generating substantial amounts of plastic waste. Reverse osmosis (RO) systems discard large volumes of treated water, dialysis consumables are predominantly single-use, and much of the resulting waste ultimately enters landfills or incineration streams. As the global population requiring kidney replacement therapy continues to grow, the environmental footprint of dialysis can no longer be considered a peripheral issue.

The recent Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference on Green Dialysis provides a timely and comprehensive framework for addressing this challenge (1). Barraclough and colleagues envision systemic opportunities to reduce environmental harm while maintaining or ideally improving patient outcomes (Figure). Environmental stewardship should not be viewed as competing with patient care but rather as an extension of value-based care that considers clinical outcomes alongside environmental, social, and economic costs.

A major strength of the KDIGO report is its emphasis on strengthening infrastructure and supply chains rather than relying on individual behavioral changes alone (1). Procurement decisions, dialysis machine design, water-treatment systems, packaging materials, and manufacturing practices account for much of the dialysis-related environmental impact. Engaging industry partners to redesign products and develop circular economy approaches will likely yield far greater benefits than asking clinicians or patients to compensate for inefficient systems.

However, implementation will not be straightforward. The report appropriately highlights opportunities to improve RO efficiency and promote reuse of reject water (1), but these recommendations must be balanced against patient safety considerations. Many dialysis facilities intentionally operate below maximal water recovery rates because increasing recovery may increase scaling, membrane fouling, and risks to water quality. Similarly, while RO reject water is often suitable for nonclinical applications, widespread adoption of reuse programs will require regulatory frameworks that currently do not exist in many countries.

The same principle applies to dialysis delivery models. Home dialysis is often promoted as an environmentally preferable modality because it reduces patient transportation and facility-related energy consumption. Home therapies transfer portions of water use, energy consumption, and waste management responsibilities to patients and families. Moreover, uptake remains limited by barriers such as concerns about self-care, insufficient home space, caregiver burden, and lack of support infrastructure. Expanding home dialysis will therefore require investments in patient education, training, reimbursement reform, and ongoing support rather than simply advocating for modality conversion.

Policy remains another critical determinant of success. Telehealth and remote patient monitoring have the potential to reduce transportation-related emissions while improving access to care. However, adoption is often limited by inadequate reimbursement, regulatory barriers, and uneven access to technology. Expanding sustainable nephrology practices will require collaboration among policymakers, payors, and health systems to create incentives that support broader implementation.

Importantly, the KDIGO report also identifies actions that clinicians can implement today (1). Incremental dialysis represents one such opportunity. Evidence increasingly supports individualized dialysis initiation and carefully selected incremental treatment strategies that preserve residual kidney function while reducing resource consumption. Similarly, emerging data suggest that lower dialysate flow rates may maintain dialysis adequacy with substantially reduced water use. Although long-term outcome data are still limited, these approaches demonstrate that personalized care and environmental sustainability can go hand in hand.

Waste reduction offers another immediately actionable target. Improved segregation of hazardous and nonhazardous waste, optimization of consumable use, reduction of unnecessary packaging, and expansion of recycling programs can produce measurable environmental benefits without compromising clinical outcomes. These interventions are often inexpensive and readily achievable, making them attractive starting points for dialysis programs seeking to improve sustainability.

The KDIGO conference delivered a clear message: Sustainability should become part of everyday dialysis care, not remain a niche interest. The environmental impact should be measured alongside traditional quality metrics, considered during procurement decisions, incorporated into research, and recognized by professional societies and regulators as an important component of high-quality kidney care.

Green dialysis is not about compromising care. It is about delivering high-quality treatment while using resources more efficiently; reducing waste; and creating resilient, sustainable systems capable of meeting future health care needs. As climate-related threats to kidney health continue to grow, sustainability must be recognized as a professional and ethical responsibility of the nephrology community. ■

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The authors report no conflicts of interest.

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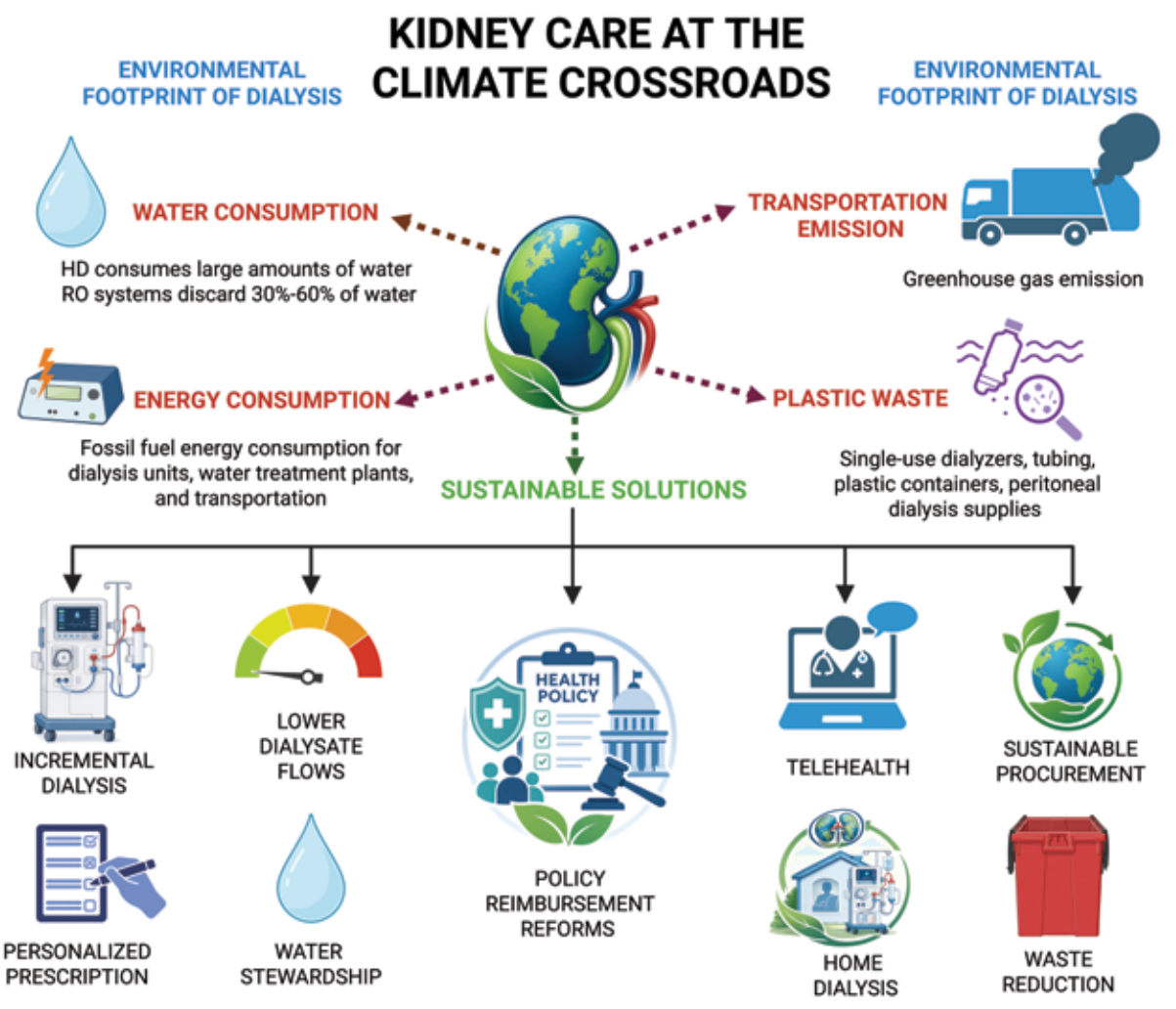
Figure. The environmental footprint of dialysis and opportunities for sustainable kidney care



HD, hemodialysis.

Creatine: Guilty by Association or Innocent Bystander?

By Nayan Arora

https://doi.org/10.62716/kn.004012026

Creatine is no longer a supplement confined to weight and locker rooms. Once used primarily by strength athletes, this niche ergogenic aid has entered mainstream wellness culture, fueled by social media, influencers, and growing interest in its effects on muscle mass and its purported benefits to cognition and healthy aging. As its popularity expands, so too has scrutiny regarding its kidney safety, largely driven by observed elevations in serum creatinine among users.

In the *Journal of Renal Nutrition* (1), Tsiaras and colleagues expand on earlier work (2, 3) by presenting a systematic review and meta-analysis of 20 studies (19 randomized controlled trials and 1 double-blind crossover study) encompassing 786 participants, evaluating the impact of creatine supplementation on kidney function. Three outcomes were assessed: serum creatinine, urea, and estimated glomerular filtration rate (eGFR). Supplementation was primarily creatine monohydrate and ranged from 4 days to 12 months. Notably, most trials used creatinine-based methods for determining eGFR, whereas three used creatinine-independent methods: two [^{51}Cr]-EDTA clearance and one cystatin C-derived eGFR. The principal finding was straightforward: Creatine supplementation produced a significant, albeit modest, increase in serum creatinine by 0.13 mg/dL (95% confidence interval, 0.07–0.18; $p < 0.01$) without corresponding changes in urea or eGFR. The authors concluded that creatine supplementation raises serum creatinine as a metabolic byproduct without evidence of impaired kidney function in healthy adults and recommended alternative markers, such as cystatin C, to assess kidney function in those who use creatine.

The authors should be commended on restricting their analysis to randomized trials, representing a meaningful improvement from prior studies. Additionally, the authors appropriately identified that the systematic review and meta-analysis by Naeini et al. (3) double-counted placebo participants in multi-arm studies, which can bias pooled estimates. Tsiaras et al. (1) address this methodologically, preserving data integrity. The duration-based and physical activity subgroup analyses are clinically useful and reinforce the safety signal across contexts. Evaluating three complementary kidney markers, rather than creatinine alone, provides a more comprehensive assessment of kidney function, and the key finding of a rise in serum creatinine, not accompanied by changes in eGFR or urea, supports the assertion that creatinine generation and kidney function are not synonymous.

However, the study is not without limitations. Creatine is the direct metabolic precursor to creatinine and undergoes spontaneous, nonenzymatic conversion to creatinine at approximately 2% of total body stores per day. Supplementation with 3 g to 20 g of creatine monohydrate predictably increases the total body creatine pool and with it, the daily production of creatinine. Thus, relying on studies that assess the impact of creatine on kidney function, using serum creatinine, is fundamentally flawed. The central limitation to this study is that pooling serum creatinine as a "kidney function" outcome is inherently circular. Creatinine may be the prosecution's star witness in the case against creatine, but it is hardly an impartial one. When the intervention directly influences the biomarker used to assess harm, distinguishing signal from artifact becomes exceedingly difficult.

The eGFR forest plot combines studies using fundamentally different methods: creatinine-based equations, creatinine clearance, cystatin C-derived eGFR, and [^{51}Cr]-EDTA clearance. Pooling these together introduces systematic heterogeneity, reflected by the I^2 statistic (63.71%), an issue acknowledged by the authors. Notably, the two studies using the gold standard of [^{51}Cr]-EDTA clearance (4, 5) both found no effect of creatine on kidney function, even in older adults and those consuming high-protein diets with resistance training. Similarly, the included study using cystatin C demonstrated preservation or improvement in eGFR in creatine users (6). A second, small randomized trial using cystatin C-based eGFR calculations in healthy adults, receiving either creatine or placebo, not included in the analysis, also demonstrated improvement in cystatin C-based eGFR with unchanged creatinine-based eGFR (7).

The duration subgroup analysis is reasonable, albeit arbitrary. Given that loading phases typically last 5 to 7 days, a more physiologically meaningful cutoff may be 1 week or less versus 1 week or more, as used by Naeini et al. (3), who found that the creatine effect was significant during the first week but not during weeks 1 through 12. With only 786 total participants and a mean supplementation duration of approximately 3 weeks, the study cannot adequately address long-term safety. The study only included healthy adults, therefore cannot necessarily be extrapolated to those with pre-existing kidney diseases, a population clearly of interest to the nephrology community. Finally, this study primarily assessed the impact of creatine monohydrate, which is the most-used form of creatine supplementation, although it does not address creatine ethyl ester, which has a greater impact on serum creatinine levels (8).

Ultimately, this study provides the most comprehensive randomized controlled trial–level synthesis to date and aligns well with the broader evidence base. The question is no longer whether creatine predictably increases serum creatinine as a pharmacokinetic consequence of creatine turnover—it does. The question is whether it causes meaningful kidney injury. Based on current randomized evidence, the answer appears to be no. The remaining challenge is to determine whether this conclusion extends to long-term users and vulnerable individuals, such as those with pre-existing chronic kidney disease.

If we accept the principle of "innocent until proven guilty," then creatine has been acquitted, at least on the charge of nephrotoxicity. ■

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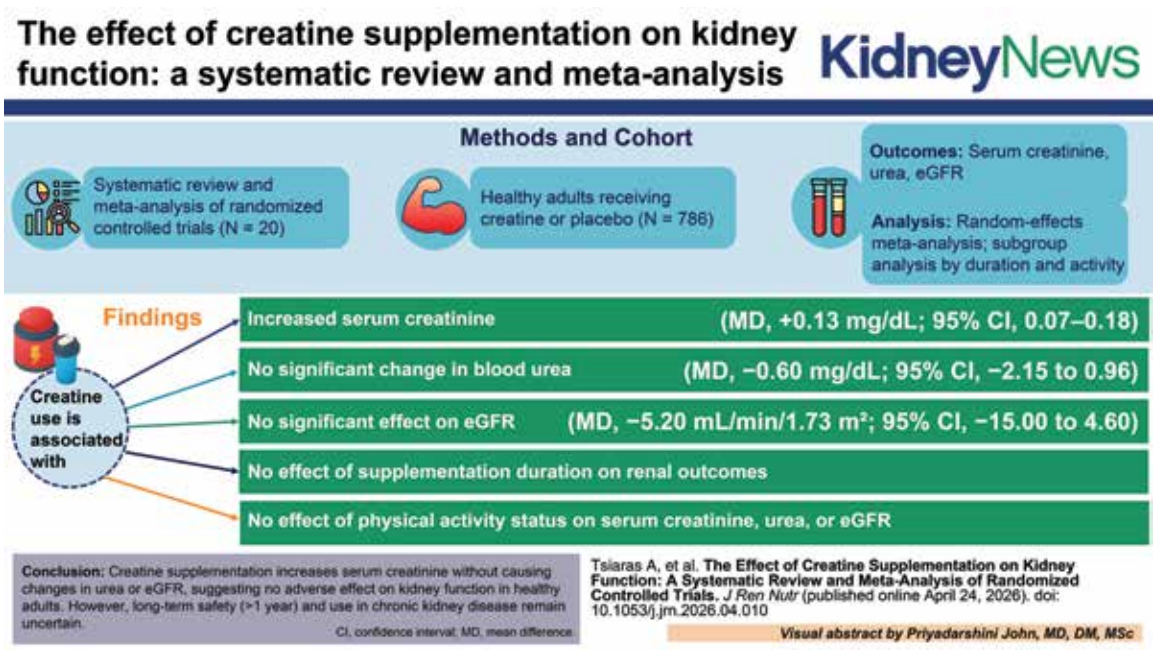
The author reports no conflicts of interest.



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When PUSH Comes to Shove: Pouring Effort Into Prevention

By Anna Zisman

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For a disease as common and costly as nephrolithiasis—affecting approximately 1 in 10 people and prone to recurrence—our preventive tool kit is remarkably thin. At its foundation sits the most universal advice in stone management: Drink more water. The rationale is not faith but rather physical chemistry: Higher urine volume lowers supersaturation and makes crystals less likely to form and grow. Borghi and colleagues confirmed as much 3 decades ago (1). The real question has never been whether hydration works but whether patients can maintain it. The Prevention of Urinary Stones With Hydration (PUSH) trial takes that question head-on (2), and its answer warrants a careful read.

In the largest stone prevention trial to date, 1658 participants were randomized to an intensive behavioral program—financial incentives, a "smart" water bottle to track hydration, health coaching, and reminders—or to guideline-concordant care. Wisely, the investigators chose symptomatic recurrence, not the easier surrogate of urine volume, as the primary endpoint. Over 2 years, events occurred in 19% of the intervention group and 20% of the controls (hazard ratio, 0.96). Urine volume rose more with intervention, but the difference was modest and faded as incentives tapered. Radiographic outcomes and landmark analyses confirmed the null outcome.

The authors must be commended for a well-executed trial. But before we conclude that hydration support does not work, we must ask whether the trial could have detected the effect it sought—and here, the experienced stone clinician must pause. Clinically, we do not advise hydration in isolation. Effective prevention is built on individualization drawn from 24-hour urine results: limiting sodium in the patient with hypercalciuria, alkalinization for the patient with low urine pH, adjusting oxalate and protein intake where appropriate, and pharmacotherapy where necessary (3). PUSH did not test that paradigm. Both arms continued usual care, whereas the intervention simply pushed on the lever (i.e., motivating fluid intake) harder. Optimizing these recommendations in isolation may have too little purchase on overall stone risk to move a clinical endpoint in the short term.

There are two additional points to highlight. First, this was not a study of hydration versus no hydration. Controls received counseling, the same smart bottles, and frequent clinician contact—the stone clinic effect (4)—and the incremental volume difference (600 mL versus 360 mL at 6 months) was narrow and narrowing. Second, as I have previously argued for the Hydrochlorothiazide for Kidney Stone Recurrence Prevention (NOSTONE) trial (5), stone disease recurs slowly; a recent 10- to 12-year cohort found that the benefit of medical therapy became evident at 5 years (6). This is the inherent mismatch between the timescale of stone pathophysiology and the timescale on which randomized clinical trials are funded and executed.

Thus, the findings from PUSH do not justify abandoning emphasis on fluid intake and urinary volume, which remain inexpensive and biologically sound interventions. PUSH tested a motivational hydration program, not the principles of supersaturation. What the findings should temper is our faith that adherence can be purchased with incentives, as the advantage evaporated with cessation of payments. The path forward is longer trials, enrichment by stone type, and attention to urine chemistry with management tailored to the individual patient. We can all drink to that. ■

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The author reports no conflicts of interest.

The real question has never been whether hydration works but whether patients can maintain it.

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Are P-CABs Associated With Nephrotoxicity in People With CKD?

By Namrata Krishnan and Mark A. Perazella

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Potassium-competitive acid blockers (P-CABs) are a new class of rapid onset, potent antisecretory agents that are used to treat gastrointestinal acid-related disorders (1). They act by reversibly and noncovalently binding to the K^+-binding site of the H^+/K^+-ATPase enzyme (proton pump) in the gastric parietal cell and do not require acid activation by food (1). In contrast, proton pump inhibitors (PPIs) are prodrugs (enteric-coated capsules or tablets) that are inactive until they reach the acidic gastric environment, where they subsequently become activated, covalently bind to cysteine residues on the proton pumps, and suppress acid production (2) (Figure). P-CABs have been shown to be more effective than PPIs for erosive esophagitis and other acid-related disorders (3, 4). Although there are a number of PPIs clinically available, the only US Food and Drug Administration-approved P-CAB is vonoprazan.

The pharmacology of these two drug classes explains the observed clinical pharmacodynamic differences (Table). P-CABs are rapidly absorbed and have a high oral bioavailability with a peak plasma concentration (T_{max}), reached within 1 to 3 hours of ingestion (1, 4, 5). They undergo metabolism by the hepatic cytochrome P450 pathway, primarily CYP3A4. They generally have a longer plasma half-life compared with PPIs. Following hepatic metabolism, P-CABs are eliminated mainly by the kidney and in feces (1, 4, 5).

PPIs are acid labile and are absorbed in the small intestine and reach stomach parietal cells through blood delivery (2, 5, 6). Most have excellent oral bioavailability and are highly protein bound. The T_{max} ranges from 1 to 5 hours, depending on the formulation used and/or meal ingested (2, 5). These drugs are primarily metabolized by the cytochrome P450 CYP2C19 and CYP3A4 enzymes, and genotypic variation can affect their efficacy in individuals (2, 5, 6). For example, CYP2C19 genetic polymorphisms can impact the drug's efficacy. PPIs have a relatively short half-life of approximately 1 to 2 hours but inhibit acid production for more than 24 hours due to irreversible proton pump binding. PPI metabolites are excreted mainly via urine (~80%) and in feces (2, 5, 6).

Table. Pharmacodynamic differences between PPIs and P-CABs

PPIs	P-CABs
Irreversible, covalent binding to the H^+/K^+-ATPase pump	Reversible and competitive K^+ site blocker on the H^+/K^+-ATPase pump
Prodrug; needs conversion to active form	Direct action on pump
Slow onset of action over 3 to 5 days	Rapid onset of action within hours
Good day-time control but night-time acid breakthrough	Longer and stronger acid suppression
Best taken on an empty stomach	Can be taken anytime of the day
Interacts with CYP2C19; therefore, genetic variation	Minimal CYP2C19 effect; not affected by genetic polymorphism

Therefore, P-CABs appear to have advantages over PPIs—faster onset of effect, longer duration of acid inhibition, flexible oral administration, and less individual variation (1, 3, 4). These benefits come at a higher drug cost. An unanswered and important question is how P-CABs compare with PPIs in regard to nephrotoxicity. Renal complications described with PPIs include acute tubulointerstitial nephritis, hypomagnesemia from gastrointestinal magnesium loss, and chronic kidney disease (CKD) due to a currently unclear mechanism (7, 8).

A recent *Kidney International Reports* publication evaluated the association of P-CAB and PPI use in people with CKD and kidney function deterioration (9). Using Korean National Health Insurance data, people with CKD (N = 34,077), who were newly initiating P-CABs (N = 4107) or PPIs (N = 16,428) between 2019 and 2022, were identified. Among the cohort, 60% were older than 65 years, and slightly more were male. The primary outcome was risk of composite kidney replacement therapy initiation, favoring P-CAB use (37% lower risk with P-CABs; hazard ratio, 0.63 [95% confidence interval, 0.45–0.88]). This is the largest study to date comparing renal outcomes between the two classes of drugs. Additionally, the study design used a target trial emulation approach, allowing the researchers to emulate a randomized trial, establish causality, and limit potential biases. This study suggests superior safety of P-CABs with regard to CKD progression compared with PPIs. Given the emerging kidney safety data, P-CABs may represent a reasonable alternative to PPIs in people with CKD requiring long-term acid suppression. ■

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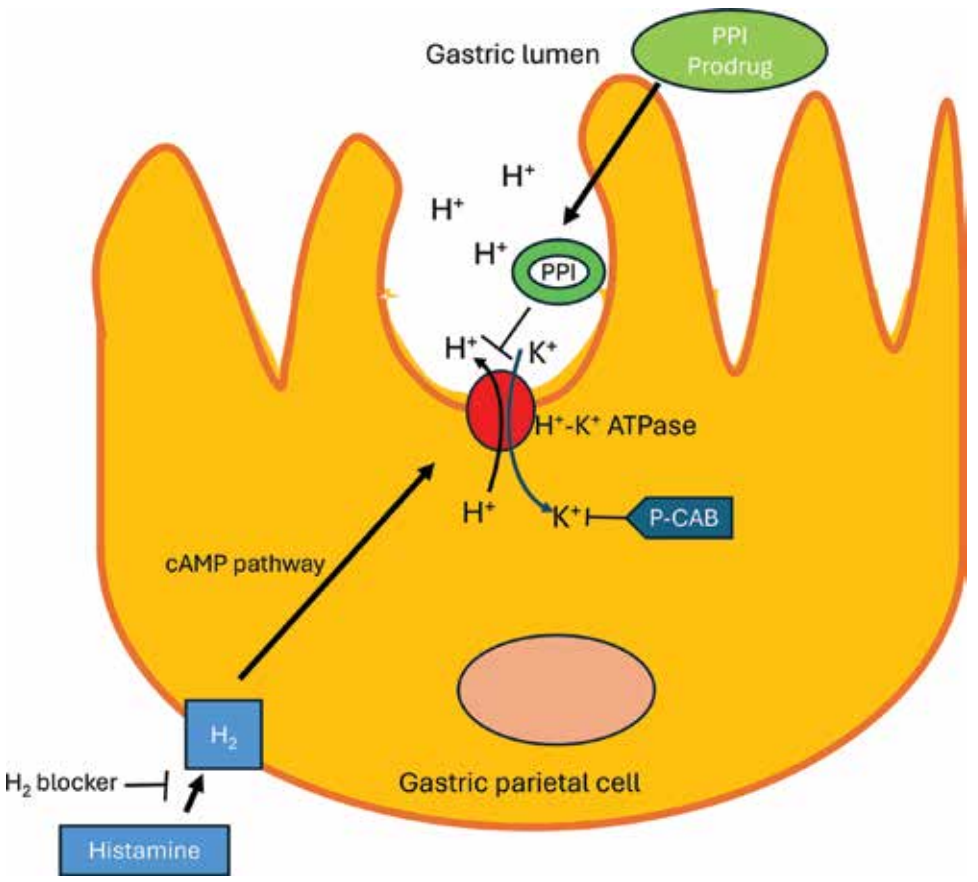
The authors report no conflicts of interest.

Figure. Mechanism of action of PPIs and P-CABs



P-CABs act by reversibly and competitively binding to the K^+ site on the H^+/K^+-ATPase enzyme and do not require acid activation by food. In contrast, PPIs are prodrugs (enteric-coated capsules or tablets) that are inactive until they reach the acidic gastric environment, where they subsequently become activated. The active moiety binds covalently to cysteine residues of the proton pumps and inhibits acid production.
cAMP, cyclic adenosine monophosphate.

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6-Q067

Sparsentan in FSGS: A New Era or an Unfinished Story?

By Zahoor Ahmed

https://doi.org/10.62716/kn.003842026

The recent US Food and Drug Administration (FDA) approval of sparsentan (Filspari) for focal segmental glomerulosclerosis (FSGS) marks a pivotal moment in nephrology, offering, for the first time, a targeted therapy that moves beyond conventional renin-angiotensin-aldosterone system (RAAS) inhibition (1). Yet, as with many advances in glomerular disease, this milestone brings both promise and important unanswered questions.

Sparsentan is a first-in-class, single-molecule dual antagonist of the endothelin type A and angiotensin II type 1 receptors (2). This dual blockade addresses two central and synergistic pathways implicated in podocyte injury: glomerular hypertension and proteinuria (2, 3). Preclinical studies have demonstrated that sparsentan improves glomerular hemodynamics, preserves podocyte integrity, and attenuates inflammatory and fibrotic signaling that exceed those observed with RAAS inhibition alone (4).

The clinical foundation for sparsentan's approval rests on two key trials. In the phase 2 DUET study (NCT01613118), sparsentan achieved a significantly greater reduction in proteinuria compared with irbesartan over 8 weeks (45% versus 19%; p = 0.006), along with higher rates of partial remission of proteinuria (28% versus 9%; p = 0.04) (5). These findings were reinforced in the phase 3 DUPLEX trial (NCT03493685), in which sparsentan demonstrated superior antiproteinuric efficacy at 36 weeks, with higher rates of both partial and complete remission of proteinuria. Importantly, these benefits were observed across diverse patient subgroups, including those with genetic forms of FSGS, traditionally considered treatment-resistant (2).

Despite these encouraging results, the story becomes more nuanced when examining long-term kidney outcomes. The DUPLEX trial did not demonstrate a statistically significant difference in the estimated glomerular filtration rate (eGFR) slope at 108 weeks between sparsentan and irbesartan (2) (Figure). This discordance between robust proteinuria reduction and the absence of clear improvement in the serum creatinine trajectory underscores a persistent challenge in nephrology. Several factors may explain this paradox. FSGS is a heterogeneous disease with variable underlying mechanisms ranging from genetic mutations to immune-mediated injury, potentially reducing treatment effects (2, 3). Additionally, the initial hemodynamic dip in the eGFR associated with dual blockade, coupled with a stronger-than-expected response in the control arm, may have obscured long-term differences. It is also plausible that longer follow-up is required for the benefits of sustained proteinuria reduction to translate into measurable preservation of kidney function (2).

From a safety perspective, sparsentan has demonstrated a profile comparable with irbesartan, with no major increase in serious adverse events. Although hypotension and hyperkalemia were more frequent, these were generally manageable and did not result in increased discontinuation rates (5).

The FDA label, however, introduces an important clinical nuance: The indication is currently limited to patients without nephrotic syndrome, reflecting subgroup analyses from DUPLEX that did not demonstrate clear benefit in nephrotic-range disease. This distinction highlights the importance of patient selection and reinforces that sparsentan is not a universal solution for all FSGS phenotypes (1).

In conclusion, sparsentan represents a significant therapeutic advance in FSGS, redefining the role of targeted dual-pathway inhibition in glomerular kidney disease. However, whether this translates into durable kidney protection remains uncertain. Thus, sparsentan is both a breakthrough and a reminder in glomerular disease that reducing proteinuria is essential, but it may not be sufficient. ■

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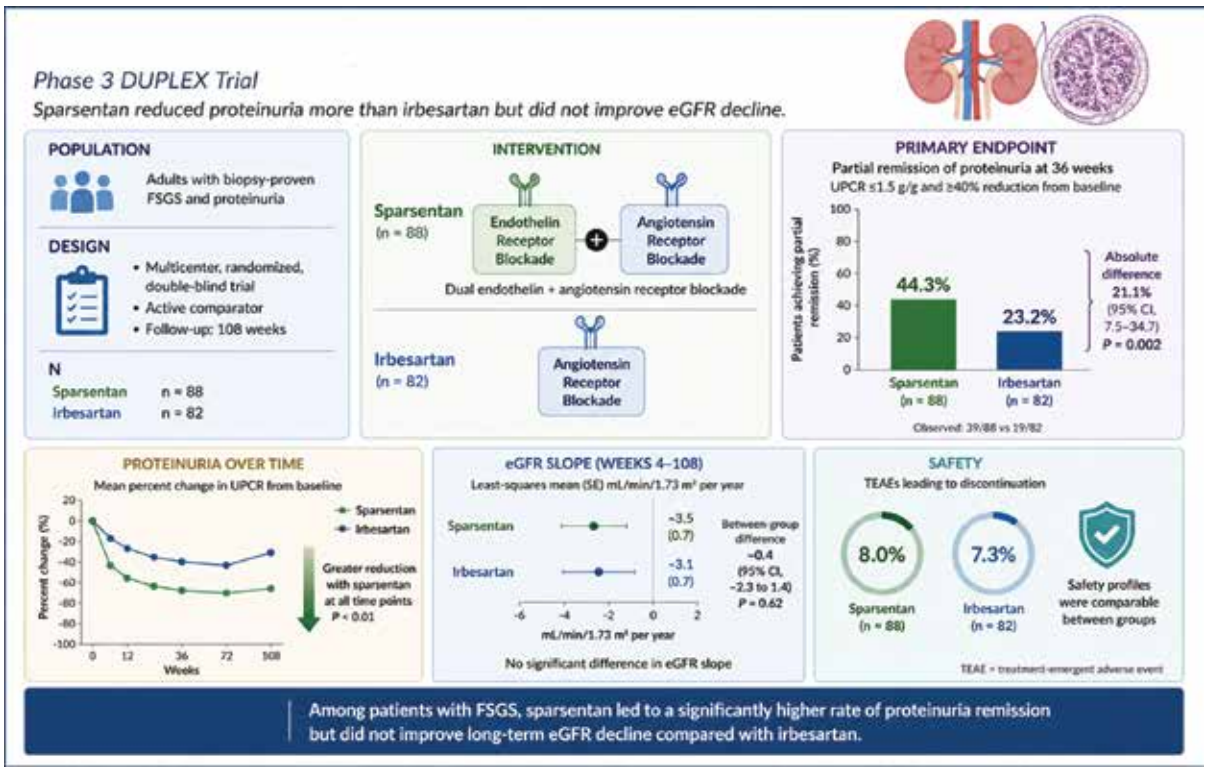
The author reports no conflicts of interest.

Figure. Sparsentan versus irbesartan in FSGS



CI, confidence interval; SE, standard error; UPCR, urine protein-to-creatinine ratio.

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Peritoneal Dialysis Connection Technology Should Be Uniform

By Katherine Kwon and Osama El Shamy

https://doi.org/10.62716/kn.003812026

A clinical scenario with potential for patient harm plays out daily at hospitals across the country: A patient on peritoneal dialysis (PD) is admitted to a hospital that does not stock their brand of supplies. The floor staff, who have limited experience performing PD exchanges, do not recognize the need for an adapter set and attempt a connection between disparate systems, creating a risk of touch contamination. These near-misses are not captured by any safety monitoring system. We both have seen this exact scenario in our clinical practice.

Vantive (formerly Baxter) and Fresenius are the two largest manufacturers of PD supplies in the United States. Each uses a proprietary PD connector system that is incompatible with the other. Because PD remains a minority modality in the United States, most hospitals make the business decision to stock only one system. Hospital admission is not the only scenario in which a patient may be limited to supplies from an incompatible system. In September 2024, Hurricane Helene significantly impacted Baxter's North Cove manufacturing site, creating shortages for patients using Baxter's PD supplies. Some dialysis units turned to Fresenius for their PD supplies during that time, despite the known incompatibility of their connector systems. The Centers for Disease Control and Prevention's Health Alert Network specifically identified use of unfamiliar supplies as a potential source of patient harm during the shortage (1). Although lack of interoperability creates this potential risk, neither company has a market incentive to change to a uniform connector technology, and to date, no regulatory body has compelled it.

Commercially available adapter sets do allow patients to use dialysate bags from the other company. However, this is a workaround solution that adds complexity to the PD process and introduces opportunities for technique errors and subsequent patient harm. In the inpatient setting, staff need to recognize where incompatible catheters are in use and seek out the adapter set. Adding the adapter set to the patient's catheter is an additional clinical competency that can be a struggle to maintain in a low-volume environment. In one published incident, a patient's transfer set was changed during admission due to hospital formulary and not changed back at discharge. The patient subsequently connected an incompatible bag from their home supplies and experienced a touch contamination (2).

Potentially harmful events from incompatible supplies may not be captured by clinical safety reporting structures, but they are important nonetheless. The late safety expert James Reason, PhD, said that "High reliability organizations. . . are constantly preoccupied with the possibility of failure" (3). A single universal standard would reduce complexity and eliminate potential harms from incompatible connections before they occur. Touch contamination is a common contributor to peritonitis development, the leading cause of PD discontinuation. In fact, the market is seeking to address the problem; Simergent's Archimedes APD [automated PD] cycler introduces a third style of connector, specifically designed to reduce touch contamination, which can safely connect to Vantive supplies and requires an adapter to connect with Fresenius supplies (4). However, adding a third style of connector increases complexity and introduces another vulnerability into the supply chain.

There is precedent for compelling design changes in connection technology to enhance patient safety. When case reports of patient deaths emerged from the misconnection of enteral devices with tracheostomy and other devices, a multidisciplinary group including clinicians, industry, and regulatory bodies developed the ENFit standard for enteral tubes (5). This was designed to ensure that enteral devices were incompatible with other devices, preventing inappropriate connections. In the PD context, we are advocating for improved compatibility but critically, within the limited use case of intraperitoneal infusion and drainage of dialysate.

A similar multidisciplinary approach could devise a voluntary standard. There are many potential avenues to achieve and track this:

- Leaders from ASN or the International Society for Peritoneal Dialysis could convene the dialysis supply manufacturers, patient advocates, and End-Stage Renal Disease (ESRD) Networks to agree on a single connector design.
- ESRD Networks could establish a near-miss registry to better gauge patient risk with the current fragmented systems.
- The US Food and Drug Administration's Center for Devices and Radiological Health could also engage the rulemaking process to require a universal PD connector standard.
- A requirement for truly interoperable PD supplies could be included in the Conditions for Coverage for dialysis units, set by the Centers for Medicare & Medicaid Services.

The Figure illustrates the potential stakeholders that could participate in creating a voluntary industry standard. In the case of the ENFit standard, a nonprofit organization was created as a convener to guide the development of the standards (5). Expanding the initiative to the international community would require participants from other countries.

This is an opportunity to act preemptively. Using previous experiences addressing safety through connector engineering, we can come together to make PD incrementally safer and easier for patients and staff. The vulnerable population of patients using PD can be better protected from supply-chain disruptions or formulary limitations. Universal connector technology is one way of advancing safer PD. Our patients deserve our advocacy. ■

Katherine Kwon, MD, FASN, is a nephrologist in private practice in St. Joseph, MI, and is the secretary-treasurer of the Renal Physicians Association. Osama El Shamy, MD, FASN, is a nephrologist at the Perelman School of Medicine at the University of Pennsylvania, Philadelphia.

Dr. Kwon reports having joint venture home dialysis units with Fresenius Kidney Care and Premier Dialysis. Dr. El Shamy reports having a speaker agreement with Vantive and serving on the medical advisory board for Light Line Medical Inc. and as a member of the International Society for Peritoneal Dialysis (ISPD)–North America Chapter council, as well as the North America representative at the ISPD council at-large.

The opinions reflected in this article are solely those of the authors.

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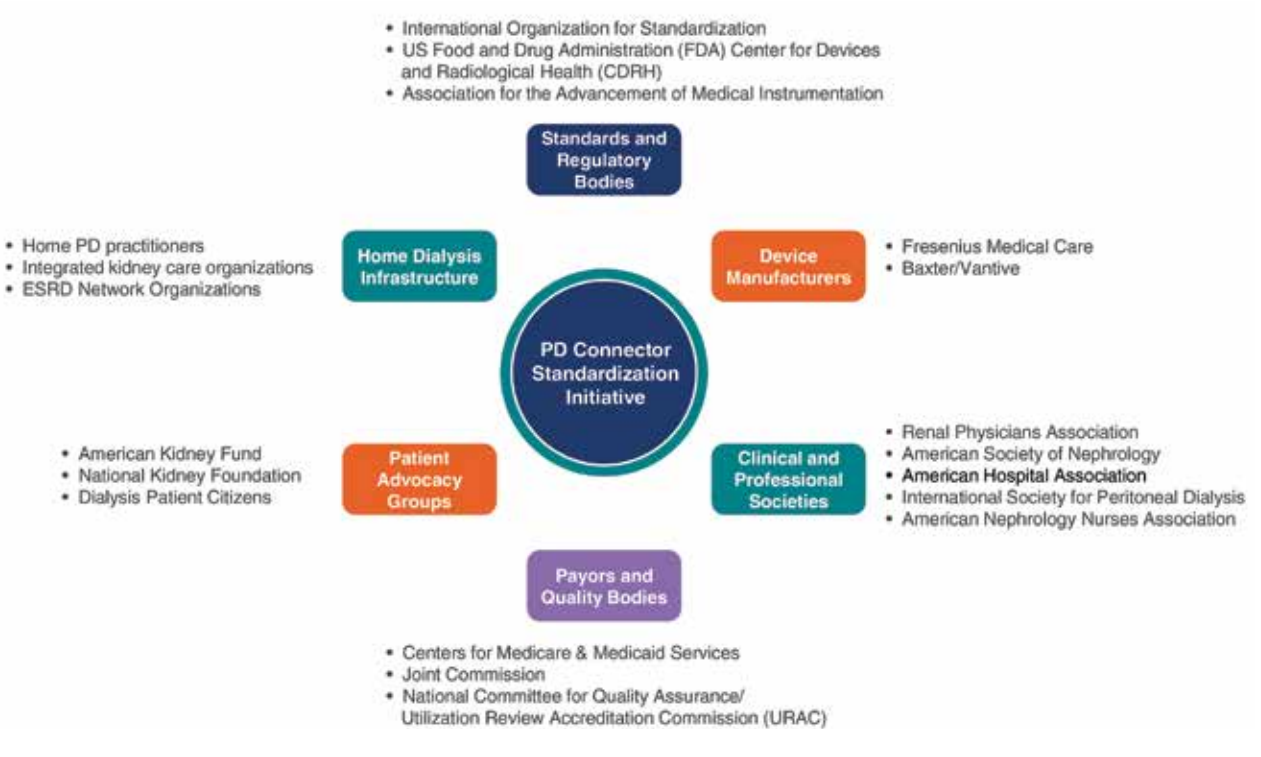
Figure. Proposed multidisciplinary group to explore common PD connection technology



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Nephrocardiologic Explanation of the Findings of the TRACK Trial

By Parta Hatamizadeh

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The kidney and cardiovascular systems are profoundly interdependent. Indeed, according to the second principle of nephrocardiology, any patient with a "nephrology-related condition" (NRC) has some type and severity of one or more cardiovascular disease (CVD), and any patient with a CVD has some type and severity of one or more NRC, whether overt or covert, diagnosed or undiagnosed (1). However, consistent with the first principle of nephrocardiology, it is crucial to remember that both NRCs and CVDs encompass a diverse group of conditions with various pathophysiologic mechanisms, which result in dissimilar diagnostic, therapeutic, and prognostic properties. Therefore, a holistic view of the interaction between the two fields of nephrology and cardiovascular medicine, with all the "elements," "aspects," and "multidirectional interactions," as described in the fundamentals of the emerging field of nephrocardiology (2, 3), is necessary to formulate correct diagnostic and management plans.

Results of the Treatment of Cardiovascular Disease With Low Dose Rivaroxaban in Advanced Chronic Kidney Disease (TRACK) trial (4) are a testament to this important fact. In this randomized trial, adults with stage 4 or 5 chronic kidney disease (CKD), who were considered "at increased risk of cardiovascular events," were randomly assigned to receive either rivaroxaban or placebo. Primary efficacy outcomes were cardiovascular death, nonfatal myocardial infarction, stroke, or a peripheral artery disease event. The primary safety outcome was major bleeding. The study was terminated prematurely due to lack of efficacy and increased safety concerns in the rivaroxaban arm.

Findings of the TRACK study appeared to contrast with previous studies of rivaroxaban on general patient populations with predominantly atherosclerotic vascular diseases, which demonstrated positive results (5–7). The discrepancy between the findings can be explained by two important topics of nephrocardiology. The first is the variety of cardiovascular conditions that are associated with CKD and the importance of distinguishing them from one another. The inclusion criteria as well as the outcome variables of the TRACK trial, such as "cardiovascular events" and "cardiovascular death," are nonspecific. In the earlier stages of CKD, atherosclerotic lesions are a major part of cardiovascular involvement; in advanced stages of CKD (the patient population in TRACK), however, cardiac structural changes, including left ventricular hypertrophy, arterial calcification, valvular calcification, and conduction abnormalities, predominate (8). Therefore, in contrast to prior studies, TRACK participants' primary cardiovascular involvement was not atherosclerotic disease.

Second, according to the second "aspect" of the "pathophysiology element" of nephrocardiology, a cardiovascular clinical phenotype can have different pathophysiologic mechanisms in the presence versus the absence of an NRC (2, 3). Contrary to the general population, in whom atherosclerotic lesions of the major epicardial coronary arteries are the primary pathophysiologic mechanism of ischemic heart disease, in advanced CKD, several other mechanisms also contribute to ischemic heart disease, including medial arterial calcification, microvascular disease, and anemia. Because these mechanisms do not cause susceptibility to thromboembolic events as much as atherosclerotic plaques do, anticoagulation therapy with rivaroxaban or any other anticoagulant medication is less likely to be relevant.

The same aspect of the pathophysiology element of nephrocardiology applies to the aforementioned nonspecific outcome variables of the TRACK study. They are less relevant to thromboembolic events in people with advanced CKD compared with the general patient population in prior studies; hence, rivaroxaban is less efficient at preventing them.

In designing the nephrocardiologic clinical trials of people with advanced CKD, it is imperative to consider the differences in the pathophysiology of the clinical phenotype in question, in people with and without advanced CKD, and to plan the intervention accordingly. Moreover, it is vital to be specific about inclusion and exclusion criteria, as well as the outcome variables in such studies. A common and negatively impactful imperfection in the medical literature and study designs is the confusion between cardiovascular events and "ischemic cardiovascular events." Unfortunately, those two concepts are frequently used interchangeably, and they are not the same. As noted, the cardiovascular complications of advanced CKD are diverse and not limited to ischemic heart disease, which itself is not limited to coronary artery atherosclerosis. Therefore, the findings of TRACK underscore the importance of the "principles" and "pillars" of "nephrocardiology" and how they can help handle the complexity of this field in clinical practice and research design. ■

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The author reports no conflicts of interest.

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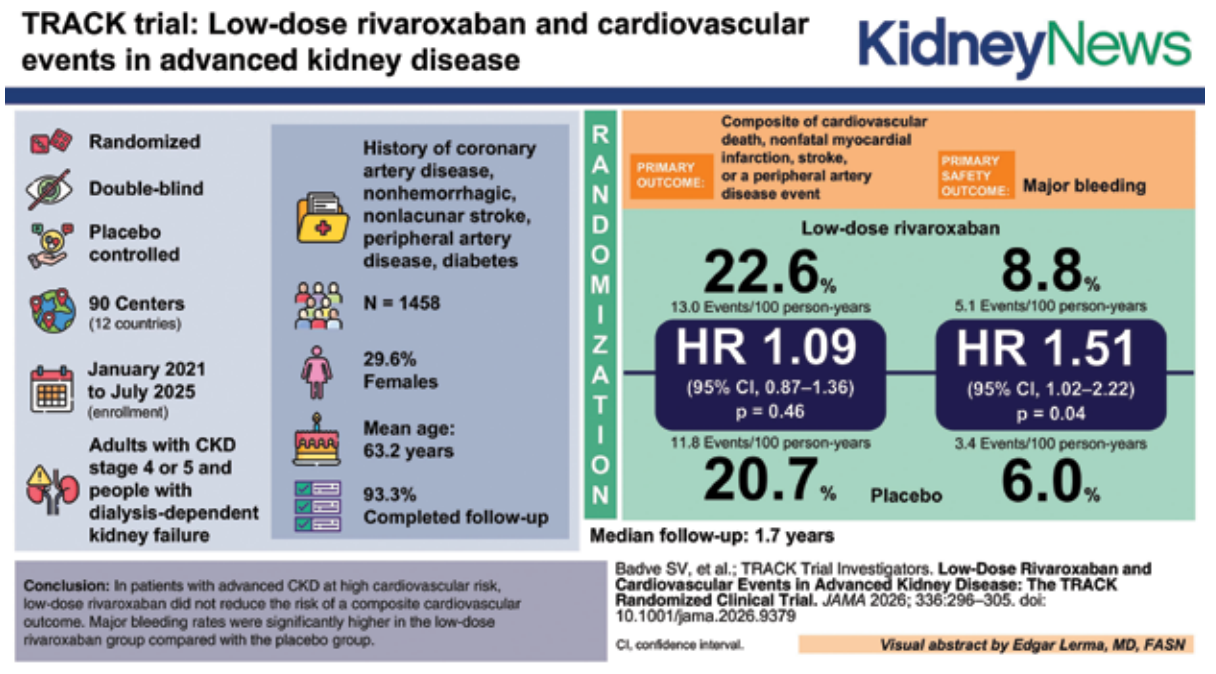

ASN Advocacy Works to Strengthen Quality Incentives, Remove Barriers for Living Donors, and Sustain Reliable Care for Transplant Patients

By Paul Renner

https://doi.org/10.62716/kn.004712026

ASN Quality Committee meets to address regulatory concerns affecting kidney care

On July 13, members of the ASN Quality Committee met at the ASN headquarters in Washington, DC, for the committee's annual in-person meeting. Each summer, the Quality Committee convenes to review and discuss ASN's responses to the Centers for Medicare & Medicaid Services' (CMS') major proposed rules that shape kidney care. This year, the two proposed rules include: 1) the End-Stage Renal Disease Prospective Payment System (ESRD PPS) and Quality Incentive Program (QIP) and 2) the Medicare Physician Fee Schedule (PFS).

These rules are vast in scope, affecting physician payment and clinical practice across the full spectrum of kidney care. The committee meeting included rigorous discussion of how effective certain quality metrics could be for improving care, what side-effects changes might bring, and how much proposed changes to payment methodology may impact kidney care. Understanding these regulations and their implications was an important first step in shaping ASN's response.

In this year's ESRD PPS proposed rule (1), CMS proposes increasing the dialysis base payment rate to $299.55, reflecting a 1.1% increase compared with the calendar year 2026 base rate (1). CMS also proposes changes to the post-Transitional Drug Add-On Payment Adjustment calculation methodology, expansion and restructuring of the Low-Volume Payment Adjustment, an increase to the home and self-dialysis training add-on payment, and two permanent changes to the pediatric ESRD payment. The rule also includes an extensive set of Requests for Information seeking stakeholder engagement to shape these policies.

This year's Medicare PFS proposed rule (2) would reduce physician payment conversion factors to $33.17 for clinicians participating in Advanced Alternative Payment Models (APMs) and $32.84 for non-APM clinicians, representing decreases of 1.19% and 1.68%, respectively (2). Although the rule includes the statutory payment updates of 0.75% for APM clinicians and 0.25% for non-APM clinicians, those increases are outweighed by the expiration of the temporary 2.5% physician payment increase enacted by Congress for 2026. Separately, CMS estimates a 0% specialty-specific impact for nephrology based on the proposed relative value unit and policy changes; this estimate does not reflect the effect of the reduced conversion factors.

Additional highlights from the proposed PFS include:

- **Proposed G2211 replacement.** CMS proposes replacing add-on code G2211 with two new modifiers, which would offer a 16% payment increase for eligible office visits and a 32% increase for clinicians in the Medicare Shared Savings Program or the upcoming Long-Term Enhanced Accountable Care Organizations Design Model.
- **Proposed remote care changes.** The rule proposes tightening standards and requirements for remote patient monitoring and remote therapeutic monitoring.
- **Proposed Merit-Based Incentive Payment System (MIPS) transition.** CMS proposes sunsetting traditional MIPS reporting beginning in performance year 2029 to transition clinicians toward MIPS Value Pathways.

ASN will continue working with the Quality Committee and other volunteer leaders to develop comments on both proposed rules. The ESRD PPS and QIP comments were due August 24, and Medicare PFS comments are due September 14.

From legislation to regulation: ASN collaborates in HOLD Act implementation

As the ASN Quality Committee worked to address regulations affecting medical practice and reimbursement, ASN has additionally focused on supporting the effective implementation of the Honor Our Living Donors (HOLD) Act. The HOLD Act, which began as a bipartisan bill in the House of Representatives, was designed to remove financial barriers that many living donors face in the process of donating life-saving organs.

The bill, which ASN supported, was signed into law on February 3, and in response, the Health Resources and Services Administration (HRSA) proposed modifications to the eligibility guidelines within the existing framework of the Living Organ Donation Reimbursement Program (LODRP) (3). ASN provided comments to HRSA to celebrate this advancement and to help ensure that the details of the regulation effectively execute the new law (4).

Specifically, ASN emphasized finalizing the change to use donor income for reimbursement rather than recipient income and the need to ensure clear thresholds for reimbursement eligibility. ASN recommends providing clear coverage up to $6000 for donors with household incomes that are at or below 500% of the US Department of Health and Human Services Poverty Guidelines, eliminating the proposed priority categories. ASN additionally recommends including nephrologists, dialysis organizations, and patient organizations in communications about changes to LODRP.

ASN urges CMS to clarify work exemptions and include patients undergoing transplant

In comments to CMS, ASN called for the clear exemption of Medicaid community engagement requirements for individuals waiting for an organ transplant or for those who recently underwent a transplant (5). These patients frequently experience complicated and high-risk conditions, for which interruptions in Medicaid coverage could disrupt life-saving therapies or lead to the removal of patients from transplant consideration.

CMS had already recognized the need to provide exemptions to work requirements under certain circumstances, such as exempting patients who are medically frail or those who have complicated and high-stakes medical needs. These considerations align with the clinical state of patients undergoing transplant. ASN also intends to continue collaborating with the kidney community to advocate that any such exemptions from CMS are granted to all people living with kidney failure. In addition to protecting patients, clarifying exemptions could reduce confusion among states and decrease administrative burden. For all of these reasons, ASN urged CMS to expressly include organ transplant waitlist and recent organ recipient statuses as qualifying bases for exemptions. ■

Paul Renner is with the policy team at ASN.

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AI in Kidney Care Is Ready. Is Reimbursement?

By Charat Thongprayoon, Ambarish Athavale, and Wisit Cheungpasitporn

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Artificial intelligence (AI) has rapidly evolved from an emerging technology into a practical clinical tool (1). In nephrology, AI is being developed and applied across nearly every aspect of kidney care, including predicting chronic kidney disease progression (2), identifying people at risk for acute kidney injury, optimizing dialysis care, improving kidney transplantation, assisting with digital pathology, and supporting clinical documentation through generative AI (1). Substantial evidence now supports AI's ability to perform many predictive and decision-support tasks with high accuracy, and several AI-enabled tools have entered clinical practice across health care, with increasing applications in nephrology (3).

Yet widespread adoption has remained limited (4). Increasingly, the principal barrier is no longer algorithm development but implementation, particularly sustainable economic incentives. Successful implementation requires integration into clinical workflows, clinician trust, regulatory oversight, and reimbursement. Without a viable economic model, even transformative technologies seldom achieve routine clinical use (1, 2, 4, 5).

The reimbursement gap

Implementing AI requires substantial investment (6). Health systems must fund software, electronic health record integration, cybersecurity, governance, model maintenance, and clinician training (6). Although these investments may ultimately improve efficiency and patient outcomes, they impose considerable upfront costs (6). For many AI applications, the practical question is no longer whether they can work, but who will pay for them (7).

Encouragingly, reimbursement pathways are beginning to emerge. New *Current Procedural Terminology* codes and evolving payment policies reflect increasing recognition that selected AI-supported clinical services are beginning to receive reimbursement (6, 7). Although these mechanisms remain in their early stages and will continue to evolve, they signal an important shift toward integrating AI into routine clinical care.

Beyond reimbursement: The role of value-based care

Dedicated reimbursement is only part of the equation. The ongoing transition from fee-for-service to value-based care may ultimately prove even more important. In addition to improving risk identification and predicting disease progression, AI has also demonstrated the ability to enhance transplant surveillance, reduce preventable hospitalizations, and support more efficient care coordination (1, 2, 5). If these capabilities improve outcomes while lowering costs, AI may create value even without direct reimbursement.

Medicare's Advancing Chronic Care With Effective, Scalable Solutions (ACCESS) model (8) illustrates this opportunity. Although ACCESS does not directly reimburse AI technologies, it rewards improvements in quality and total cost of care. Health systems that leverage AI to prevent complications, reduce hospitalizations, and improve quality metrics may realize financial returns through value-based payment.

A convergence of opportunity

Recent policy developments suggest that nephrology is approaching an important inflection point. In July, the Centers for Medicare & Medicaid Services proposed recognizing "Software as a Medical Service" as a distinct category under the Hospital Outpatient Prospective Payment System, including a new status indicator for qualifying algorithm-driven services (9). Although the proposal remains preliminary, it represents an important step toward a more standardized Medicare reimbursement pathway for clinical AI. As AI becomes increasingly clinically useful, regulatory frameworks are maturing, reimbursement pathways are emerging, and value-based payment models are beginning to reward technologies that improve outcomes rather than increase service volume (6, 7).

The next generation of successful AI tools will not necessarily be those with the highest predictive performance but those that integrate seamlessly into clinical workflows, reduce clinician burden, improve patient outcomes, and demonstrate measurable value to health care systems. For nephrologists, the future of AI will depend not only on advances in model development but also on implementation science, reimbursement policy, and rigorous clinical evaluation. AI in kidney care may be ready. The question is whether our payment systems are ready as well. ■

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The authors report no conflicts of interest.

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Ditching the Stick: A New Era for Venous Blood Gas Conversions

By Biff F. Palmer

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When rounding on the wards and guiding medical students or junior faculty through the nuances of acid-base physiology, the arterial blood gas (ABG) has long been our undisputed gold standard. It gives us the precise pH, partial pressure of carbon dioxide (pCO_2), and bicarbonate (HCO_3^-) values we need. However, obtaining that arterial sample through a radial or femoral puncture is notoriously cumbersome and technically challenging and carries genuine risks for the patient, including hematomas, thrombosis, and infection.

Because of these limitations, many of us have increasingly leaned on the venous blood gas (VBG). It is easier, faster, and much kinder to the patient. But interpreting it usually involves a bit of clinical hand-waving. For years, the standard rule of thumb has been to simply subtract 5 mm Hg from the venous pCO_2 ($vpCO_2$) to estimate the arterial pCO_2. We also broadly accept the typical baseline differences: The venous pH is usually about 0.05 units lower than the arterial pH, whereas the venous HCO_3^- is slightly higher, typically by about 2 to 3 mEq/L. This difference in HCO_3^- concentration makes perfect physiologic sense; CO_2 produced peripherally is carried from the tissues to the lungs primarily in the form of HCO_3^- (1).

A recent article by Batlle et al. has finally brought rigorous math to our daily bedside estimates (2). To ensure robust statistical reliability, the research team used an unprecedentedly massive dataset of 5419 concurrent ABG and VBG samples to map the exact relationship between venous and arterial values. Their data prove that the old rule of a static 5-mm Hg subtraction for pCO_2 is fundamentally flawed, as the gap between venous and arterial pCO_2 widens significantly at higher values. Instead, they offer precision conversions. For instance, arterial pH estimated from venous samples achieved a remarkable 95% limit of agreement ranging from just –0.05 to +0.04 pH units.

The beauty of this research lies in its immediate clinical utility. By calculating estimated arterial pCO_2 ($epCO_2$) values using their derived formulas, such as $epCO_2$ = (0.9224 × $vpCO_2$) – 3.642, we can meet acceptable clinical expectations without subjecting patients to unnecessary arterial punctures. The authors even replicated how blood gas laboratories report HCO_3^-, calculating an estimated arterial HCO_3^- by plugging the derived arterial pH and pCO_2 back into the Henderson-Hasselbalch equation. As the authors elegantly conclude, "The data show that the VBG can be transformed with reasonable confidence intervals to arrive at a corresponding ABG."

For those who prefer to avoid complex regression algebra during a busy shift, the lead author has conveniently packaged these data into a dedicated mobile app (https://play.google.com/store/apps/details?id=com.mihapp.blood_gas_calc). You simply plug in the venous numbers, and it calculates the highly reliable arterial estimates.

This article is a major win for both patient comfort and diagnostic accuracy. It updates our everyday clinical tool kit and provides valuable, evidence-based material for drafting the next batch of nephrology examination questions and clinical case studies.

Biff F. Palmer, MD, FASN, is a professor in the Departments of Education and Internal Medicine at the Texas Health Science Center, El Paso, and an adjunct professor with The University of Texas Southwestern Medical Center, Dallas, where he also serves as the course director of the Kidney-Genitourinary block.

The author reports no conflicts of interest.

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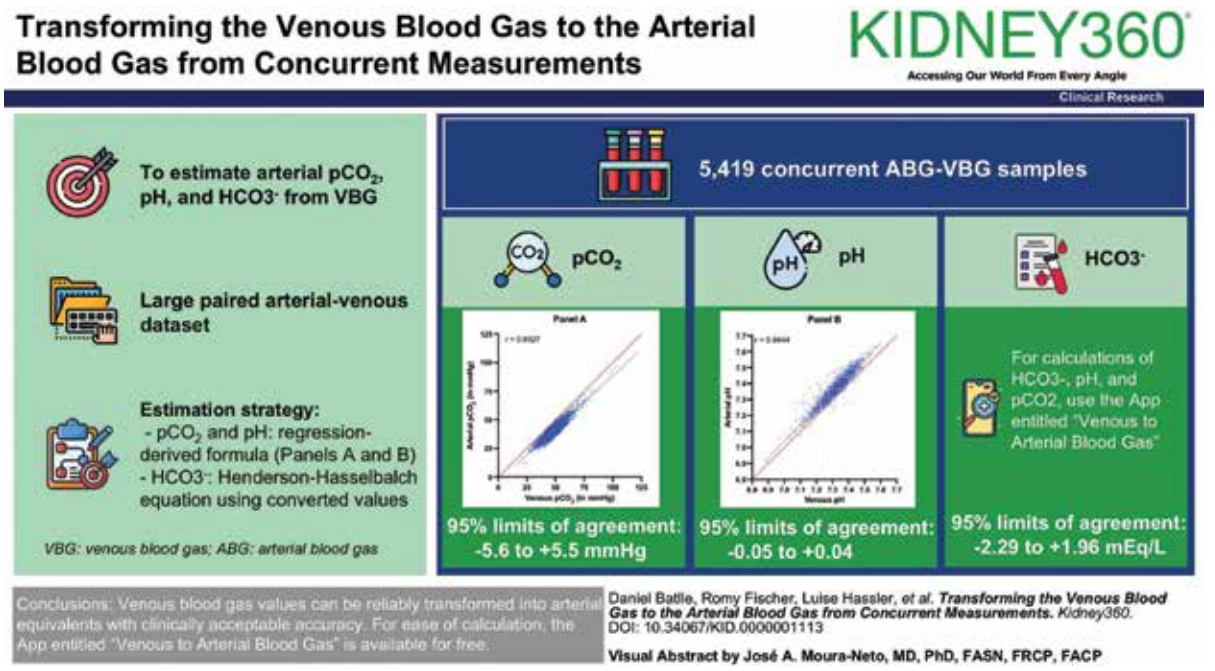

From Prediction to Precision: Can We Reliably Quantify Bleeding Risk Before Kidney Biopsy?

By Austin G. Stack and Leonard Browne

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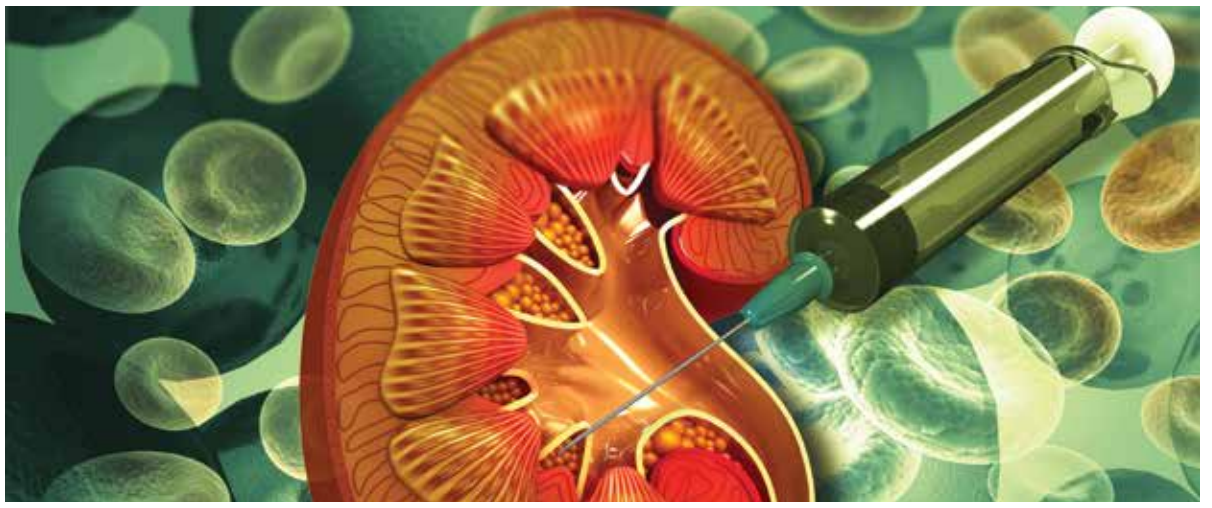

Percutaneous kidney biopsy remains the diagnostic cornerstone of modern nephrology (1). Despite advances in imaging, pathology, and biomarker discovery, biopsy continues to provide information that cannot be obtained through noninvasive means. Yet concerns regarding bleeding complications often influence clinical decision-making, patient counseling, and postprocedure monitoring. In this context, the study by Thorne and colleagues represents an important advance by providing the first, to our knowledge, external validation of a kidney biopsy bleeding risk calculator and demonstrating its potential utility in routine clinical practice (2).

The investigators evaluated a previously developed risk prediction model incorporating seven readily available clinical variables—age, hemoglobin, platelet count, weight, height, kidney size, and native versus transplant kidney status—in an independent cohort of 715 patients from Halifax, Nova Scotia, Canada, from 2012 to 2019 (3). The model demonstrated good discrimination (C-statistic, 0.78) and acceptable calibration (calibration slope, 0.72), supporting its ability to distinguish patients at higher and lower risk of major bleeding. Given the differences in patient populations, clinical practices, and observed bleeding rates between the Halifax cohort (4.1%) and the original London, Ontario, Canada, cohorts (1.9% and 1.8%), the need for recalibration is not unexpected and may reflect differences in baseline risk rather than a weakness of the original model. Recalibration, using a combined cohort of 1732 biopsies, further improved performance, yielding an optimism-corrected C-statistic of 0.84. Importantly, adding kidney function (serum creatinine) did not meaningfully improve predictive performance, underscoring the robustness and parsimony of the original model. However, single creatinine measurements may not adequately capture the extent and severity of kidney damage, the presence of acute kidney injury (AKI), or dynamic changes in kidney function observed in routine clinical practice.

Several strengths deserve emphasis. First, external validation is the critical but often neglected step in prediction model development (4). Many risk scores perform well in derivation cohorts yet fail when applied elsewhere. By demonstrating consistent performance in a geographically distinct population with different biopsy practices, operators, and patient characteristics, the authors provide compelling evidence of generalizability. Second, the study adheres to contemporary standards for prediction modeling, including assessment of discrimination, calibration, decision-curve analysis, bootstrap validation, and model recalibration. Third, the model relies exclusively on variables routinely available before biopsy, making implementation straightforward and scalable. Finally, inclusion of both native and transplant biopsies broadens applicability across nephrology practice.

Notwithstanding these strengths, several limitations warrant consideration. Although the combined cohort was relatively large, only 48 major bleeding events occurred, limiting statistical precision and increasing uncertainty around estimates. The retrospective design introduces the possibility of residual confounding and incomplete capture of clinically relevant variables. Practice patterns differed between centers, including needle gauge (18-G versus 16-G needles), operator specialty (nephrologist versus radiologist), and use of desmopressin, factors that may influence bleeding risk but were incompletely characterized (2). Sex and AKI were not included in the original model or evaluated during model extension (5). Given previous evidence identifying female sex and AKI as risk factors for major bleeding following kidney biopsy, their potential predictive value warrants further evaluation. Furthermore, the model revealed overprediction of risk for patients with higher-risk ranges, although the clinical importance of this finding is likely modest given that such patients may not proceed to biopsy in routine practice.

The practical implications for nephrology are substantial. First, this tool facilitates individualized patient counseling, moving discussions beyond generic complication rates toward personalized risk estimates. Second, risk stratification may inform procedural planning and postbiopsy observation protocols. The authors highlight how the model has already supported shorter observation periods in patients with lower risk, an approach that could improve efficiency and reduce health care utilization. Third, the calculator may identify patients who would benefit from optimization of modifiable risk factors, such as anemia or thrombocytopenia, before biopsy. Finally, widespread adoption could promote more standardized approaches to biopsy safety across centers.

As nephrology increasingly embraces precision medicine, validated clinical prediction tools will become essential components of care. The work by Thorne et al. (2) moves the field beyond expert judgment alone toward evidence-based quantification of biopsy risk. Although further validation in larger and more diverse populations is certainly desirable, this study provides encouraging evidence that bleeding risk after kidney biopsy can be estimated reliably and used to support shared clinical decision-making. It represents an important step toward safer, more personalized kidney biopsy practice. ■

Austin G. Stack, MD, is chair of medicine and a professor in the Department of Nephrology, and Leonard Browne, PhD, is a senior research fellow in the School of Medicine at University Hospital Limerick, Ireland.

The authors report no conflicts of interest.

External validation and recalibration of a risk calculator for major bleeding after diagnostic kidney biopsy

KidneyNews

Quaternary care enter (Halifax, Nova Scotia, Canada)

2012–2019

Adults who underwent diagnostic kidney biopsy (N = 715)

Major bleeding was defined as the need for blood transfusion, surgical intervention or embolization, or death.

PREDICTION MODEL

Risk of bleeding complications after kidney biopsy

- Age
- Weight
- Height
- Platelet count
- Hemoglobin
- Kidney size
- Native versus transplant graft kidney

2.7% Major bleeding risk

VALIDATION COHORT

0.78 C-Statistic overall discrimination performance (95% CI, 0.69–0.85)

0.72 Calibration slope (95% CI, 0.41–1.02)

Recalibration improved performance in the combined cohort; model performance improved with the combined dataset.

0.84 C-Statistic optimism-corrected (95% CI, 0.79–0.88)

0.82 Bias-corrected calibration slope (95% CI, 0.73–0.88)

Conclusion: In this study, a risk calculator for predicting major bleeding complications from kidney biopsy demonstrated good model performance in an external validation that improved with recalibration in a combined cohort. CI, confidence interval.

Thorne J, et al. **External Validation and Recalibration of a Risk Calculator for Major Bleeding After Diagnostic Kidney Biopsy**. *Kidney Med* 2026; 8:101352. doi: 10.1016/j.xkme.2026.101352

Visual abstract by Edgar Lerma, MD, FASN

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Association of Autosomal Dominant Polycystic Kidney Disease and Aortic Disease

By Konrad Timon

https://doi.org/10.62716/kn.004112026

Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited cause of kidney failure worldwide, affecting approximately 1 in 1000 to 2500 people globally (1). While named for the progressive formation of fluid-filled cysts in both kidneys, its extrarenal complications are equally well-recognized. Well-documented, potentially devastating cardiovascular manifestations, including mitral valve prolapse, cardiomyopathy, and intracranial aneurysms, have prompted screening recommendations in certain clinical settings (2, 3). By contrast, the association between ADPKD and aortic disease, including aortic dissection (AD) and aortic aneurysm (AA), remains uncertain despite decades of interest. Given the high mortality of both conditions, clarifying whether ADPKD independently predisposes patients to aortic disease is essential to guide clinical vigilance and timely intervention.

A cohort study published in the *American Journal of Kidney Diseases* by Nakayama and colleagues offers compelling evidence of an independent association between ADPKD and incident AD or AA (4). Drawing on a nationwide Japanese insurance claims database of over 2.5 million individuals, participants were followed from an index date, defined as a health checkup, at least 6 months after insurance enrollment until the occurrence of aortic disease, insurance program disenrollment, or the end of the study. A key strength was the ability to account for covariates including hypertension and reduced kidney function, both established predictors of aortic disease that have historically confounded attempts to isolate the contribution of ADPKD itself (5). Three cause-specific hazard models, multiple subgroup analyses, and rigorous sensitivity analyses further supported the robustness of the findings.

Across all three models, individuals with ADPKD faced a statistically significant higher risk of AD or AA, with the fully adjusted model demonstrating a 76% increased risk (hazard ratio [HR], 1.76; 95% confidence interval [CI], 1.13–2.73). When analyzed separately, the risk of aortic dissection more than doubled (HR, 2.53; 95% CI, 1.13–5.66). Notably, the fully adjusted model failed to demonstrate a statistically significant increase in AA risk alone (HR, 1.56; 95% CI, 0.94–2.60)—a finding that the authors do not fully explore and one that may warrant further investigation. Subgroup analysis revealed that individuals with a body mass index (BMI) of 25 kg/m² or more were at substantially higher risk (HR, 3.06; 95% CI, 1.59–5.90), although the authors rightly caution that low event numbers and the likelihood of kidney enlargement artificially inflating BMI limit interpretation of this finding (6).

Several limitations deserve acknowledgment. The Japanese study population warrants caution when extrapolating findings to non-Asian populations, given known ethnic differences in the incidence of aortic disease (7). Phenotypic variability driven by genetic variant, a key feature of ADPKD, was also unaccounted for.

Clinically, however, the implications are meaningful. These findings support a lower threshold for vascular imaging in patients with ADPKD presenting with atypical pain and lend additional weight to rigorous blood pressure control, already a cornerstone of ADPKD management, as a potential modifier of aortic risk. Overall, this study makes a strong case that aortic disease deserves a firm place in the routine clinical conversation about ADPKD. ■

Konrad Timon, MD, is with St. Vincent's University Hospital, Dublin, Ireland.

The author reports no conflicts of interest.

Given the high mortality of both conditions, clarifying whether ADPKD independently predisposes patients to aortic disease is essential to guide clinical vigilance and timely intervention.

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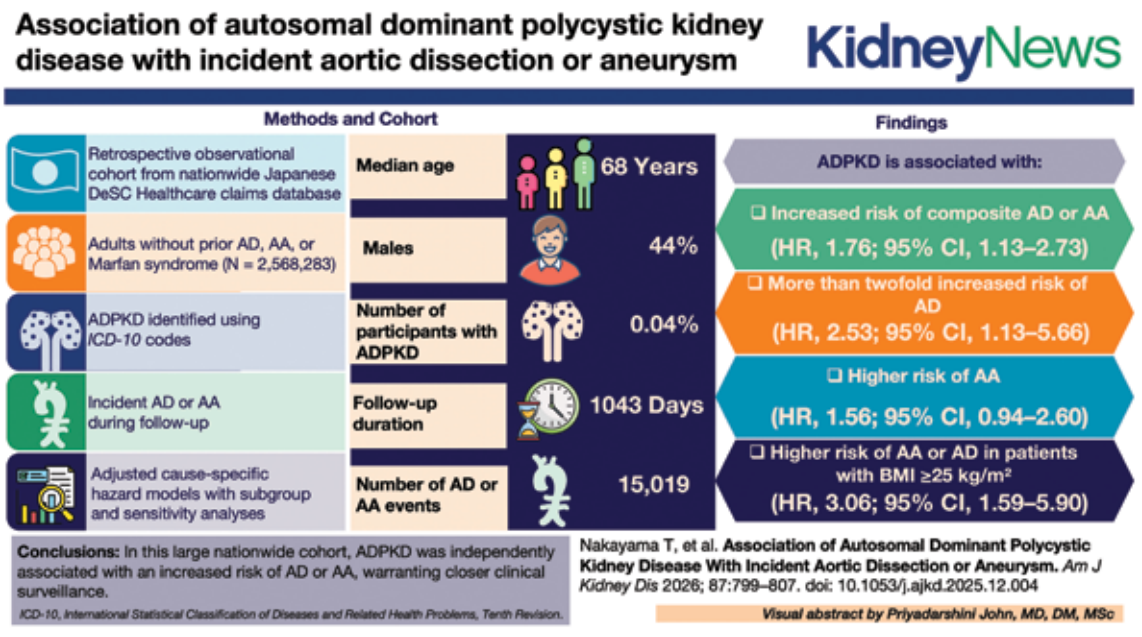


The Reset Button Reaches Nephrology: CAR-T Cell Therapy for Autoimmune Kidney Disease

By Jaymin Patel

https://doi.org/10.62716/kn.004022026

In 2024, an adolescent with rapidly progressive lupus nephritis was weaned off hemodialysis after a single infusion of engineered T cells, with no new immunosuppressant, no transplant, and no regimen to taper (1). For a specialty that has spent decades titrating mycophenolate, that should stop us in our tracks.

Chimeric antigen receptor T (CAR-T) cell therapy reached autoimmunity with startling speed: one patient with refractory lupus in 2021 (2); a five-patient series in 2022 with every patient drug-free (3); and by 2024, a 15-patient series across lupus, scleroderma, and myositis with durable, medication-free remission and mostly low-grade toxicity (4). The conceptual leap matters most. Instead of chronic suppression, deep CD19-directed B cell depletion appears to produce an immune "reset," in which B cells return from naïve precursors, autoantibodies seroconvert, and disease quiets, sometimes for years without any therapy (Figure).

The most transformative therapy for our most feared immune kidney diseases is being built largely outside nephrology, by hematology, rheumatology, and industry.

This is emphatically a nephrology story. The diseases now in trials—lupus nephritis, antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis, membranous nephropathy, and monoclonal gammopathies—are disproportionately ours, and the kidney endpoints are no longer afterthoughts. In the most mature cohort, a B cell maturation antigen (BCMA)–CD19 compound product achieved stringent complete remission in 10 of 12 patients with refractory lupus. That bar is high: drug-free clinical remission plus a complete renal response (proteinuria <0.5 g/g, preserved kidney function). Repeat biopsies showed cleared immune-complex deposits and resolved chronic glomerular injury, with the index response nearing 6 years (5). In refractory myeloperoxidase (MPO)-ANCA vasculitis with crescentic glomerulonephritis that had failed cyclophosphamide, rituximab, and avacopan, a point-of-care anti-CD19 product induced complete remission with an 87% fall in proteinuria (6). These are histologic and functional renal outcomes, not surrogate serologies.

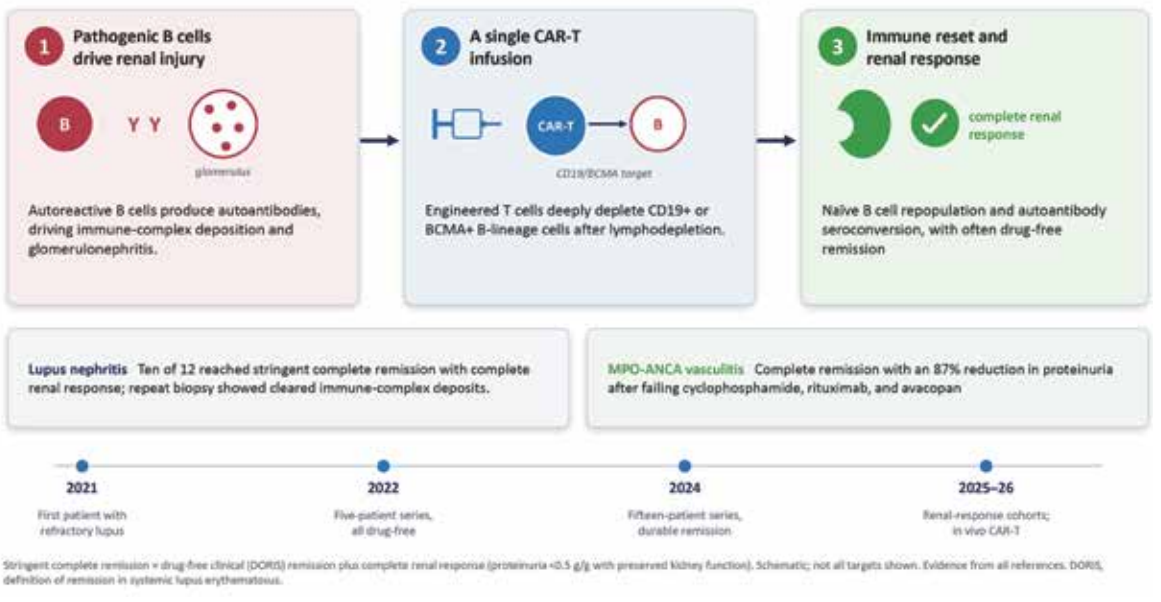
Enthusiasm should be disciplined: Nearly all data are small, single-arm, and short-term, with real risks from B cell aplasia and lymphodepletion. Whether or not we prescribe these therapies, nephrologists will manage their renal toxicities, including acute kidney injury and CAR-T cell–associated proteinuria—complications for which nephrology is already being consulted.

The next wave may reshape who can offer cell therapy at all. Autologous manufacturing is slow, costly, and centralized—each dose built individually from a patient's own cells— which is a recipe for inequity in a field already serving the underserved. Off-the-shelf allogeneic constructs and in vivo CAR-T cells, in which lipid nanoparticles generate CAR-T cells directly inside the patient without apheresis or lymphodepletion, attack that bottleneck: By removing the slow, individualized manufacturing step, they could make treatment faster, cheaper, and far more widely available. An early in vivo approach has already depleted B cells in refractory lupus (7).

Here is the fellow's stake. The most transformative therapy for our most feared immune kidney diseases is being built largely outside nephrology, by hematology, rheumatology, and industry. If we want a seat, we must claim it now: Learn the immunobiology, co-manage cell therapy fluently, push for nephrology on the trials, insist that kidney endpoints define success, and be the loudest voices on access.

The teenager who left dialysis is not a guarantee; she is a question—whether nephrology helps write the next chapter of immune kidney disease or reads about it in someone else's journal. ■

Figure. CD19/BCMA-directed CAR-T cell therapy in lupus nephritis and ANCA-associated vasculitis



Stringent complete remission = drug-free clinical (DORIS) remission plus complete renal response (proteinuria <0.5 g/g with preserved kidney function). Schematic; not all targets shown. Evidence from all references. DORIS, definition of remission in systemic lupus erythematosus.

Jaymin Patel, MD, is a nephrology fellow in the Division of Nephrology and Hypertension at the University of Cincinnati College of Medicine, OH. His clinical and academic interests include glomerular disease, immunology, medical education, and service to the underserved.

The author reports no conflicts of interest.

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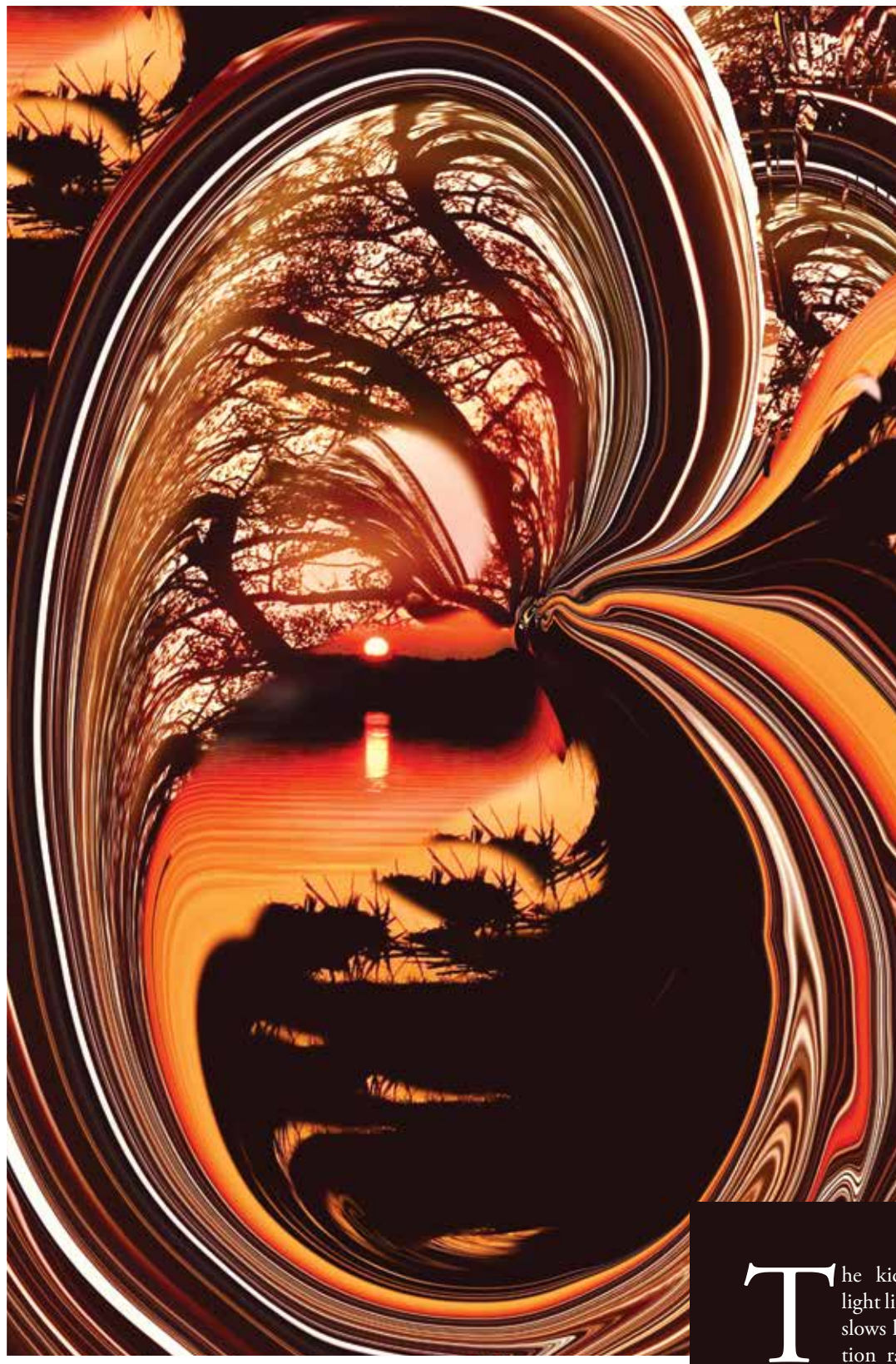
CREATIVE CORTEX

Sunset Kidney

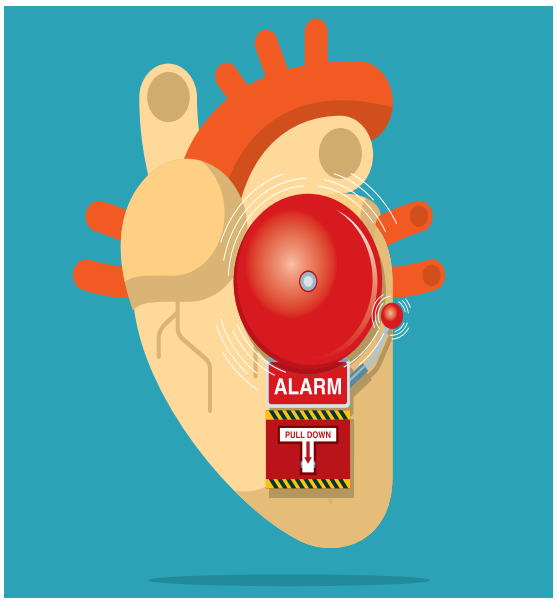
By Anil Saxena

https://doi.org/10.62716/kn.003172026



Artwork by AnilzArt. Anil Saxena, MD, is a digital artist based in Dubai, United Arab Emirates. His abstract artwork blends trained medical expertise with vibrant color palettes, creating visually captivating landscapes of human identity and transformation. Saxena's work has been exhibited internationally and featured on the covers of medical journals.

The kidney drifts into sunset—amber light lingering on its last labors. Filtration slows like a tired river, glomerular filtration rate descending with quiet grace. Not collapse, but a gentle surrender of day to dusk. In this glowing pause lies a plea: Notice the fading light, tend the horizon, and let care arrive before night forgets the sun. ■



Rising Rate of Heart Failure Admissions in Advanced CKD

https://doi.org/10.62716/kn.004732026

Despite declining mortality, rates of heart failure (HF) hospitalization among people with advanced chronic kidney disease (CKD) have increased significantly in recent years, according to a study in *Kidney International Reports*.

Using Swedish Renal Registry data from 2011 to 2021, the researchers identified four groups of individuals with advanced CKD: 25,591 with stage G4 and 13,968 with stage G5 nondialysis-dependent CKD, 10,635 receiving hemodialysis, and 4511 receiving peritoneal dialysis. Trends in HF-related hospitalization and death were analyzed and compared with those in an age- and sex-matched general population.

At baseline, HF was present in 27% of people with stage G4 CKD, 25% with stage 5 CKD, 33% on hemodialysis, and 25% on peritoneal dialysis. Compared with the general population, the incidence rate of HF hospitalization was 6.8 per 100 patient-years in the G4 cohort and 9.5 in the G5 cohort, compared with 5.2 and 5.4 in the hemodialysis and peritoneal dialysis groups, respectively. Individuals with G5 CKD had the highest incidence of HF-related death: 3.7 per 100 patient-years, compared with approximately 2.6 per 100 patient-years in the other cohorts.

Rates of renin-angiotensin system inhibitor and beta-blocker use remained stable and relatively low throughout the period studied, while diuretic use declined in the nondialysis-dependent CKD cohorts. HF-related hospitalization increased by 51% in the G4 cohort, 36% in the G5 cohort, and 30% in the hemodialysis cohort, with higher rates than in the matched general population. Meanwhile, HF-related mortality declined steadily in the CKD groups: by up to 21% in the G4 cohort and 66% in the peritoneal dialysis cohort. HF mortality was 11.6 to 17.0 times higher than in the general population.

HF is the most common cardiovascular complication of CKD, with prevalence increasing as kidney function declines. The new analysis suggests that rates of HF-related hospitalization among people with advanced CKD have increased in recent years, more rapidly than in the general population. "These findings emphasize the growing excess cardiovascular burden in patients with advanced CKD, and underscore the urgent need for optimized evidence-based treatment strategies tailored to this very high-risk population," the researchers conclude [Lankinen R, et al. 10-Year trends in heart failure among patients with dialysis and nondialysis CKD. *Kidney Int Rep* 2026; 11:106695. doi: 10.1016/j.ekir.2026.106695].

Early Rasburicase May Improve Outcomes in Tumor Lysis Syndrome

https://doi.org/10.62716/kn.004742026

Early treatment with the recombinant antihyperuricemic agent rasburicase reduces the risk of kidney replacement therapy or death in patients with cancer and tumor lysis syndrome (TLS), reports a study in *The British Medical Journal*.

The "STOP-TLS" emulated target trial included 1276 adults with TLS admitted to 36 US hospitals between 2014 and 2023. All had active hematologic malignancy or metastatic solid tumors, a high tumor burden, or laboratory or clinical features of TLS. Of these, 55.3% started rasburicase within 12 hours after TLS onset. Patients with early rasburicase therapy were compared with those with later or no rasburicase on a composite outcome of acute kidney injury (AKI) requiring kidney replacement therapy or death during index hospitalization.

Median time to rasburicase administration in the early treatment group was 5 hours. Median uric acid level was 0.71 mmol/L in the early rasburicase group versus 0.59 mmol/L for those who started treatment after 12 hours. The two groups appeared well-balanced in terms of disease severity after inverse probability of treatment weighting.

Patients receiving early rasburicase were less likely to reach the composite outcome of kidney replacement therapy or death: 32.7% versus 42.0%; adjusted odds ratio (AOR), 0.67. Early treatment was also associated with a lower rate of moderate to severe AKI: 33.1% versus 56.0%; AOR, 0.39. In addition, patients receiving early rasburicase had lower 90-day mortality (AOR, 0.71) and a shorter time to anticancer therapy (adjusted hazard ratio, 1.36). Sensitivity analyses yielded consistent findings.

The STOP-TLS results suggest that early rasburicase therapy can lower the risk of AKI requiring kidney replacement therapy or death in patients with TLS, while improving key secondary outcomes. The authors call for further studies to clarify the optimal timing, dosing, and patient selection criteria for this treatment [Shenoy T, et al. Early treatment with rasburicase and risk of kidney replacement therapy and death in adults with tumour lysis syndrome: Emulated target trial. *BMJ* 2026; 394:e100040. doi: 10.1136/bmj-2026-100040].

Can Early Nephrology Consultation Prevent Severe AKI in Patients at Risk?

https://doi.org/10.62716/kn.004752026

A structured early nephrology consultation (ENC)—triggered by a machine-learning risk score—does not reduce the risk of severe acute kidney injury (AKI) in patients who are hospitalized, reports a clinical trial in *JAMA Network Open*.

The randomized trial enrolled 180 patients admitted to a US medical center between 2019 and 2024. All were identified as being at high risk for AKI, based on the previously validated "Electronic Signal to Prevent AKI" (ESTOP-AKI) risk score. Patients assigned to the intervention group were targeted for a structured ENC conducted by an attending nephrologist, including assessment of volume status, kidney perfusion, medications, electrolytes, nutrition, and further testing.

Patients assigned to the comparison group received a nephrology consultation only if requested by the primary team. Over 7 days' follow-up, peak change in serum creatinine (SCr) was compared between groups, along with secondary outcomes.

On adjusted analysis, there was no significant difference in change in SCr between groups. The risk of stage 1 or higher AKI was 42% in the intervention group versus 36% with usual care. The risk of stage 2 or higher AKI was 19% versus 13%, respectively. There was also no difference in other adverse outcomes nor in 90-day readmission or mortality rates.

Patients in the ENC group underwent a total of 121 ENC consultations leading to 270 recommendations, compared with 19 consultations and 36 recommendations in the usual care group. Although there were more recommendations in the ENC group, adherence to these recommendations was low. Recommendations addressing medication dosage or discontinuation, diuretic or fluid use, or vasopressor drugs were more likely to be completely followed in the usual-care group: 68% versus 41%.

The study is one of the first, to our knowledge, to evaluate the use of a real-time, machine-learning AKI risk score to trigger a clinical nephrology intervention. While the ESTOP score identified a group of patients who were hospitalized and at high risk, ESTOP-triggered ENC did not reduce the risk of AKI and related adverse events in this trial. The researchers conclude: "Our negative results should not be interpreted as a failure of machine-learning risk scores but rather that valuable tools such as ESTOP should be embedded within interventions that reliably change clinical management" [Churpek MM, et al.; Electronic Signal to Prevent Acute Kidney Injury (ESTOP-AKI) Investigative Team. Early nephrology consultation and acute kidney injury in hospitalized patients: A randomized clinical trial. *JAMA Netw Open* 2026; 9:e2622554. doi: 10.1001/jamanetworkopen.2026.22554].

Four Doses of Dapagliflozin Reduce AKI After Cardiac Surgery

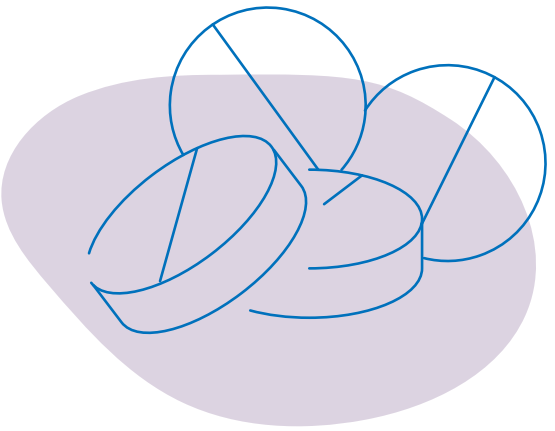
https://doi.org/10.62716/kn.004762026

A 4-day course of dapagliflozin, starting the day before cardiac surgery, can reduce the risk of acute kidney injury (AKI), reports a clinical trial in *JAMA*.

The randomized, double-blind MERCURI-2 trial included 784 patients undergoing elective cardiac surgery at seven centers in the Netherlands between 2023 and 2025. Patients assigned to the intervention group received four doses of dapagliflozin (10 mg), starting on the day before surgery and continuing through the second postoperative day. Rates of AKI, based on Kidney Disease: Improving Global Outcomes (KDIGO) criteria, were assessed over the first 7 postoperative days.

Of 778 patients with complete evaluation, the median age was 68 years, and 76% were men. AKI occurred in 28% of patients assigned to dapagliflozin versus 52% in the comparison group: relative risk (RR), 0.54. Atrial fibrillation and reoperation were the most common adverse events, occurring at similar rates in both groups. On post hoc analysis, dapagliflozin was associated with lower risk of KDIGO stage 1 and 2 AKI: RR, 0.59 and 0.33, respectively.

Previous reports have suggested that sodium-glucose cotransporter-2 inhibitors might help to reduce the risk of AKI after cardiac surgery. The MERCURI-2 trial finds a significant reduction in AKI in patients receiving four doses of dapagliflozin starting the day before elective cardiac surgery, compared with placebo. Dapagliflozin does not appear to affect secondary outcomes beyond AKI risk [Oosterom-Eijmael MJP, et al.; MERCURI-2 Study Group. Dapagliflozin and acute kidney injury following cardiac surgery: A randomized clinical trial. *JAMA*, published online July 30, 2026. doi: 10.1001/jama.2026.9268]. ■



Clarification

Clarification to "Evidence Grows for High-Quality, Plant-Heavy Diets for Kidney Health, Despite High Protein Push" (March 2026)

https://doi.org/10.62716/kn.004792026

The article "Evidence Grows for High-Quality, Plant-Heavy Diets for Kidney Health, Despite High Protein Push" by Bridget M. Kuehn, published in the March 2026 issue of *Kidney News* (1), was amended after print publication to use generic names consistently for potassium binders. This change did not affect the meaning or accuracy of the article. The updated full-text version was published online on August 19, 2026. ■

Reference

1. Kuehn BM. Evidence grows for high-quality, plant-heavy diets for kidney health, despite high protein push. *Kidney News*, March 2026; 18(3):1, 9. doi: 10.62716/kn.002992026

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APRIL, a proliferation-inducing ligand; BAFF, B cell activating factor; Gd-IgA1, galactose-deficient immunoglobulin A1; IgA, immunoglobulin A.

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