ASN American Society of Nephrology

Kidney News

September 2020 | Vol. 12, Number 9

Pandemic Exacerbates Disparities in Kidney Disease

By Bridget M. Kuehn

The same lower income and predominantly minority communities in the South and West sides of Chicago that have the highest density of dialysis units also have the highest numbers of residents testing positive for COVID-19, a recent analysis found (1).

The analysis is part of a growing body of evidence revealing how the health inequities and structural racism that help fuel disproportionately high rates of kidney diseases and other chronic diseases in marginalized communities are also contributing to a disproportionate burden of COVID-19.

"Kidney disease is really just the perfect lens to view health disparities in the United States," said analysis co-author Holly Mattix-Kramer, MD, MPH, associate professor of public health sciences and medicine at Loyola University in Chicago and National Kidney Foundation (NKF) president. "The COVID-19 epidemic, it just reflects those disparities and then, to compound it, people who have kidney disease are more likely to be hospitalized if they get COVID-19 and more likely to die."

To manage these intertwined epidemics and their root causes, kidney patients in marginalized communities and their clinicians may need resources that extend beyond traditional kidney care. These include access to accurate information about COVID-19, improved access to healthcare, and COVID-19 testing.

Support in identifying and addressing health inequities during COVID-19 and beyond is also needed from professional societies. The American Society of Nephrology recently testified to the US House of Representatives Committee on Ways and Means on the "Disproportionate Impact of COVID-19 on Communities of Color" and called on Congress to pass legislation to address disparities in healthcare, the Health Equity and Accountability Act of 2020. Additionally, the society issued a statement against racism and signed on to statements against racism issued by the Council of Medical Specialty Societies and the Association of American Medical Colleges.

In August, the ASN Council unanimously approved a plan for how the society and the broader ASN Alliance for Kidney Health can help address systemic racism in nephrology. A key element of this plan is to expand the focus from supporting diversity, equity, and inclusion to confronting

Continued on page 2

COVID-19 Reshapes Residency Education, Exposure to Nephrology

By Melanie Padgett Powers

The COVID-19 pandemic has upended all areas of society, including medical residency education. Residency programs were forced to change almost overnight this spring, presenting new challenges as teaching went online and some aspects, like electives and clinics, were halted at many institutions. But there were bright spots and technology advances that residency programs may continue to embrace long after the pandemic.

While challenging, moving residency conferences to platforms like Zoom allowed for more participation and flexibility. "Zoom is very convenient; you can log in from anywhere," said Sylvia Wu, MD, a third-year internal medicine resident at Donald and Barbara Zucker School of Medicine at Hofstra/Northwell in New York, who is applying for a nephrology fellowship. "During one of our morning conferences, our chairman invited colleagues from different institutes, which was a valuable experience."

Trainees can catch up on online conferences if they missed them, can rewatch them, and can look for education outside their program or institution. Plus, residents on maternity and

Continued on page 3

Inside

ASN American Society of Nephrology

KidneyNews

ASN Kidney News is published by the American Society of Nephrology
1401 H Street, NW, Suite 900, Washington, DC 20005. Phone: 202-640-4660

www.asn-online.org

ASN Kidney News is the authoritative source for analysis of trends in medicine, industry, and policy affecting all practitioners in nephrology. The statements and opinions expressed in *ASN Kidney News* are solely those of the authors and not of the American Society of Nephrology (ASN) or the editorial policy of the editors. The appearance of advertisements in *ASN Kidney News* is not a warranty, endorsement, or approval of the products or services advertised or of their effectiveness, quality, or safety. The American Society of Nephrology disclaims responsibility for any injury to persons or property resulting from any ideas or products referred to in the articles or advertisements.

The American Society of Nephrology is organized and operated exclusively for scientific and educational purposes, including enhancing the field of nephrology by advancing the scientific knowledge and clinical practice of that discipline through stimulation of basic and clinical investigation, providing access to new knowledge through the publication of journals and the holding of scientific meetings, advocating for the development of national health policies to improve the quality of care for renal patients, cooperating with other national and international societies and organizations involved in the field of nephrology, and using other means as directed by the Council of the Society.

Postmaster: Please send address changes to *ASN Kidney News*, c/o Customer Service, American Society of Nephrology 1401 H Street, NW, Suite 900, Washington, DC 20005.

Publications mail agreement No. 40624074. Return undeliverable Canadian addresses to PO Box 503, RPO West Beaver Creek, Richmond Hill ON L4B 4R6

ASN Kidney News (ISSN print 1943-8044 and online 1943-8052) is an official publication of the American Society of Nephrology, 1401 H Street, NW, Suite 900, Washington DC 20005, and is published monthly 11 times a year except November. Periodicals postage paid at Washington, DC and at additional mailing offices. Subscription rates: $12 per year. To order, please email bhenkel@asn-online.org. Subscription prices subject to change. Annual ASN membership dues include $12 for *ASN Kidney News* subscription.

★ WINNER OF 2 DESIGN AWARDS ★

WINNER 2019 APEX AWARDS FOR PUBLICATION EXCELLENCE

GD USA HEALTH + WELLNESS DESIGN AWARDS

Pandemic Exacerbates Disparities

Continued from page 1

health disparities and social determinants of health. "ASN, the ASN Alliance for Kidney Health, and the rest of the kidney community must tackle systemic racism from every perspective," asserts ASN Executive Vice President Tod Ibrahim.

"Addressing systemic racism is the right thing to do, it's the smart thing to do, it will make the entire community stronger, and the time is now."

Disproportionate burdens

Individuals who are Black, Hispanic, Native American, or Pacific Islander already represent half of all patients with kidney failure, according to a recent analysis co-authored by Lilia Cervantes, MD, associate professor of medicine at Denver Health Medical Center and the University of Colorado School of Medicine in Denver (2). These same populations are also overrepresented among COVID-19 patients.

National data from the US Centers for Disease Control and Prevention show that Native American/Alaska Native, Black, and Hispanic people are about three times more likely than white people to test positive for COVID-19 and are 4.6 to 5.3 times more likely to be hospitalized (3). Black patients were twice as likely to die as white patients, and American Indian/Alaska Natives were 1.4 times more likely to die.

Data from New York City's public hospital system also found Black and Hispanic patients had disproportionately higher rates of positive COVID-19 tests, hospitalizations, and deaths (4). More than one in 10 of those hospitalized with COVID-19 and 15% of those who died had chronic kidney disease.

"It has become increasingly clear that the disproportionate burden of COVID-19 infection, hospitalization, and death among Black people and other people of color is driven by longstanding health and socioeconomic inequities," said Roopa Kalyanaraman Marcello, MPH, director of research and evaluation in the Office of Population Health at NYC Health + Hospitals. "Systemic racism and inequities in the social determinants of health—employment, income, education, housing, and access to culturally competent healthcare—have resulted in conditions that put these groups at higher risk of infection and adverse outcomes from COVID-19."

Lower income individuals are more likely to be essential workers, be unable to work from home, to use public transportation, and to live in multigenerational or multifamily housing, increasing the risk of exposure, Cervantes said. Many may not have access to personal protective equipment or may feel unable to advocate for safety precautions in the workplace, she said.

Many individuals in marginalized communities also lack access to COVID-19 testing, health insurance, and healthcare. Lower income workers may not be able to afford co-pays if they do have insurance, said Deidra Crews, MD, ScM, associate vice chair for diversity and inclusion and associate professor of medicine at Johns Hopkins Medicine, during NKF's Kidneys and COVID-19: Navigating Health Disparities in Minority Communities webcast (5). They may not be able to take a day off to seek testing or care, she said.

"Some people have to take two or three buses just to get to a healthcare facility so . . . getting tested is almost out of the question," said Francesca Weaks, MS, DrPH, policy and research manager for the National Association for the Advancement of Colored People, during the webcast. "They are more likely to be frontline workers and go to work sick rather than get a test."

Individuals in historically underserved communities may be wary of COVID-19 exposure at health facilities or may mistrust healthcare institutions because of previous experiences of discrimination, Crews said. Recent high-profile incidents of racism may further exacerbate Black patients' distrust of the system and the effects of COVID-19 on Black communities, noted Crews and Tanjala Purnell, MPH, PhD, associate director of Johns Hopkins Urban Health Institute, in a recent commentary (6).

Immigrants, particularly undocumented immigrants, face a unique set of hurdles in accessing care. They are excluded from Medicare, the Affordable Care Act, and most forms of Medicaid, Cervantes said. Those with kidney failure may only be able to access dialysis in an emergency room when they are critically ill and receive coverage through emergency Medicaid, despite such care being associated with higher costs and worse outcomes (7).

"Right now, [undocumented immigrants with kidney failure] are being unnecessarily exposed to COVID-19 because they have to come into an emergency department once a week," Cervantes said. In addition to the risk to the patient, this exposure may contribute to further community spread and added burdens on emergency department and nephrology clinicians (8).

Undocumented immigrants, who often live in mixed status households, may also be reluctant to seek medical care or testing for COVID-19 or kidney diseases because they are worried about deportation, especially after recent changes were made to the Public Charge Rule. The changes, which were temporarily suspended during the pandemic, have already had a chilling effect on Medicaid participation (9).

"They don't know if coming in for emergency care will impact their ability to later on change their immigration status," Cervantes said.

Additionally, misinformation about COVID-19 has been rampant in marginalized communities. "There is a tremendous amount of misinformation," Crews said. "It is overwhelming and dangerous."

Proactive and protective policies

Nephrologists may need to reach beyond their traditional toolbox to help patients, argued Mattix-Kramer, including working more closely with social workers to help patients coping with economic and other challenges associated with the pandemic. In addition to addressing pandemic-related fallout, Crews and Purnell also advocated for nephrologists to acknowledge the emotional toll for patients coping with high-profile incidents of racism.

"Nephrologists can support their patients by first acknowledging that these are tremendously difficult times and inviting them to share how they are coping," Crews said in an e-mail interview. "We can also inquire about any changes in our patients' abilities to meet basic needs relevant to their health, such as food and shelter. If needs are identified, then we should refer or connect our patients to resources to help them meet these needs."

John Wagner, MD, MBA, Service Line Lead in Nephrology at NYC Health + Hospitals, also recommended that nephrologists take time to discuss COVID-19 preventive measures with their kidney disease patients. This discussion should include encouraging them to get up to date on vaccinations, including the seasonal influenza vaccine; recommending those starting dialysis to consider home-based options; and encouraging in-center dialysis patients to review and follow protective procedures at their facilities.

Healthcare institutions should also reach out to communities at high risk of COVID-19 and kidney disease to help prevent infections and ensure timely care. Crews suggested institutions and nephrologists work with trusted community leaders or faith leaders to debunk COVID-19 myths and ensure that socially disadvantaged communities have the information and resources they need to stop the spread of the virus. For example, Johns Hopkins Center for Health Equity is partnering with members of its Community Advisory Board to disseminate information about COVID-19; resources for assistance with food, housing and other needs; and support for people coping with the grief, Crews said. The center has used webinars, teleconferences, and its website to share this information (10).

Cervantes and her colleagues have also partnered with community-based organizations in Colorado that are working to reduce the burden of kidney disease among Hispanic patients with diabetes to spread information about COVID-19. She emphasized the need to work with organizations that can provide culturally concordant information in accessible language to the many different immigrant communities in the United States.

"By creating trusting relationships with these communities, you are not only able to facilitate communication about COVID-19, but you're also welcoming them to the hospital if they get sick," she said. "Many of these patients wait until they're too sick from COVID-19 [to go to the hospital]. Treating them earlier or seeing them sooner is better."

"We are advocating for routine testing of patients who are on dialysis if they live in areas that have a high risk," said the NKF's Mattix-Kramer. She explained this may help identify asymptomatic individuals who may pose a risk of infecting fellow patients or other close contacts and ensure that these individuals can self-isolate and are carefully monitored for worsening illness.

Some states are pursuing policy changes to increase healthcare access for marginalized populations, Cervantes said. For example, several states have revised the definition of emergency care to include kidney failure in order to expand coverage for undocumented immigrants. Some states are also providing economic relief to undocumented immigrants who have lost jobs, cannot pay rent, or have been ill who do not qualify for federal aid.

"They realize that it doesn't make sense to have someone come in [to an emergency department] on a weekly basis from a quality of life perspective or a cost analysis perspective," she said. "We can only be as healthy as the most vulnerable among us and so if we're not protecting our undocumented patients, then this virus will continue to spread."

Greater kidney patient and nephrologist advocacy is needed to support more funding for community outreach to educate high-risk communities about both kidney disease and COVID-19 as well as policies and funding to improve care for kidney patients.

"The nephrology community as a whole really needs to have a much stronger voice politically," said Mattix-Kramer.

References

1. Bhayani S, et al. Dialysis, COVID-19, poverty, and race in Greater Chicago: An ecological analysis. *Kidney Medicine* 30 July 2020, doi:10.1016/j.xkme.2020.06.005
2. Novick TK, et al. "COVID-19 and kidney disease disparities in the United States." *Advances in Chronic Kidney Disease* 2020 doi:10.1053/j.ackd.202.06.005
3. US Centers for Disease Control and Prevention. COVID-19 Hospitalization and Death by Race and Ethnicity. https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-race-ethnicity.html
4. Kalyanaraman Marcello R, et al. Characteristics and outcomes of COVID-19 patients in New York City's public hospital system. Preprint. *medRxiv*. 2020;2020.05.29.20086645. Published 2020 Jun 2. doi:10.1101/2020.05.29.20086645
5. National Kidney Foundation. Kidneys and COVID-19: Navigating Health Disparities in Minority Communities. https://kidney.zoom.us/webinar/register/rec/WN_HaoazmBfRuiRO-MLnV2b5Q?meetingId=uJBENZegqFxOTqf1yR31BKgbXZrbT6a81CBM8vtbnbLbDBF4klDtraLJ3s0fbg0&playId=&action=play&_x_zm_rtaid=nvwOwBSwTumTEji-Ba5-1A.1590680269213.c805579f9e7f372e11754aae1f932be2&_x_zm_rhtaid=489
6. Crews D and Purnell T. COVID-19, racism, and racial disparities in kidney disease: Galvanizing the kidney community response. *J Am Soc Neph* 2020; 31:8 doi: 10.1681/ASN.2020060809
7. Nguyen OK, et al. Association of scheduled vs emergency-only dialysis with health outcomes and costs in undocumented immigrants with end-stage renal disease. *JAMA Intern Med* 2019; 179:175–183. doi:10.1001/jamainternmed.2018.5866
8. Rizzolo K, et al. Dialysis care for undocumented immigrants with kidney failure in the COVID-19 era: Public health implications and policy recommendations. *Am J Kidney Dis* 2020; 76:255–257. doi:10.1053/j.ajkd.2020.05.001
9. National Conference of State Legislatures. Immigration and Public Charge: Rule Suspended During Pandemic. August 5, 2020. https://www.ncsl.org/research/immigration/immigration-and-public-charge-dhs-proposes-new-definition.aspx
10. Johns Hopkins Center for Health Equity. COVID-19 Resources Page https://www.healthequityhub.com/covid19-resources
11. Longino K and Kramer H. Racial and ethnic disparities, kidney disease, and COVID-19: A call to action" [published online ahead of print, 2020 Jul 21]. *Kidney Med* 2020 doi:10.1016/j.xkme.2020.07.001

COVID-19

Continued from page 1

paternity leave can choose to watch at their convenience, even though it's not required, said Samira Farouk, MD, FASN, assistant professor of medicine and medical education at Mount Sinai in New York.

"In the past, we didn't really have mechanisms to record lectures," Farouk said. "It's really allowed us to capture a lot of our teaching materials." Farouk co-wrote a paper on medical education during the pandemic for *Advances in Chronic Kidney Disease* (1).

While residents on nephrology elective at Mount Sinai are welcome to attend divisional and fellowship conferences as well, now anyone interested can watch online. "Even if folks are not officially with us, the links are always available, so you don't have to be on a nephrology elective," Farouk said. "If you're a second-year internal medicine resident, you got the email, you thought the topic was interesting, you can always log in to view that recording later. I think this has really opened up the venues for learning."

In fact, at Farouk's hospital, they created an all-virtual nephrology residency elective that can be implemented if COVID-19 cases spike and the hospital is forced to shut down programs again. They may also use the online version if too many residents seek a nephrology elective, especially as the hospital follows physical distancing guidelines, and they cannot accommodate everyone in person.

In the virtual program, an attending would serve as virtual elective leader. The residents would do virtual rounds each morning and be assigned real patients. Nephrology faculty worked with electronic medical records (EMR) staff so they will be able to create a separate EMR list for those patients for virtual service. "We would really have a robust curriculum over the two- or three-week elective students may join us for," Farouk said.

While some nephrology programs had already embraced the use of social media and online gaming to enhance education, that may also increase in residency education. In 2018, the Northwell nephrology fellowship program created a group chat via the WhatsApp platform. It included the program's eight fellows and seven selected faculty members. At least one multiple-choice question was provided each week.

"To our surprise, there was more discussion in that group than lectures we were giving live," said Kenar Jhaveri, MD, FASN, professor of medicine and associate chief in the Division of Kidney Diseases and Hypertension at the Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, who has a special interest in innovative nephrology education. "It actually became more lively during COVID because that was one of the only sources the fellows had for learning," he said. "Faculty were excited and were posting COVID-related questions with references and explanations. So, we keep doing more of such tools as adjunct while we continue the didactic and live lectures when possible. We feel these parallel learning methods might be adjuncts, but then they might become primary during times like COVID."

While Northwell's WhatsApp chat is for fellows, residency programs could develop similar channels. Jhaveri studied Northwell's use of WhatsApp for teaching and reported on it in *Clinical Kidney Journal* in February 2020 (2).

Another program that has been widely adopted during the pandemic has been telehealth. While not new, telehealth has provided a safe way for physicians to continue to take care of patients. At the height of the pandemic, most internal medicine residents were treating COVID-19 patients. But as the cases decrease in some states, residents are going back to their previous responsibilities.

This opens the opportunity for more residents to get involved in telehealth visits, said Matthew Sparks, MD, FASN, assistant professor of medicine, director of medical student research, and associate program director of nephrology fellowship at Duke University. Sparks didn't use telehealth before the pandemic. Suddenly, he was seeing 80% of his patients via telehealth phone calls.

Margaret DeOliveira, MD, a fourth-year internal medicine/pediatrics resident at Duke who is applying for a nephrology fellowship, said it was interesting to see just how quickly telehealth became the prominent way to interact with many patients.

DeOliveira believes telehealth is here to stay, which means it should be taught to residents. "While there is a learning curve, I think it does open up interesting possibilities for how telehealth can be more fully integrated into residency education programs in the future and how all levels of training will be fully integrated into this new system," she said.

Wu agreed: "We hadn't been exposed to telemedicine prior to the pandemic, but we got fully immersed in it very quickly," she said. "I think it's good to learn telemedicine during residency. That's a career path that you can think about—

Continued on page 4 >

COVID-19

Continued from page 3

doing remote visits."

One of the challenges of telehealth that needs to be worked out, Sparks said, is how to precept a televisit with residents and fellows. "Do we come on the phone on a three-way call? At what point do you do that? Do you call the patient later and verify?"

Adoption of telehealth could potentially improve a patient's experience. "There are some patients who have transportation issues," Jhaveri said. "Let's just visit their homes through a televisit and only bring them in once a year for a physical exam. Why have them come to every doctor's visit and put them at risk for falls and infections?"

Jhaveri said he's excited about using telehealth with dialysis patients, which could enhance physician work-life balance—and attract more residents to the field. Instead of nephrologists rounding to dialysis centers about four times a month per patient, they can, for example, in some stable patients, do three visits via telehealth and see the patient once a month in person. This was allowed and covered by payers during the pandemic and should be made permanent, he said.

Facing the challenges

Of course there have been challenges during the pandemic, and residents' lack of exposure to nephrology has weighed on faculties' minds. "Even before COVID, there were challenges with residency education and recruitment in nephrology," Jhaveri said. Much of that exposure was through a nephrology rotation, but those are electives at most programs.

"During COVID, unfortunately, all electives were canceled for residents, so whatever exposure they could have had to nephrology was also taken away," he said. "And that was the biggest challenge that we faced because we had no residents doing any electives in nephrology, both inpatient and outpatient. None of these residents had time to do any electives because they were so busy taking care of COVID patients."

It is possible that residents connected with nephrologists more in the emergency department and ICU, as consults increased. Jhaveri said nephrology consults increased at their health system by 39% at the peak of COVID. He's heard similar numbers from other institutions. "We saw the residents noticing a lot of us—not just at this hospital but at other hospitals—doctors on the frontlines fighting COVID because 37% of hospitalized COVID patients had acute kidney injury," he said (3).

As nephrology didactic sessions started back up this summer, Farouk's first one was about the impact of COVID-19 on the kidneys. All three classes of residents were invited to attend via Zoom, and more than 50 showed up, interested to hear a nephrologist's firsthand perspective on the virus.

"I think that was also another way to show them an important side of our field, and moving forward, for medical students and residents thinking about subspecialty choices, I think the impact of the pandemic and how it was approached by each specialty is going to have an important role in how they choose a specialty," Farouk said.

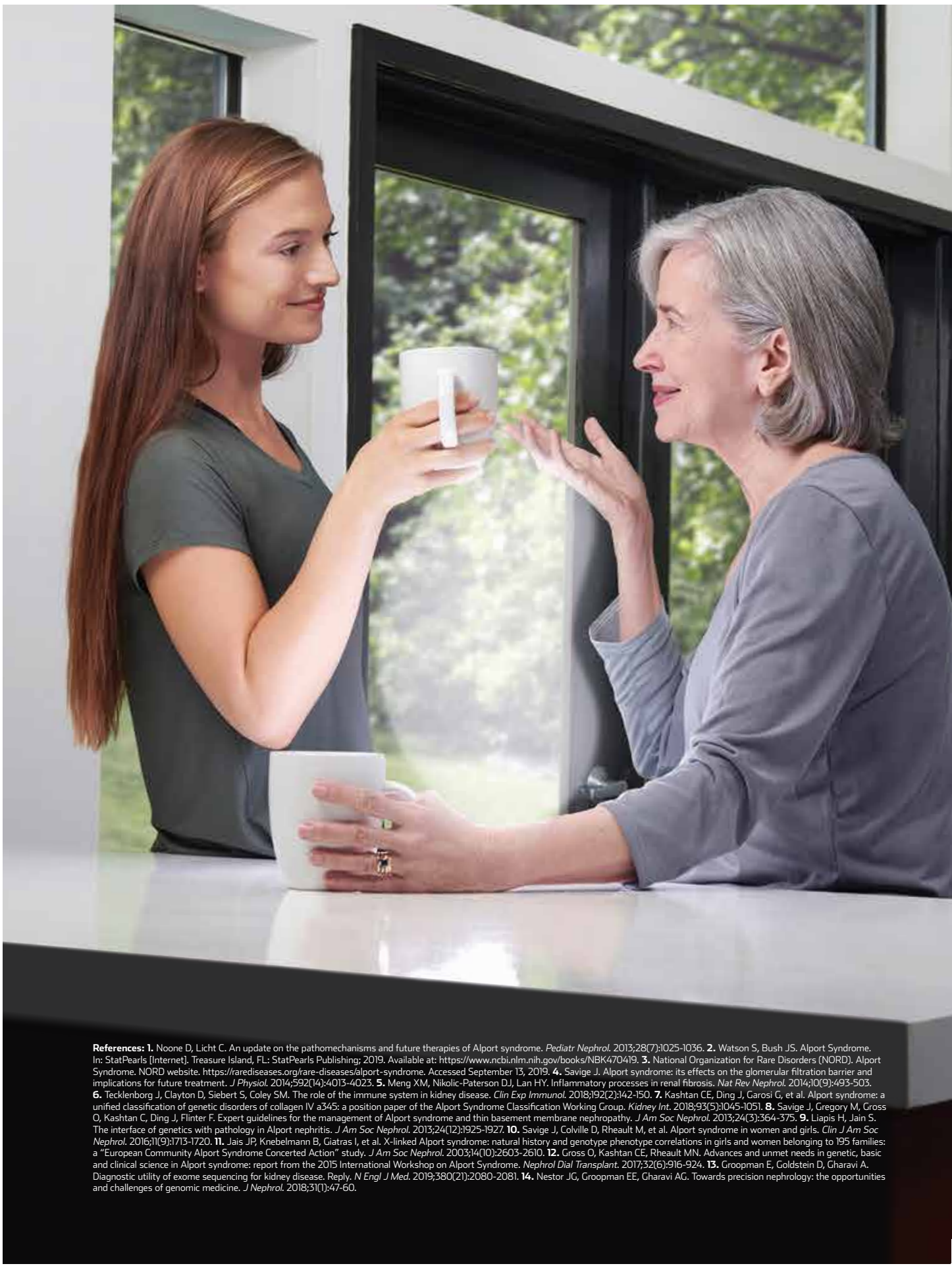
But with the intense pace of care, there wasn't much time for personal interaction in the emergency department and ICU. In fact, that loss of face-to-face communication has been a detriment during the pandemic.

"Having less personal contact with people has been hard. … I think that's where we are realizing that education is not just knowledge—it's getting to know people, it's social, it's connections, it's mentorship," Sparks said. "I think that it's important for us to realize that we have to change how we interact with trainees so that we can still provide all those intangible things that make a fellowship program and a residency program amazing and contribute to the career development of the trainee."

Jhaveri said it's too early to know how the COVID-related changes might affect nephrology recruitment. "This just happened in February, March, and April of 2020 for the northeastern US. We will only know when we see the fellowship applications," he said. "If we see an increase in applications in nephrology, then maybe seeing nephrologists be heroes in the frontlines of the COVID war worked (4). ■

References

1. Hilberg R, et al. Medical education during the COVID-19 pandemic: Learning from a distance. *Adv Chronic Kidney Dis* 2020; in press. doi: https://doi.org/10.1053/j.ackd.2020.05.017
2. Jhaveri KD, et al. 'WhatsApp®'ening in nephrology training. *Clin Kidney J* 2019; 13:8–13. doi: 10.1093/ckj/sfz045
3. Hirsch JS, et al. Acute kidney injury in patients hospitalized with COVID-19. *Kidney Int* 2020; 98:209–218. doi: 10.1016/j.kint.2020.05.006
4. Parikh R, et al. The war we call COVID-19: A letter from the front in New York. *Am J Kidney Dis* 2020; 76:A13–A14. doi: 10.1053/j.ajkd.2020.05.007



References: 1. Noone D, Licht C. An update on the pathomechanisms and future therapies of Alport syndrome. *Pediatr Nephrol*. 2013;28(7):1025-1036. **2.** Watson S, Bush JS. Alport Syndrome. In: StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing; 2019. Available at: https://www.ncbi.nlm.nih.gov/books/NBK470419. **3.** National Organization for Rare Disorders (NORD). Alport Syndrome. NORD website. https://rarediseases.org/rare-diseases/alport-syndrome. Accessed September 13, 2019. **4.** Savige J. Alport syndrome: its effects on the glomerular filtration barrier and implications for future treatment. *J Physiol*. 2014;592(14):4013-4023. **5.** Meng XM, Nikolic-Paterson DJ, Lan HY. Inflammatory processes in renal fibrosis. *Nat Rev Nephrol*. 2014;10(9):493-503. **6.** Tecklenborg J, Clayton D, Siebert S, Coley SM. The role of the immune system in kidney disease. *Clin Exp Immunol*. 2018;192(2):142-150. **7.** Kashtan CE, Ding J, Garosi G, et al. Alport syndrome: a unified classification of genetic disorders of collagen IV a345: a position paper of the Alport Syndrome Classification Working Group. *Kidney Int*. 2018;93(5):1045-1051. **8.** Savige J, Gregory M, Gross O, Kashtan C, Ding J, Flinter F. Expert guidelines for the management of Alport syndrome and thin basement membrane nephropathy. *J Am Soc Nephrol*. 2013;24(3):364-375. **9.** Liapis H, Jain S. The interface of genetics with pathology in Alport nephritis. *J Am Soc Nephrol*. 2013;24(12):1925-1927. **10.** Savige J, Colville D, Rheault M, et al. Alport syndrome in women and girls. *Clin J Am Soc Nephrol*. 2016;11(9):1713-1720. **11.** Jais JP, Knebelmann B, Giatras I, et al. X-linked Alport syndrome: natural history and genotype phenotype correlations in girls and women belonging to 195 families: a "European Community Alport Syndrome Concerted Action" study. *J Am Soc Nephrol*. 2003;14(10):2603-2610. **12.** Gross O, Kashtan CE, Rheault MN. Advances and unmet needs in genetic, basic and clinical science in Alport syndrome: report from the 2015 International Workshop on Alport Syndrome. *Nephrol Dial Transplant*. 2017;32(6):916-924. **13.** Groopman E, Goldstein D, Gharavi A. Diagnostic utility of exome sequencing for kidney disease. Reply. *N Engl J Med*. 2019;380(21):2080-2081. **14.** Nestor JG, Groopman EE, Gharavi AG. Towards precision nephrology: the opportunities and challenges of genomic medicine. *J Nephrol*. 2018;31(1):47-60.

Gold-Standard Test Shows High Rates of Primary Aldosteronism

Primary aldosteronism is more common than previously recognized, and prevalence rises with severity of hypertension, reports a study in the *Annals of Internal Medicine*.

The cross-sectional study included participants from studies at four US medical centers: 298 with normotension, 115 with stage 1 hypertension, 203 with stage 2 hypertension, and 408 with resistant hypertension. All underwent an oral sodium suppression test, regarded as a gold-standard confirmatory test for primary aldosteronism. The study definition of "biochemically overt" primary aldosteronism was a urinary aldosterone level greater than 12 µg/24 h.

In all four blood pressure categories, participants with higher renin-independent aldosterone production had higher blood pressure, increased potassium excretion, and lower serum potassium. Mean adjusted urinary aldosterone level was 6.5 µg/24 h in the normotensive group, 7.3 µg/24 h in participants with stage 1 hypertension, 9.5 µg/24 h in those with stage 2 hypertension, and 14.6 µg/24 h in those with resistant hypertension.

Adjusted prevalence of biochemically overt primary aldosteronism was 11.3% in the normotensive group, 15.7% in participants with stage 1 hypertension, 15.7% in those with stage 2 hypertension, and 22.0% in those with resistant hypertension. The aldosterone–renin ratio had low sensitivity and negative predictive value for biochemically overt primary aldosteronism.

Patients with primary aldosteronism have nonsuppressible, renin-independent aldosterone production, associated with hypertension and adverse cardiovascular outcomes. The aldosterone–renin ratio is the currently recommended screening test for primary aldosteronism.

The new study, using the oral sodium suppression test, finds a high prevalence of unrecognized, biochemically overt primary aldosteronism. The findings "show the existence of a pathologic continuum of nonsuppressible renin-independent aldosterone production that parallels the severity of hypertension," the researchers write. They believe that primary aldosteronism should not be regarded as a "rare and categorical disease," but rather as a common contributor to hypertension across the full range of severity [Brown JM, et al. The unrecognized prevalence of primary aldosteronism: a cross-sectional study. *Ann Intern Med* 2020; 173:10–20]. ■

Cost-Effectiveness Study Supports Sequential Living-Donor Evaluation

When more than one potential living kidney donor comes forward, it is more cost-effective to evaluate them all at once, rather than one at a time, reports a study in *Kidney International*.

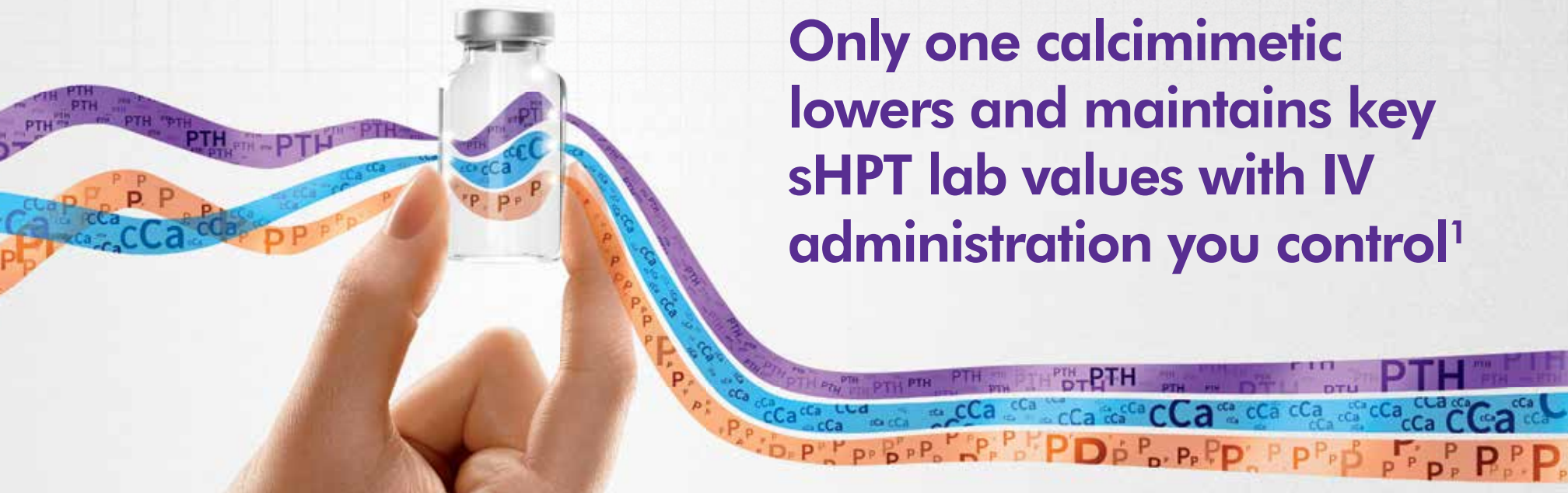
The researchers created a simple decision tree to assess the economic impact of simultaneous versus sequential evaluation of multiple potential living kidney donors. In many transplant programs, donors are evaluated one at a time, to avoid the costs of performing unnecessary evaluations.

The costs of evaluation were indeed higher when two candidates were evaluated simultaneously: $1266 (Canadian dollars) higher than sequential evaluation. However, simultaneous evaluation was also associated with a shorter time to kidney transplantation: 1 month shorter than with sequential evaluation.

The reduction in time to transplantation avoided $6931 in dialysis costs; total savings were $5665 per intended recipient. Other benefits included a 1% increase in living-donor kidney transplants and improved quality of life for recipients, due to less time on dialysis.

For potential recipients who had not yet started dialysis, simultaneous evaluation was also associated with a 2% reduction in the rate of dialysis initiation. Simultaneous evaluation of three or four potential donors had similar benefits.

Evaluating multiple potential living kidney donors simultaneously is the "dominant strategy" in terms of cost-effectiveness, compared to sequential evaluation. Savings accrue from having the recipient spend less time on dialysis, or from starting dialysis in the first place. The investigators conclude: "Evaluating up to four living donor candidates simultaneously rather than sequentially is one cost-effective solution to reduce the overall costs of healthcare and improve outcomes in this population" [Habbous S, et al. Evaluating multiple living kidney donor candidates simultaneously is more cost-effective than sequentially. *Kidney Int* 2020; DOI: https://doi.org/10.1016/j.kint.2020.06.015]. ■



Only one calcimimetic lowers and maintains key sHPT lab values with IV administration you control[1]

Not an actual Parsabiv™ vial.
The displayed vial is for illustrative purposes only.

Measure corrected serum calcium prior to initiation of Parsabiv™. Do not initiate in patients if the corrected serum calcium is less than the lower limit of normal. Monitor corrected serum calcium within 1 week after initiation or dose adjustment and every 4 weeks during treatment with Parsabiv™. Measure PTH 4 weeks after initiation or dose adjustment of Parsabiv™. Once the maintenance dose has been established, measure PTH per clinical practice.

Indication

Parsabiv™ (etelcalcetide) is indicated for the treatment of secondary hyperparathyroidism (HPT) in adult patients with chronic kidney disease (CKD) on hemodialysis.

Limitations of Use:

Parsabiv™ has not been studied in adult patients with parathyroid carcinoma, primary hyperparathyroidism, or with CKD who are not on hemodialysis and is not recommended for use in these populations.

Important Safety Information

Contraindication: Parsabiv™ is contraindicated in patients with known hypersensitivity to etelcalcetide or any of its excipients. Hypersensitivity reactions, including pruritic rash, urticaria, and face edema, have occurred.

Hypocalcemia: Parsabiv™ lowers serum calcium and can lead to hypocalcemia, sometimes severe. Significant lowering of serum calcium can cause QT interval prolongation and ventricular arrhythmia. Patients with conditions that predispose to QT interval prolongation and ventricular arrhythmia may be at increased risk for QT interval prolongation and ventricular arrhythmias if they develop hypocalcemia due to Parsabiv™. Closely monitor corrected serum calcium and QT interval in patients at risk on Parsabiv™.

Significant reductions in corrected serum calcium may lower the threshold for seizures. Patients with a history of seizure disorder may be at increased risk for seizures if they develop hypocalcemia due to Parsabiv™. Monitor corrected serum calcium in patients with seizure disorders on Parsabiv™.

Concurrent administration of Parsabiv™ with another oral calcimimetic could result in severe, life-threatening hypocalcemia. Patients switching from cinacalcet to Parsabiv™ should discontinue cinacalcet for at least 7 days prior to initiating Parsabiv™. Closely monitor corrected serum calcium in patients receiving Parsabiv™ and concomitant therapies known to lower serum calcium.

Worsening Heart Failure: In Parsabiv™ clinical studies, cases of hypotension, congestive heart failure, and decreased myocardial performance have been reported. Closely monitor patients treated with Parsabiv™ for worsening signs and symptoms of heart failure.

Upper Gastrointestinal Bleeding: In clinical studies, 2 patients treated with Parsabiv™ in 1253 patient years of exposure had upper gastrointestinal (GI) bleeding at the time of death. The exact cause of GI bleeding in these patients is unknown and there were too few cases to determine whether these cases were related to Parsabiv™.

Patients with risk factors for upper GI bleeding, such as known gastritis, esophagitis, ulcers or severe vomiting, may be at increased risk for GI bleeding with Parsabiv™. Monitor patients for worsening of common Parsabiv™ GI adverse reactions and for signs and symptoms of GI bleeding and ulcerations during Parsabiv™ therapy.

Adynamic Bone: Adynamic bone may develop if PTH levels are chronically suppressed.

Adverse Reactions: In clinical trials of patients with secondary HPT comparing Parsabiv™ to placebo, the most common adverse reactions were blood calcium decreased (64% vs. 10%), muscle spasms (12% vs. 7%), diarrhea (11% vs. 9%), nausea (11% vs. 6%), vomiting (9% vs. 5%), headache (8% vs. 6%), hypocalcemia (7% vs. 0.2%), and paresthesia (6% vs. 1%).

Please see Brief Summary of full Prescribing Information on adjacent page.

IV = intravenous; sHPT = secondary hyperparathyroidism; PTH = parathyroid hormone; P = phosphate; cCa = corrected calcium.

Reference: 1. Parsabiv™ (etelcalcetide) prescribing information, Amgen.

Parsabiv™
(etelcalcetide) Injection for intravenous use
2.5mg/0.5mL | 5mg/1mL | 10mg/2mL

Visit **ParsabivHCP.com** for more information.

BRIEF SUMMARY OF PRESCRIBING INFORMATION

Parsabiv™
(etelcalcetide) Injection for intravenous use
2.5mg/0.5mL | 5mg/1mL | 10mg/2mL

Please see package insert for full Prescribing Information.

INDICATIONS AND USAGE

PARSABIV is indicated for the treatment of secondary hyperparathyroidism (HPT) in adult patients with chronic kidney disease (CKD) on hemodialysis.

Limitations of Use:

PARSABIV has not been studied in adult patients with parathyroid carcinoma, primary hyperparathyroidism, or with chronic kidney disease who are not on hemodialysis and is not recommended for use in these populations.

CONTRAINDICATIONS

Hypersensitivity

PARSABIV is contraindicated in patients with known hypersensitivity to etelcalcetide or any of its excipients. Hypersensitivity reactions, including pruritic rash, urticaria, and face edema, have occurred with PARSABIV *[see Adverse Reactions (6.1) in PARSABIV full prescribing information]*.

WARNINGS AND PRECAUTIONS

Hypocalcemia

PARSABIV lowers serum calcium *[see Adverse Reactions (6.1) in PARSABIV full prescribing information]* and can lead to hypocalcemia, sometimes severe. Significant lowering of serum calcium can cause paresthesias, myalgias, muscle spasms, seizures, QT interval prolongation, and ventricular arrhythmia.

QT Interval Prolongation and Ventricular Arrhythmia

In the combined placebo-controlled studies, more patients treated with PARSABIV experienced a maximum increase from baseline of greater than 60 msec in the QTcF interval (0% placebo versus 1.2% PARSABIV). In these studies, the incidence of a maximum post-baseline predialysis QTcF > 500 msec in the placebo and PARSABIV groups was 1.9% and 4.8%, respectively *[see Adverse Reactions (6.1) in PARSABIV full prescribing information]*. Patients with congenital long QT syndrome, history of QT interval prolongation, family history of long QT syndrome or sudden cardiac death, and other conditions that predispose to QT interval prolongation and ventricular arrhythmia may be at increased risk for QT interval prolongation and ventricular arrhythmias if they develop hypocalcemia due to PARSABIV. Closely monitor corrected serum calcium and QT interval in patients at risk receiving PARSABIV.

Seizures

Significant reductions in corrected serum calcium may lower the threshold for seizures. Patients with a history of seizure disorder may be at increased risk for seizures if they develop hypocalcemia due to PARSABIV. Monitor corrected serum calcium in patients with seizure disorders receiving PARSABIV.

Concurrent administration of PARSABIV with another oral calcium-sensing receptor agonist could result in severe, life-threatening hypocalcemia. Patients switching from cinacalcet to PARSABIV should discontinue cinacalcet for at least 7 days prior to initiating PARSABIV *[see Dosage and Administration (2.4) in PARSABIV full prescribing information]*. Closely monitor corrected serum calcium in patients receiving PARSABIV and concomitant therapies known to lower serum calcium.

Measure corrected serum calcium prior to initiation of PARSABIV. Do not initiate in patients if the corrected serum calcium is less than the lower limit of normal. Monitor corrected serum calcium within 1 week after initiation or dose adjustment and every 4 weeks during treatment with PARSABIV *[see Dosage and Administration (2.2) in PARSABIV full prescribing information]*. Educate patients on the symptoms of hypocalcemia, and advise them to contact a healthcare provider if they occur.

If corrected serum calcium falls below the lower limit of normal or symptoms of hypocalcemia develop, start or increase calcium supplementation (including calcium, calcium-containing phosphate binders, and/or vitamin D sterols or increases in dialysate calcium concentration). PARSABIV dose reduction or discontinuation of PARSABIV may be necessary *[see Dosage and Administration (2.2) in PARSABIV full prescribing information]*.

Worsening Heart Failure

In clinical studies with PARSABIV, cases of hypotension, congestive heart failure, and decreased myocardial performance have been reported. In clinical studies, heart failure requiring hospitalization occurred in 2% of PARSABIV-treated patients and 1% of placebo-treated patients. Reductions in corrected serum calcium may be associated with congestive heart failure, however, a causal relationship to PARSABIV could not be completely excluded. Closely monitor patients treated with PARSABIV for worsening signs and symptoms of heart failure.

Upper Gastrointestinal Bleeding

In clinical studies, two patients treated with PARSABIV in 1253 patient-years of exposure had upper gastrointestinal (GI) bleeding noted at the time of death while no patient in the control groups in 384 patient-years of exposure had upper GI bleeding noted at the time of death. The exact cause of GI bleeding in these patients is unknown, and there were too few cases to determine whether these cases were related to PARSABIV.

Patients with risk factors for upper GI bleeding (such as known gastritis, esophagitis, ulcers, or severe vomiting) may be at increased risk for GI bleeding while receiving PARSABIV treatment. Monitor patients for worsening of common GI adverse reactions of nausea and vomiting associated with PARSABIV *[see Adverse Reactions (6.1) in PARSABIV full prescribing information]* and for signs and symptoms of GI bleeding and ulcerations during PARSABIV therapy. Promptly evaluate and treat any suspected GI bleeding.

Adynamic Bone

Adynamic bone may develop if PTH levels are chronically suppressed. If PTH levels decrease below the recommended target range, the dose of vitamin D sterols and/or PARSABIV should be reduced or therapy discontinued. After discontinuation, resume therapy at a lower dose to maintain PTH levels in the target range *[see Dosage and Administration (2.1) in PARSABIV full prescribing information]*.

ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the labeling:

- Hypocalcemia *[see Warnings and Precautions (5.1) in PARSABIV full prescribing information]*
- Worsening Heart Failure *[see Warnings and Precautions (5.2) in PARSABIV full prescribing information]*
- Upper Gastrointestinal Bleeding *[see Warnings and Precautions (5.3) in PARSABIV full prescribing information]*
- Adynamic Bone *[see Warnings and Precautions (5.4) in PARSABIV full prescribing information]*

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

The data in Table 2 are derived from two placebo-controlled clinical studies in patients with chronic kidney disease and secondary hyperparathyroidism on hemodialysis. The data reflect exposure of 503 patients to PARSABIV with a mean duration of exposure to PARSABIV of 23.6 weeks. The mean age of patients was approximately 58 years, and 60% of the patients were male. Of the total patients, 67% were Caucasian, 28% were Black or African American, 2.6% were Asian, 1.2% were Native Hawaiian or Other Pacific Islander, and 1.6% were categorized as Other.

Table 2 shows common adverse reactions associated with the use of PARSABIV in the pool of placebo-controlled studies. These adverse reactions occurred more commonly on PARSABIV than on placebo and were reported in at least 5% of patients treated with PARSABIV.

Table 2: Adverse Reactions Reported in ≥ 5% of PARSABIV-Treated Patients

Adverse Reaction*	Placebo (N = 513)	PARSABIV (N = 503)
Blood calcium decreased[a]	10%	64%
Muscle spasms	7%	12%
Diarrhea	9%	11%
Nausea	6%	11%
Vomiting	5%	9%
Headache	6%	8%
Hypocalcemia[b]	0.2%	7%
Paresthesia[c]	1%	6%

*Included adverse reactions reported with at least 1% greater incidence in the PARSABIV group compared to the placebo group

[a] Asymptomatic reductions in calcium below 7.5 mg/dL or clinically significant asymptomatic reductions in corrected serum calcium between 7.5 and < 8.3 mg/dL (that required medical management)

[b] Symptomatic reductions in corrected serum calcium < 8.3 mg/dL

[c] Paresthesia includes preferred terms of paresthesia and hypoesthesia

Other adverse reactions associated with the use of PARSABIV but reported in < 5% of patients in the PARSABIV group in the two placebo-controlled clinical studies were:

- Hyperkalemia: 3% and 4% for placebo and PARSABIV, respectively.
- Hospitalization for Heart Failure: 1% and 2% for placebo and PARSABIV, respectively.
- Myalgia: 0.2% and 2% for placebo and PARSABIV, respectively.
- Hypophosphatemia: 0.2% and 1% for placebo and PARSABIV, respectively.

Description of Selected Adverse Reactions

Hypocalcemia

In the combined placebo-controlled studies, a higher proportion of patients on PARSABIV developed at least one corrected serum calcium value below 7.0 mg/dL (7.6% PARSABIV, 3.1% placebo), below 7.5 mg/dL (27% PARSABIV, 5.5% placebo), and below 8.3 mg/dL (79% PARSABIV, 19% placebo). In the combined placebo-controlled studies, 1% of patients in the PARSABIV group and 0% of patients in the placebo group discontinued treatment due to an adverse reaction attributed to a low corrected serum calcium.

Hypophosphatemia

In the combined placebo-controlled studies, 18% of patients treated with PARSABIV and 8.2% of patients treated with placebo had at least one measured phosphorus level below the lower normal limit (i.e., 2.2 mg/dL).

QTc Interval Prolongation Secondary to Hypocalcemia

In the combined placebo-controlled studies, more patients treated with PARSABIV experienced a maximum increase from baseline of greater than 60 msec in the QTcF interval (0% placebo versus 1.2% PARSABIV). The patient incidence of maximum post-baseline predialysis QTcF > 500 msec in the placebo and PARSABIV groups was 1.9% and 4.8%, respectively.

Hypersensitivity

In the combined placebo-controlled studies, the subject incidence of adverse reactions potentially related to hypersensitivity was 4.4% in the PARSABIV group and 3.7% in the placebo group. Hypersensitivity reactions in the PARSABIV group were pruritic rash, urticaria, and face edema.

Immunogenicity

As with all peptide therapeutics, there is potential for immunogenicity. The detection of anti-drug binding antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to etelcalcetide with the incidence of antibodies to other products may be misleading.

In clinical studies, 7.1% (71 out of 995) of patients with secondary hyperparathyroidism treated with PARSABIV for up to 6 months tested positive for binding anti-etelcalcetide antibodies. Fifty-seven out of 71 had pre-existing anti-etelcalcetide antibodies.

No evidence of altered pharmacokinetic profile, clinical response, or safety profile was associated with pre-existing or developing anti-etelcalcetide antibodies. If formation of anti-etelcalcetide binding antibodies with a clinically significant effect is suspected, contact Amgen at 1-800-77-AMGEN (1-800-772-6436) to discuss antibody testing.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

There are no available data on the use of PARSABIV in pregnant women. In animal reproduction studies, effects were seen at doses associated with maternal toxicity that included hypocalcemia. In a pre- and post-natal study in rats administered etelcalcetide during organogenesis through delivery and weaning, there was a slight increase in perinatal pup mortality, delay in parturition, and transient effects on pup growth at exposures 1.8 times the human exposure for the clinical dose of 15 mg three times per week. There was no effect on sexual maturation, neurobehavioral, or reproductive function in the rat offspring. In embryo-fetal studies, when rats and rabbits were administered etelcalcetide during organogenesis, reduced fetal growth was observed at exposures 2.7 and 7 times exposures for the clinical dose, respectively.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

Animal Data

There were no effects on embryo-fetal development in Sprague-Dawley rats when etelcalcetide was dosed at 0.75, 1.5, and 3 mg/kg/day by the intravenous route during organogenesis (pre-mating to gestation day 17) at exposures up to 1.8 times human exposures at the clinical dose of 15 mg three times per week based on AUC. No effects on embryo-fetal development were observed in New Zealand White rabbits at doses of etelcalcetide of 0.375, 0.75, and 1.5 mg/kg by the intravenous route (gestation day 7 to 19), representing up to 4.3 times human exposures based on AUC. In separate studies at higher doses of 4.5 mg/kg in rats (gestation days 6 to 17) and 2.25 mg/kg in rabbits (gestation days 7 to 20), representing 2.7 and 7 fold clinical exposures, respectively, there was reduced fetal growth associated with maternal toxicities of hypocalcemia, tremoring, and reductions in body weight and food consumption.

In a pre- and post-natal development study in Sprague-Dawley rats administered etelcalcetide at 0.75, 1.5, and 3 mg/kg/day by the intravenous route (gestation day 7 to lactation day 20), there was a slight increase in perinatal pup mortality, delay in parturition, and transient reductions in post-natal growth at 3 mg/kg/day (representing 1.8-fold human exposures at the clinical dose of 15 mg three times per week based on AUC), associated with maternal toxicities of hypocalcemia, tremoring, and reductions in body weight and food consumption. There were no effects on sexual maturation, neurobehavioral, or reproductive function at up to 3 mg/kg/day, representing exposures up to 1.8-fold human exposure based on AUC.

Lactation

Risk Summary

There are no data regarding the presence of PARSABIV in human milk or effects on the breastfed infant or on milk production. Studies in rats showed [^{14}C]-etelcalcetide was present in the milk at concentrations similar to plasma. Because of the potential for PARSABIV to cause adverse effects in breastfed infants including hypocalcemia, advise women that use of PARSABIV is not recommended while breastfeeding.

Data

Presence in milk was assessed following a single intravenous dose of [^{14}C]-etelcalcetide in lactating rats at maternal exposures similar to the exposure at the human clinical dose of 15 mg three times per week. [^{14}C]-etelcalcetide-derived radioactivity was present in milk at levels similar to plasma.

Pediatric Use

The safety and efficacy of PARSABIV have not been established in pediatric patients.

Geriatric Use

Of the 503 patients in placebo-controlled studies who received PARSABIV, 177 patients (35.2%) were ≥ 65 years old and 72 patients (14%) were ≥ 75 years old.

No clinically significant differences in safety or efficacy were observed between patients ≥ 65 years and younger patients (≥ 18 and < 65 years old). No differences in plasma concentrations of etelcalcetide were observed between patients ≥ 65 years and younger patients (≥ 18 and < 65 years old).

OVERDOSAGE

There is no clinical experience with PARSABIV overdosage. Overdosage of PARSABIV may lead to hypocalcemia with or without clinical symptoms and may require treatment. Although PARSABIV is cleared by dialysis, hemodialysis has not been studied as a treatment for PARSABIV overdosage. In the event of overdosage, corrected serum calcium should be checked and patients should be monitored for symptoms of hypocalcemia, and appropriate measures should be taken *[see Warnings and Precautions (5.1) in PARSABIV full prescribing information]*.

AMGEN®

PARSABIV™ (etelcalcetide)

Manufactured for:
KAI Pharmaceuticals, Inc., a wholly owned subsidiary of Amgen, Inc.
One Amgen Center Drive
Thousand Oaks, California 91320-1799

Patent: http://pat.amgen.com/Parsabiv/

Physician Fee Schedule Changes a Win for Nephrologists, Home Dialysis

By David White

Nephrologists will see payment increases in some services starting January 1, 2021, according to the proposed rule on the annual physician fee schedule released last month by the Centers for Medicare & Medicaid Services (CMS). In general, nephrology will see an overall 6% increase with an approximately 30% increase for home dialysis services.

Anupam Agarwal, MD, FASN, ASN President, praised the move by CMS: "Finally, after years of advocacy by ASN, Medicare is supporting nephrologists with rates that better reflect our work. Most importantly, this is a big win for home dialysis, a top priority for ASN."

Payment and codes

CMS also proposed changes to the payment of transitional care management (TCM) and what codes can be billed with TCM services (Table 1). CMS added 14 End Stage Renal Disease (ESRD) codes to the list that may be billed with the TCM. TCM accounts for all the services by clinicians during the 30-day post-discharge period for patients discharged from hospitals. This includes the 7- or 14-day face-to-face visit. This visit does not have to meet a documentation level of service such as a 99214 or 99215 other than the medical decision-making component.

The increase in nephrology payments was due to the upward adjustment of relative value units (RVUs) being updated and applied to nephrology billing codes. However, the calculation of RVUs to adjust home dialysis rates became a source of great confusion at the time of the release of the proposed rule. The text of the proposed rule stated the RVU adjustment for CPT 90966 showed an increase from 4.26 to 8.04 RVUs—signaling an 89% increase for home dialysis rates. However, attached to the proposed rule was an Excel spreadsheet showing an increase to 5.52 RVUs for home dialysis establishing parity with two to three in-center MCP visits or a 31% reimbursement increase. This confusion led some in the kidney community to speculate that there had been a behind-the-scenes battle over "how much" to raise home dialysis reimbursement.

Telehealth

The kidney community had expected a set of recommendations regarding which telehealth waivers or expansions made under the public health emergency (PHE) owing to COVID-19 might be made permanent for those CMS has the authority to extend and and an indication of those the agency believes Congress will need to take action to extend. For the most part, this did not happen. Instead, CMS placed most ESRD-related service expansions in a newly created Category 3—the future of which is far from clear in the proposed rule. CMS invited comment on the fate of items in Category 3 as to whether commenters want the waivers/expansions to be made permanent. The American Society of Nephrology (ASN) is preparing comments on telehealth expansions and other nephrology-related changes under the PHE. Those comments are due to Medicare by October 5, 2020.

For the most part, the following are the telehealth changes to Medicare in the PHE:

- Geographic and site restrictions were waived. Telehealth services were available across the country, allowing originating sites to be everywhere including the home and dialysis facilities.
- Provider lists were expanded, adding care team members to those originally approved to conduct and bill for telehealth services.
- Services were expanded, adding over 80 additional codes, including those for home and in-center dialysis.
- Modalities including video were expanded to include audio only in some cases.
- Supervision and licensing requirements were relaxed.
- Payment parity was established for audio only when asynchronous video/audio is not possible.
- Telehealth was opened to new patients in addition to existing patients.

Making these changes permanent requires action by either CMS or Congress depending on the change.

- Geographic and site restrictions would need congressional action to become permanent.
- Changes to the modality (audio/video) requirements do not require congressional action; however, CMS is unlikely to take action without congressional approval. Federal law only requires it to be a telecommunications system, but in regulations CMS has required it to be an "interactive" telecommunications system—not audio only—while also using language prohibiting phones from meeting that definition. The phone language, however, was amended and is likely to remain permanently.
- Permanent expansion of providers able to provide telehealth and bill for it would also require congressional action.
- Permanent expansion of services (expanding CPT codes approved for telehealth), for the most part, can be done by CMS.

Medicare appears to be cautiously awaiting both congressional approval and healthcare stakeholder support.

Quality Payment Program

As of 2019, and the release of the proposed physician fee schedule for calendar year 2020, CMS has included the Quality Payment Program (QPP) within the fee schedule rule. Previously, it had its own separate set of rule-making. The QPP, the value-based payment system that went into effect on January 1, 2017, has two payment pathways: Merit-based Incentive Payment System (MIPS) and Advanced Alternative Payment Models (AAPM). Not many major changes were proposed for calendar year 2021, and most of those included were prescribed by statute when Congress created the program in 2015. Here are a few proposed changes:

- Beginning Merit-based Incentive Payment System (MIPS) Value Pathways (MVPs) implementation was delayed until 2022 instead of 2021.
- Increasing the performance threshold from 45 points for the 2020 performance year to 50 points for 2021 (10 points less than the 60-point threshold finalized for 2021 in the CY 2020 PFS Rule due to the PHE).
- Revising performance category weights for Quality (decreases from 45% to 40%) and Cost (increases from 15% to 20%).
- Removing the CMS Web Interface as a collection type and submission type for reporting MIPS quality measures beginning with the 2021 performance period.
- Sunsetting the Alternative Payment Model (APM) Scoring Standard and allowing MIPS-eligible clinicians in APMs the option to participate in MIPS and submit data at the individual, group, or APM Entity level.
- Updating third party intermediary approval criteria as well as remedial action and termination criteria.

New APM Performance Pathway (APP) in 2021; Complex Patient Bonus COVID-19 Update

CMS also proposes implementing an APP ahead of schedule in 2021. Performance category weights under the APP would be: 50% for Quality, 30% for Promoting Interoperability, and 20% for Improvement Activities.

The APP would be:

- complementary to MVPs, composed of a fixed set of measures for each performance category.
- available only for MIPS-eligible clinicians in MIPS, APMs, and
- reported by individual eligible clinicians, groups, or APM Entities.

Medicare is also proposing to make a one-year only adjustment for 2021 to increase the complex patient bonus from a 5- to 10-point maximum for clinicians, groups, virtual groups, and APM Entities for 2020 performance only to offset the additional complexity of the patient population due to COVID-19.

Table 1. ESRD codes that may be paired with TCM services beginning in calendar year 2021

Code Family	CPT Code	Descriptor
End Stage Renal Disease Services (for ages less than 2 months through 20+ years)	90951	ESRD related services with 4 or more face-to-face visits per month; for patients <2 months of age
	90954	ESRD related services with 4 or more face-to-face visits per month; for patients 2-11 years
	90955	ESRD related services with 2-3 face-to-face visits per month; for patients 2-11 years
	90956	ESRD related services with 1 face-to-face visit per month; for patients 2-11 years
	90957	ESRD related services with 4 or more face-to-face visits per month; for patients 12-19 years
	90958	ESRD related services with 2-3 face-to-face visits per month; for patients 12-19 years
	90959	ESRD related services with 1 face-to-face visit per month; for patients 12-19 years
	90963	ESRD related services for home dialysis per full month; for patients <2 years of age
	90964	ESRD related services for home dialysis per full month; for patients 2-11 years
	90965	ESRD related services for home dialysis per full month; for patients 12-19 years
	90966	ESRD related services for home dialysis per full month; for patients 20 years and older
	90967	ESRD related services for dialysis less than a full month of service; per day; for patients <2 years of age
	90968	ESRD related services for dialysis less than a full month of service; per day; for patients 2-11 years
	90969	ESRD related services for dialysis less than a full month of service; per day; for patients 12-19 years
Complex Chronic Care Management Services	G2058	Chronic care management services, each additional 20 minutes of clinical staff time directed by a physician or other qualified healthcare professional, per calendar month

Courtesy Department of Health and Human Services, Centers for Medicare & Medicaid Services, 42 CFR parts 410, 414, 415, 423, 424, and 425

Telehealth in Rural America: Q and A

A recent report from the Department of Health and Human Services (HHS) shows the impact the COVID-19 public health emergency has had on the expansion and increased utilization of telehealth. Medicare fee-for-service primary care visits provided through telehealth in April 2020 jumped to 43.5%, compared to far less than 1% in February 2020, before the public health emergency (1).

Kidney News invited Scott Bieber, DO, ASN Quality Committee chair, and Terrence Jay O'Neil, MD, FASN, ASN Quality Committee member, two nephrologists practicing in rural communities, to discuss how their practices are providing kidney care via telehealth and the particular challenges that rural Americans face. Dr. Bieber's practice covers the entire panhandle of northern Idaho, from the border of Canada to the lake regions of Coeur d' Alene and Sandpoint all the way south to farming regions of the Palouse in Moscow and east to the mining towns around Kellogg and the mountainous border between Idaho and Montana. Dr. O'Neil's practice area runs from Marion, Virginia, in the east to Sevierville, Tennessee, in the west, and from Harlan, Kentucky, south to near Asheville, North Carolina.

We have seen exponential growth in use of telehealth during the COVID-19 pandemic. How has that worked in your areas?

Bieber: In Coeur d' Alene, where our main practice site is located, telehealth has for the most part gone very well with some rare exceptions for patients who live outside the city in areas where cell access is spotty in their homes and they maybe do not have Internet or WiFi. In the outreach clinics of Kellogg and Moscow, it has been worse. The entire city of Kellogg lacks access to high speed Internet, and there are some real gaps in cell phone coverage inside the city (my cell does not get signal from our outreach clinic there). Most of the people who live out there are in the mountains and their coverage is zero. Similar problems exist over in the Palouse. Some patients do not have cell phone coverage at their farms or homes and have no Internet access. This means the telephone is the only way we can reach them.

O'Neil: In East Tennessee, I have been working with the James Quillen Veterans Affairs Medical Center (VAMC) to create a tele-video preventive renal care education program for veterans with identified chronic kidney disease at risk for progressive kidney insufficiency. This tele-video program is intended to replace a program created 6 years ago that used a model of group meetings of veterans and their families at the VAMC main campus and each of the six community-based outpatient clinics. The James Quillen VAMC has been very involved in creating a telehealth infrastructure to provide face-to-face voice or (where possible) voice-and-video telehealth to East Tennessee veterans. There have been problems, however, that have tended to deny access to such programs to those most in need—the rural less-well-off Appalachian region veterans.

Are you experiencing what is called the digital divide, or constraints due to broadband access? What have been your experiences? Have you had to change approaches due to broadband challenges?

Bieber: Yes. When it comes to telehealth, of course a telephone call is better than nothing, but a video connection is better than a telephone call alone. Being able to visually see the patient makes a big difference in my ability to recognize and troubleshoot potential problems. In general, due to poor connectivity, we have not been able to provide reliable telehealth services to those patients in the outreach clinics. We leave the choice for a phone call or in-person visit up to the patient and nearly all patients have decided it is better to come to see us in the clinic.

O'Neil: Yes. According to HighSpeedInternet.com, the average download speed in Tennessee is 12 MBPS and only 82% of Tennesseans have access to a bandwidth of 25 MBPS or more. Keep in mind that download speeds are considerably greater than upload speeds, and secure adequate video at the provider end requires a symmetrical upload for good audio and video. The bandwidth considered best for a business-grade tele-video connection is 50 MBPS. DSL connections are generally inadequate and found mostly in the urban regions around Memphis and Nashville.

If cable broadband access is not available, cellular can substitute, but only when there is adequate signal strength. A review of the (generally overly generous) commercial accessibility maps such as the Multi-Providers Cellular Coverage Maps shows that there are significant pockets of north-central and eastern Tennessee where coverage is sparse or nonexistent. Many veterans live in exactly those areas. Also, cellular data charges escalate rapidly beyond the ability of rural veterans of reduced means who own cell phones to support tele-video connections as they use up gigabytes of data rapidly. And there are many still using landline dial-ups.

There is currently no mechanism in place to pay veterans for the cost of enhanced data/bandwidth plans, even where such plans are available. The current ISP business model is effectively a regional monopoly, and in many areas of rural Tennessee Internet providers have no economic incentive to put expensive cable installations in areas where population density and income would not return a good profit on investment.

What technology do your patients own or have access to (computers, tablets, phones)? How well do they use them?

Bieber: Most people here have a cell phone, but many do not have a smart phone or Internet-capable phone. I continue to be surprised at the number of people who live here who simply do not want to have a smart phone and prefer a standard old school flip phone. Most have a computer or tablet at home but that is hit-and-miss as well. Many do not have one and if they do it is sort of irrelevant to what we can do for them with telehealth because their Internet provider can't deliver a reliable real time video connection.

O'Neil: Veterans living in the more urban and suburban regions of Tennessee have cable access of some sort. Fairly quickly as one gets into the mountains adjacent to North Carolina, Kentucky, and Virginia, however, the population may have a landline phone or a burner cell phone. Many do not have any computers of any kind. Where there is available Internet access, the VAMC has been loaning Internet-capable iPads. However, many of the same families who lack any form of computer also lack Internet connectivity. The VAMC provides automated blood pressure (BP) cuffs and weighing scales with memory, and if the connection is adequate, those can telemeter the BP and daily weights back to the telehealth office for transmittal to the primary care provider.

How about cell phone coverage? What are the least-served areas? What do you do in those cases?

Bieber There are many areas in Idaho that do not get cell phone coverage. The least served areas are the mountainous areas and rural farming areas, particularly the farther away you get from major highways or interstates, but even some of the highways I travel have cell phone coverage gaps. Those patients usually elect to come and see us in person, or we do a telephone encounter over a landline.

O'Neil: Much like the situation Dr. Bieber described in Idaho, veterans living in several east and northeast Tennessee regions lack adequate cell phone coverage. Where landlines exist (and some do not have even that), audio-only telehealth is practiced, but with the caveat that face-to-face medical encounters are still required for basic physical parameter documentation (BP, pulse, weight) and physical examination of organs at risk (eyes, ears) as well as crucial laboratory monitoring.

What other thoughts and observations would you like to share?

Bieber: This is a complicated problem. On the one hand, it seems there are certain people who are being left behind due to lack of cell phone and Internet services in the area in which they reside. On the other hand, part of what draws many of these patients to live in areas that are underserved is their desire to be "off the grid," so to speak. Many of them are perfectly happy not having Internet or cell phones. From a healthcare provider's perspective, what I feel is most important is that we meet patients where they are with regard to technical abilities and continue to have the flexibility to decide what type of encounter is going to work best for that particular patient and clinical situation. I hope that rules and regulations continue to work to facilitate more options for patients to choose how they receive their care.

O'Neil: I agree with Dr. Bieber's comments regarding Idaho. Additionally, whereas it is true that many of those who live in digitally underserved areas of Tennessee choose to do so, many are in health and demographic groups most at risk for progressive disease and premature death or disability. Their particular reason for living in those areas may indeed be due to a desire to be less digitally accessible, but many are there because the communities they reside in have suffered collapsed mining economies and they lack either the means or the motivation to move.

In the 1930s and 1940s, large stretches of the Appalachian and Blue Ridge Mountain regions had no access to electricity, and the people living in those areas adapted. However, farm productivity was low, and it became a recognized national priority through the Tennessee Valley Authority program to ensure that electricity was accessible by every American, however rural. Today, digital connectivity correlates strongly with educational attainment and prosperity. A program to alter or supplement the private for-profit ISP business model would be justified to ensure that the minimum Internet connectivity judged technically necessary to support distance learning and medical telehealth is available to every American.

Reference

1. https://aspe.hhs.gov/pdf-report/medicare-beneficiary-use-telehealth

"Interventional Nephrology: Evolution, Challenges, and Opportunities" is the theme of this special issue of *Kidney News*. The field of interventional nephrology covers an area that is common to nephrologists, vascular surgeons, and interventional radiologists. In 2000, the American Society of Diagnostic and Interventional Nephrology (ASDIN) was founded, with the mission of promoting excellence in dialysis access care and improving outcomes for patients with kidney disease.

We have gathered here articles by several interventional nephrologists who share their thoughts and experiences in this growing and exciting field. In looking at the recently published KDOQI Vascular Access Guidelines, we have included the viewpoints of a clinician and a patient, as well as thoughtful consideration of the guidelines' application in the international arena as written by Dr. Dalia Dawoud, Mr. Evan Coaker, and Dr. Vivekanand Jha, respectively. Dr. Vandana Niyyar gives a primer on hemodialysis access. And with the recent development of percutaneous AVF, Dr. Umar Waheed discusses the current understanding of and experiences with the available pAVF technologies.

Also included are discussions of common problems and dilemmas in dialysis access for the general nephrologist. Dr. Bhavnish Bucktowarsing tackles a common problem of high flow AVF that interventional nephrologists typically encounter, while Dr. Aisha Shaikh and Dr. Loay Salman debate the controversial topic of ligating AV accesses when they are no longer in use. Last but not least, a topic that is germane to all nephrologists—as we all get the call no matter what the time of day, "Doctor, can we put a PICC line in your patient?"

We hope you enjoy and benefit from these concise discussions of very practical topics.

—Anil Agarwal, MD, FASN, FASDIN, and Edgar V. Lerma, MD, FASN, FASDIN, Editors

INTERVENTIONAL NEPHROLOGY

EVOLUTION, CHALLENGES, AND OPPORTUNITIES

By Anil Agarwal

Until a couple of decades ago, nephrology was extensively dependent for its procedural needs on other specialties, including surgery and radiology. Although nephrologists commonly performed kidney biopsies and nontunneled dialysis catheter placements, the non-nephrologists were mostly creating and maintaining arteriovenous and peritoneal dialysis (PD) accesses. With relatively minimal to modest communication, a multidisciplinary coordinated approach was lacking, leading to a fragmented approach to the care of dialysis access. Further, despite over half a century of tireless efforts to innovate, dialysis access was (and has been) an unrivaled challenge for patients with ESKD. As we long for perfection in achieving a consistent, reliable, inexpensive, and simple-to-use access, recent progress in the field of interventional nephrology (IN) has widened the options and choices for our patients. There is a noticeable glimmer of hope on the horizon, both for patients requiring kidney replacement therapy by dialysis and for those who remain in the midst of their daunting journey through kidney disease.

Evolution of interventional nephrology

The advent of IN in the United States about two decades ago was the product of accumulating frustration about the difficulty in provision of appropriate and timely creation and maintenance of dialysis access. A desire to improve outcomes led nephrologists to learn invasive techniques that were not taught in nephrology fellowships. This change in the paradigm of care was instantly appealing, especially to younger nephrologists, who then managed to learn access procedures from willing surgeons and interventionalists. An organized effort of a handful of these "interventional nephrologists" resulted in the formation of the American Society of Diagnostic and Interventional Nephrology (ASDIN), which over the years has become the world leader in IN and has influenced patient care around the globe.

The debate about the pros and cons of IN has largely subsided over the years, owing to a wide acceptance of this specialty (1). The impacts of IN are multidimensional. A few of the important positive impacts of IN are as follows:

Improvement in ESKD patient care

As the primary provider for patients across the spectrum of pre-ESKD care to providing care in the dialysis unit, the nephrologist is the natural care provider who truly understands the dilemmas and challenges of dialysis patients. The IN practitioner has the comprehensive tools to provide holistic care, from the management of underlying kidney disease and its complications to taking care of vascular access. Proactive planning, execution of an ESKD life plan, and seamless communication with the multidisciplinary team is implicit when the IN specialist is in charge of access. Several early articles alluded not only to the safety and efficacy but also to improved patient outcomes when interventional nephrologists provided care of dialysis access (2–4).

Reduction in inpatient resource utilization

Freestanding vascular access centers free up precious and expensive hospital beds by avoiding hospital admissions for access-related procedures.

Continued on page 12 >

Evolution, challenges, and opportunities

Continued from page 11

Reduction in exposure of patients to the hospital environment

In the COVID-19 era, keeping the patient out of the hospital is a goal worth pursuing. Leading in the midst of crisis, ASDIN was instrumental in publishing a joint statement with the Vascular Access Society of America to ensure the uninterrupted performance of dialysis access procedures (5). The ASDIN has also advocated for appropriate reimbursement for care and has created opportunities for education and training.

Reduction in healthcare expenditures

Prompt outpatient management, avoidance of unnecessary temporary dialysis catheter placements, and prevention of access thrombosis by timely intervention can save costs.

Impact on patient care worldwide

ASDIN educational programs have inspired the evolution of multiple other interventional nephrology societies specific to countries and regions. This has significantly affected the care of dialysis patients worldwide.

Challenges

The early challenges for IN were enormous, starting with difficulty in obtaining training, turf wars with established providers, and acceptance by other healthcare professionals of their unfamiliar role. Diligence and the wisdom of early interventional nephrologists in publishing the results of their interventions soon established the safety and efficacy of IN procedures done by nephrologists (2).

Now, IN faces new challenges. Interventional training, though more accessible now, is still freely available. There is a relatively small workforce of interventionalists. The scarcity of academic IN programs and a lack of focus on dialysis access has resulted in a lack of fellowship training in dialysis access. Drastic reimbursement cuts for interventional procedures over the years have dissuaded many well-intentioned nephrologists from learning these techniques. The dearth of organized research efforts in dialysis access is striking, considering there are over half a million dialysis patients in the United States alone. Provider apathy toward dialysis access is still noticeable in many areas. We need a wider focus that includes dialysis access and the inclusion of new procedural technologies for patient care.

Opportunities

There are exciting opportunities in the field of dialysis access. Special areas with new approaches are as follows:

Technological advancements

AV access: In the past, many interventional nephrologists learned traditional surgical arteriovenous (AVF) creation with success rates second to none. The very recent innovations in percutaneous endovascular AVF (endo AVF, eAVF) creation use two different devices that place AVF creation squarely in the hands of interventional nephrologists. Bioengineered vessels have become available for AVF creation. Percutaneous graft creation is in advanced stages of development (6).

PD catheter insertion: Initially, nephrologists used to blindly insert PD catheters at the bedside. This technique then evolved into laparoscopic and peritoneoscopic placement and also in open surgical placement in appropriate cases. Fluoroscopic PD catheter placement has become common in the past decade and can be performed in the interventional suite without a need for extra equipment (7). With greater emphasis on home dialysis owing to the Advancing American Kidney Health executive order, this technique has the potential to become even more widespread.

As we long for perfection in achieving a consistent, reliable, inexpensive, and simple-to-use access, recent progress in the field of interventional nephrology has widened the options and choices for our patients.

Noninvasive techniques in patient care

Traditionally, nephrologists used ultrasonography to examine the urinary tract. Progress in technology has brought about the availability of bedside handheld ultrasonography, often known as POCUS (Point Of Care UltraSound), which has become a multifunctional tool. POCUS is destined to shorten the differential diagnosis of acute kidney failure (e.g., assessment of volume status and cardiac function and diagnosis of urinary obstruction) at the bedside. Examination of vascular access and measurement of flow at the bedside would also become a matter of minutes and help in understanding vascular access better. Cannulation of access would also become easier with the use of POCUS. This discipline is certain to become the modern attraction for trainees to nephrology, besides becoming an integral part of patient examination for many subspecialties. The ASDIN Ultrasound Committee is spearheading the POCUS certification process, which should become available very soon.

Focus on the patient, rather than on technology or procedures

A life plan—not only for ESKD patients but also for patients with CKD—is extremely important (8). The prevention and management of kidney disease by the use of new technologies should remain an essential part of care.

Globalization of access care

Access issues are prevalent worldwide. As a leader through its Global Access Workgroup, the ASDIN is collaborating with international partners to create a concerted focus on access care.

Research opportunities

To improve research in dialysis access, the ASDIN started giving research grants several years ago. There is an ongoing effort in this area to make additional short-term clinical project funding available to multiple candidates every year to help solve the common clinical problems of our patients.

In summary, the scope of IN is widening. This discipline is on the rise, and the peak of the incline is not even close! The future is bright for our patients, and the days of desolation are over for dialysis access. ■

Anil Agarwal, MD, FASN, FASDIN, is chief of medicine, VA Central California Health Care System, and professor of medicine, University of California San Francisco, Fresno.

References

1. Agarwal AK. Pros and cons of interventional nephrology. *Renal and Urology News*. 2010. https://www.renalandurologynews.com/home/departments/commentary/the-pros-and-cons-of-interventional-nephrology/. Accessed July 14, 2020.
2. Beathard GA, Litchfield T. Effectiveness and safety of dialysis vascular access procedures performed by interventional nephrologist. *Kidney Int* 2004; 66:1622–1632. doi: 10.1111/j.1523-1755.2004.00928.x
3. Mishler R, et al. Dedicated outpatient vascular access center decreases hospitalization and missed outpatient dialysis treatments. *Kidney Int* 2006; 69:393–398. doi: 10.1038/sj.ki.5000066
4. Arnold WP. Improvement in hemodialysis vascular access outcomes in a dedicated access center. *Semin Dial* 2000; 13:359–363. doi: 10.1046/j.1525-139x.2000.00106.x
5. Hentschel DM, Agarwal AK, Lawson JH. Maintaining lifelines for ESKD patients: ASDIN and VASA joint statement. May 2020. https://cdn.ymaws.com/www.asdin.org/resource/resmgr/covid_19/Maintaining_lifelines_ASDIN_.pdf . Accessed July 14, 2020.
6. Agarwal AK, et al. Innovations in vascular access for hemodialysis. *Kidney Int* 2019; 95:1053–1063. doi: 10.1016/j.kint.2018.11.046
7. Abdel Aal AK, et al. Outcomes of fluoroscopic and ultrasound-guided placement versus laparoscopic placement of peritoneal dialysis catheters. *Clin Kidney J* 2018; 11:549–554. doi: 10.1093/ckj/sfx132
8. Executive order on Advancing American Kidney Health. July 10, 2019. https://www.whitehouse.gov/presidential-actions/executive-order-advancing-american-kidney-health/. Accessed July 14, 2020.
9. Lok CE, et al. KDOQI Clinical Practice Guideline for Vascular Access: 2019 Update. *Am J Kidney Dis* 2020; 75:S1–S164. doi: https://doi.org/10.1053/j.ajkd.2019.12.001

KDOQI Vascular Access Guidelines
A Clinician's Perspective

By Dalia Dawoud

In 1996, the Kidney Disease Outcomes Quality Initiative (KDOQI) was created by a multidisciplinary group of physicians with the support of the National Kidney Foundation. It was the first literature-based practice guideline and was developed with the hope of measurably improving the quality of life and clinical outcomes for dialysis patients. To achieve this objective, four work groups were created, one of which was dedicated to clinical practice guidelines related to vascular access for patients requiring hemodialysis (HD) (1). The vascular access guidelines have since undergone three updates: in 2000, 2006, and most recently, in 2019.

The 2019 vascular access guidelines have been expanded to 26 separate sets of guidelines that were based on review of more than 4600 publications. As with the earlier versions, evidence-based and opinion-based guidelines were differentiated; in the 2019 guidelines, each recommendation was qualified by using a "Grading of Recommendations Assessment, Development, and Evaluation" (GRADE) approach. Furthermore, when applicable, each guideline statement was accompanied by rationale/background information, a detailed justification, monitoring and evaluation guidance, implementation considerations, special discussions, and recommendations for future research (2).

From a clinician perspective, it is gratifying to see how the 2019 vascular access initiatives and guidelines have progressed from stringent recommendations, such as mandating specific thresholds of fistula or catheter prevalence, to a more clinically based approach that takes into consideration the individual patient context, such as patients with poor long-term prognoses and short life expectancies.

Since the Fistula First Initiative emerged from the 2001 KDOQI vascular access guideline update, a significant increase in the utilization of arteriovenous fistulas (AVF) in HD patients has been reported, from <20% of US end stage kidney disease (ESKD) patients at the time of the original guidelines to >60% prevalence of AVF in the US HD population today. A widely held opinion, however, is that these guidelines have, at times, also had a negative impact on patient care. This negative impact is mainly attributed to unintended outcomes, such as the rising numbers of upper-arm fistulas, which may negatively impact a patient's future vascular access options. Another unintended consequence is that whereas the number of AVF creations has significantly increased, it is not necessarily paralleled by subsequent use of AVFs. The increase in fistula creations has been mainly due to a reduction in initial arteriovenous graft (AVG) creations and use, rather than a reduction in central venous catheter (CVC) utilization; CVC use remains unchanged and exceeds 80% for incident HD patients, perhaps due to the high fistula failure rate (3).

The 2019 KDOQI vascular access guidelines have a much more patient-focused approach that recognizes the differences in practice patterns among clinicians, while still focusing on providing high-quality standards that offer dialysis access choices customized to individual patients' goals and preferences. The ideal access is no longer "a fistula"; it is any type of access that is reliable, can deliver adequate dialysis without complications, and is suitable for each individual patient's needs: "The right access, in the right patient, at the right time, for the right reasons."

The "ESKD Life-Plan," adopted in the 2019 document (Guideline 1), provides a patient's individualized lifetime map of dialysis modalities by creating a "P-L-A-N" (patient life-plan first, then access needs). The comprehensive vascular access plan includes an access creation plan, contingency plan, succession plan, and underlying vessel preservation plan (2).

Table 1. Differences between previous and current KDOQI guidelines

KDOQI 2006	KDOQI 2019
Emphasis on a "fistula first" approach to vascular access choice due to the AVF associations with superior patency and lower complications compared with other vascular access types. Based on observational data and potentially flawed interpretations. A population approach to care was emphasized.	Emphasis on "The right access, in the right patient, at the right time, for the right reasons." A patient-centered approach to HD vascular access that considers multiple aspects of a patient's needs and dialysis access eligibility. Based on understanding potential biases of prior data and lessons learned from unintended consequences. An individualized approach to care is emphasized, recognizing overall population benefits to proposed strategies.
A vein with a 2.5-mm minimum vein diameter and arterial diameter of 2.0 mm was suggested as a guideline for AVF creation.	No minimum diameter threshold is required to create an AVF; arteries and veins of <2 mm in diameter should undergo careful evaluation for feasibility and quality to create a functioning AVF.
Primary AVF creation (radiocephalic, followed by brachiocephalic) is specifically recommended as a first AV access before considering an alternate access. The guidelines are unclear about the selection of type and site of AV access after an initial failed attempt for a second AV access.	Emphasis on the importance of choosing the site (location) of the AV access (AVF or AVG) after careful consideration of the patient's specific characteristic, such as advanced age, comorbidities, or short life expectancy. Case scenarios and algorithms are given as examples. Secondary access sequences are suggested after considering the patient's ESKD Life-Plan.
Long-term dialysis catheters should be avoided, particularly on the same side of a maturing venous access.	The use of tunneled CVCs for short-term or long-term durations for incident patients is appropriate in valid clinical circumstances (listed).
Right internal jugular vein is the preferred site for tunneled, cuffed venous dialysis catheters, regardless of clinical situation. Subclavian veins should be used only after all other upper-extremity sites are exhausted.	In urgent dialysis start situations, under limited-use circumstances (e.g., <1 month) and when transplant is not an option, the use of a tunneled, cuffed femoral CVC may be an appropriate approach. When there are valid reasons for use, and duration of use is expected to be prolonged (e.g., >3 months) without anticipated use of AV access, CVC may be placed in the following locations in order of preference: internal jugular, external jugular, femoral, subclavian, and lumbar.
No recommendation with regard to pharmacologic therapies to assist AVF maturation.	Suggestions not to use allogeneic endothelial implants or pancreatic elastase to improve AVF maturation, patency, or clinical usability or to improve AVG graft patency or reduce thrombosis.
Grafts and fistulae should be regularly monitored for stenoses via quantitative measurement of flow within the vascular access, static venous dialysis pressures, duplex ultrasound, and/or physical examination.	There is no evidence to make a recommendation on routine AVF and AVG patency surveillance by measuring access blood flow, pressure monitoring, or imaging for stenosis, that is, additional to routine clinical monitoring, to improve access patency. The guidelines indicate "monitoring of vascular access is primary, while surveillance findings are supplementary, and action should not be based solely on surveillance findings."
Angioplasty should be performed if >50% stenosis is present in either the arterial or venous limbs. Successfully treated lesions should have <30% residual stenosis.	Preemptive angioplasty of AVFs and AVGs with stenosis, not associated with clinical indicators, to improve access patency is not recommended. There is an emphasis on intervention in the presence of clinical indicators and no intervention in the absence of clinical indicators.
Abandoning of the AVF to more recent attempts at AVF thrombectomy and AV access salvage.	Management of each episode of AV access thrombosis is at the operator's/clinician's best judgment and discretion, including consideration of the patient's dialysis access succession plan that is consistent with the ESKD Life-Plan.
Definition of a CVC dysfunction: failure to maintain extracorporeal blood flow of >300 mL/min at a pre-pump arterial pressure more negative than −250 mm Hg.	Updated definition of CVC dysfunction: failure to maintain the prescribed extracorporeal blood flow required for adequate HD without lengthening the prescribed HD treatment.
A fibrin sheath causing CVC malfunction can be treated with CVC exchange, with or without balloon disruption. No statement was made regarding disrupting fibrin sheaths to prevent or treat bacteremia.	A CVC fibrin sheath associated with adverse clinical manifestations (CVC dysfunction and/or infection); a CVC exchange, with or without balloon disruption of the fibrin sheath, should be performed.

Table continued on page 14

The guidelines also have renewed approaches of older topics to optimize the patient's access options. For example, they propose a surprising sequence of dialysis catheter locations, prioritizing femoral catheterization over subclavian catheterization in urgent dialysis start situations until the AV access or peritoneal dialysis (PD) catheter can be quickly created and used, which is justified by the potential to limit central stenosis. It is worthwhile taking the time to read the detailed justifications to the guideline's statements.

The inclusion of the subclavian vein as a possible site was also unexpected in light of the well-reported central

Continued on page 14

KDOQI Vascular Access Guideline

Continued from page 13

vein stenosis following subclavian vein catheterization. However, from a clinician perspective, subclavian vein catheterization on an extremity, where all vascular access options have been exhausted, is much more beneficial than an internal jugular catheterization on the ipsilateral side of newly created vascular access. Here, we see how the guidelines are practical and aligned with a clinician's perspective. A note under the statement reads, "If one side has pathology that limits AV access creation but allows for CVC insertion, this side should be used for the CVC to preserve the other side for AV access creation" (4).

The new guidelines emphasize the clinical implications of their implementation. A good example is the new definition of CVC dysfunction, which takes advantage of the flexibility in various HD prescriptions, according to the duration and frequencies of dialysis regimens. Moving away from the rigid cutoff of the ">300 mL/min" recommendation would decrease unnecessary or invasive interventions, such as tissue plasminogen activator (TPA) administration or catheter exchange based solely on a flow rate.

There are other differences between the prior guidelines and the current ones. The current guidelines have the benefit of almost 15 years of ample literature, including controlled randomized trials and a more rigorous evidentiary database for vascular access. Table 1 highlights some of these differences.

Whereas one might argue that some of the updated guidelines continue to support recommendations solely based on expert opinion, such as maintenance angioplasty of dialysis access to address "access flow dysfunction" complications, clinicians utilizing such opinion-based guidelines might avoid a significant increase in patient morbidity, as well as cost to the healthcare system associated with vascular access dysfunction. This seems appropriate until we have better evidence-based recommendations.

In summary, the updated 2019 vascular access guidelines have gained refinement in development, grading, and reporting. The expected conveyance from population-based practice to patient-centered practice would substantially affect overall clinical vascular access management and patient outcomes for years to come. These guidelines are a welcome and refreshing change that can be practically implemented by clinicians. ■

Dalia Dawoud, MD, MSc, FASDIN, is a nephrology specialist in Riverside, CA, affiliated with Renown Regional Medical Center and Renown South Meadows Medical Center.

Table 1, continued from page 13

KDOQI 2006	KDOQI 2019
The definition for diagnosing catheter-related bacteremia adapted the following Centers for Disease Control and Prevention (CDC) definitions for catheter-related infections, which are not based on evidence obtained from studies of dialysis patients: Definite: Same organism from a semiquantitative culture of the catheter tip [>15 colony-forming units (CFU)/catheter segment] and from a BC in a symptomatic patient with no other apparent source of infection. Probable: Defervescence of symptoms after antibiotic therapy, with or without removal of the catheter, in the setting in which BC confirms infection, but catheter tip does not (or catheter tip does, but blood does not) in a symptomatic patient with no other apparent source of infection. Possible: Defervescence of symptoms after antibiotic treatment or after removal of catheter in the absence of laboratory confirmation of bloodstream infection (BSI) in a symptomatic patient with no other apparent source of infection.	The definition for diagnosing catheter-related bacteremia is based on evidence obtained from studies of dialysis patients. It is practical, as it allows the use of the dialysis circuit to get the blood cultures (BCs), which has the benefit of preserving veins for AV access creation but also reduces contamination. Clinical manifestations and at least 1 positive BC from a peripheral source (dialysis circuit or vein) and no other apparent source, with either positive semiquantitative (>15 CFU/catheter segment, hub or tip) or quantitative (>102 CFU/catheter segment, e.g., hub or tip) culture, whereby the same organism (species and antibiogram) is isolated from the catheter segment (e.g., hub or tip) and a peripheral source (dialysis circuit or vein) blood sample. If available, the following would be supportive: simultaneous quantitative cultures of blood samples with a ratio of ≥3:1 [catheter hub/tip versus peripheral (dialysis circuit/vein)]; differential period of catheter culture versus peripheral BC positivity of 2 hours.

References

1. NKF-DOQI clinical practice guidelines for vascular access. National Kidney Foundation-Dialysis Outcomes Quality Initiative. *Am J Kidney Dis* 1997; 30:S179–S183. PMID: 9339150
2. Lok CE, et al. KDOQI clinical practice guideline for vascular access: 2019 update. *Am J Kidney Dis* 2020; 75:S1–S164. https://doi.org/10.1053/j.ajkd.2019.12.001
3. Lee T. Fistula First Initiative: historical impact on vascular access practice patterns and influence on future vascular access care. *Cardiovasc Eng Technol* 2017; 8:244–254. doi: 10.1007/s13239-017-0319-9
4. Agarwal AK, et al. Central vein stenosis: a nephrologist's perspective. *Semin Dial* 2007; 20:53–62. doi: 10.1111/j.1525-139X.2007.00242.x

Vascular Access Guidelines
A Patient's Perspective

By Evan Coaker

I have been a dialysis or transplant patient since 1988. Alport's syndrome, a familial illness, struck my family in 1971. That year, one of my older brothers became sick at 16 years of age and died later that year. My other two brothers got sick in 1973 and progressed to dialysis. Both received transplants in 1975, but my oldest brother succumbed to an opportunistic infection a year later. My younger brother is still living.

My own history began with a kidney biopsy in 1972, and I got regular bloodwork to monitor my kidney function until my blood pressure began rising in the early 1980s. In late 1987, a nephrologist spoke the words I had dreaded: "You will need to begin dialysis soon." I had begun to notice I was winded and nauseated after any kind of strenuous activity.

Of critical importance to each patient facing possible kidney replacement therapy (KRT) is an ESKD life plan. This strategy is about always having a contingency plan for likely "what-ifs." It helps to consider, with one's family and medical care team, what might be the likeliest changes and difficulties. I had the relatively rare advantage of 16 years from diagnosis to actual need for KRT. I had a chance to carefully consider my KRT modality. I chose peritoneal dialysis (PD) in 1988, uncomfortable with the idea of having a fistula, which my brothers had had, but I did not like it because of my body image as a relatively young man with no other comorbidities. Also, I had seen how my younger brother dealt with his fistula and the intrusive schedule of hemodialysis, and I decided that PD was a better fit for me, with the relative schedule independence and hidden belly catheter. It took a painful bout of peritonitis in 1989 to convince me to get on the transplantation list. In 1990 I received a transplant from a deceased donor.

The transplant lasted 12 years, and in November 2002 I went back to using PD until January 2005, when an umbilical hernia made it impractical to continue. My nephrologist said that the peritoneal membrane was not dialyzing well, and I had a slow leak under my skin. The leaking PD fluid made a pale ring around my belly button. A vascular surgeon installed a catheter in my chest, and I began hemodialysis the next week. Shortly after that the PD catheter was removed from my belly. In March my fistula surgery was delayed by an infection caused when the hernia was repaired. In May my vascular surgeon swung my left basilic vein around under the skin in a loop to connect on the inside of the elbow with the brachial artery. This fistula was often mistaken for a graft because of its loop shape. I was still using the chest catheter until about July, when I moved to Ohio to live with my family for a more reliable health and financial support system.

After I began hemodialysis with the fistula, I began to deal with questions about the appearance of my arm. My body image concerns have actually been replaced with a desire to educate anyone who asks me about the appearance of my arm. I have had people stare and whisper. I have had people ask bold questions about the swelling and scars on my forearm, sometimes with assumptions about drug use. I simply tell the story of how dialysis works and how it keeps me from becoming toxic and sick. This gives me what I feel is a constructive way to explain what I live with, as do so many other hemodialysis patients. I try to consider contingencies so that if I have a problem with my dialysis access, I have thought through my options ahead of time.

After 4 years with my first fistula, two separate aneurysms had developed that were each about the size of a tennis ball. My vascular surgeon was consulted and determined that the cause of the aneurysms was too frequent cannulation in the same areas, and suggested a straighter configuration, with more potential cannulation sites, for a new fistula. The surgery was done in the fall of 2009, but the fistula did not mature quickly. After several months, ultrasonography revealed that some feeder veins were interfering with matu-

ration. These were blocked surgically, and after another 2 months the fistula was patent. Despite the delays with the new fistula's patency, I was able to continue to use the old fistula until the new one was fully mature.

When aneurysms developed in the old fistula, and a new one was to be created, I began researching ways to protect the new fistula from aneurysms. I was told by my vascular surgeon about the buttonhole technique and spoke about it to several nurses and other patients. None of the patients knew about the technique. I was told that self-cannulation would minimize problems with the buttonhole technique. Many people have a fear of cannulating themselves, but because I have no concerns about self-cannulation, I decided that it was a good option for me. Buttonhole cannulation is similar to putting an earring through the same hole each time. The path from the hole to the fistula is called a scar tunnel. "Buttonhole" refers to its dimpled exterior appearance. Cannulation is best done each time by the same person, who knows the path and angle of approach. My first two buttonhole sites were established by someone who specialized in creating buttonhole scar tunnels. I was told that one possible complication with the technique was more frequent infections.

I have been using my buttonhole site with the same fistula ever since, and it has lasted 10 years with no aneurysms and only one infection. In 2017 I had my first and (so far) only infection, on the arterial site, and was told I could no longer use the same location. I used rope-ladder cannulation until I finished creating a new scar tunnel. Early this year, excessive scarring on the venous site required a new scar tunnel to be started. It takes about 2 weeks of careful aim with ordinary sharp dialysis needles to follow the same path and establish new scar tunnels. My current technician helped me establish the replacement scar tunnels. I did most of the cannulation during the creation of the first and second sets of scar tunnels. I marked the fistula farther down from the entry point to establish the angle of approach. I kept the ink in the same place to guide me and to keep the angle consistent. I have used freckles and other skin landmarks to guide me since then and to keep me on the "straight and narrow."

In sum, I have managed to keep my fistulas viable despite the complications I've had over the years.

Being a kidney patient has also had an impact on my professional life. I worked full time all through college as a half-time student and only took a week off in 1988 to have my peritoneal catheter installed and to heal from that surgery. After I graduated from college I worked as a software trainer for several years before moving into a sales job. I continued to work until I had my transplant, then took 4 months off to acclimate to the immunosuppressive medication. I was able to continue working until about 7 months into my second stint on PD, when I began having trouble with my energy levels, attempting to perform in an outside sales job. I have worked part time over the years since. ■

Evan Coaker is a retired software trainer & sales consultant. He worked for Quotron Systems, Inc., then Reuters America, on the Advantage AE and successor market data reporting systems, for the brokerage and trading industry, as well as NYSE floor brokers and specialists.

Vascular Access Guidelines
An International Perspective

By Vivekanand Jha

Issues related to vascular access—the timing of creation, type, site, access care, maintenance, surveillance, early identification of problems, and appropriate resolution—are important determinants of the short-term and long-term outcomes and cost of care of patients receiving maintenance hemodialysis (HD). Calling vascular access the lifeline of these individuals is not an exaggeration. In the 2019 update of its Vascular Access Guideline (1), the KDOQI Guideline Work Group made the guideline more patient-focused, using the tagline "Right Access for the Right Patient for Right Reasons at Right Time" with emphasis on multidisciplinary care; individualized assessment of risks, benefits, and quality of life; and factoring in the patient's values, beliefs, and preferences. This approach is consistent with the value given to autonomy and patient-centricity of care in North America.

The guideline development process has followed the rigorous GRADE approach (Grading of Recommendations Assessment, Development, and Evaluation), and the statements use language that best reflects the conclusions that can be drawn from the totality of evidence. These guidelines satisfy the Institute of Medicine statement, "Clinical practice guidelines are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances."

The highlight—the move away from the "fistula first, catheter last" approach and the need to think about the next access—is largely based on issues around the prevalent HD population in the region: the elderly, those with multiple chronic comorbidities, those with previously failed arteriovenous fistulas with prolonged catheter dependence, and those with limited life expectancy. The guidelines provide specific recommendations on almost all practical issues that are encountered in vascular access management.

How will these guidelines be used internationally? Clinical practice guidelines developed in the industrialized world are eagerly anticipated by medical communities in the global south because of a lack of homegrown guidelines and the fact that the biological issues around managing an individual patient are broadly similar throughout the world.

Dialysis is unique among healthcare treatments in being almost entirely dependent on public funding. The major issues around dialysis in low-income and middle-income countries (LMICs) have been service availability (2). Because of demands from various quarters, many LMICs are developing HD programs. It is reasonable to expect that vascular access care is included in the ambit of such programs. In such a situation, guidelines related to any aspect of the care of dialysis patients have implications not only for the individual patient but also for the healthcare system, which needs to balance the tradeoffs involved in providing the best possible care to an individual and to the entire population. Given that infrastructure for vascular access care is weak in LMICs (3), the policymakers and professional bodies in those countries need to decide areas in which investments should be prioritized. Local guideline adaptation should reflect that reality, which has been acknowledged in a general sense by the guidelines.

At risk of stating the obvious: the developing world is not homogeneous. Parts of the LMIC population are able to afford expensive care that uses modern technology, and it is reasonable to grow expertise in those areas. Initially, such care is likely to be restricted to the private sector, but it will grow in scope as programs mature and as countries become wealthier and are able to increase healthcare spending.

It is well known that the kidney failure population in LMICs is relatively young and has fewer comorbidities. Data from several studies have shown a high rate of early mortality and dropouts among HD patients in LMICs (4, 5). The contribution of access-related issues (catheter-related sepsis, primary arteriovenous fistula failure rates) is widely acknowledged, albeit not formally studied. To that end, guideline implementation may be an important public health intervention in an area where a lot of public money is likely to be spent.

To be effective, guidelines should be implementable in local settings. Only 9 out of 167 guideline statements start with "KDOQI recommends," signaling that clinicians should be providing the recommended course of action to most patients and that the recommendation can be adopted as policy. For the rest, physicians need to exercise judgment. An absence of experience limits their ability to do so.

Given that the chief rationale behind moving away from a fistula-first approach is patient demographics, this may still be the most appropriate population-level policy choice for LMICs.

Education directed at care delivery is another key intervention. For example, a large proportion of kidney failure patients first come to a nephrologist only when dialysis is imminent (6), and dialysis is initiated through a temporary catheter, which may be left in place for longer than the 2 weeks recommended by the guideline. Cost is offered as the justification, but patients end up spending far more in the long term because of complications such as catheter-related sepsis, vascular stenosis, and the need for repeated procedures. It is not uncommon to see young HD patients with stenosis/thrombosis at multiple sites. Education about timely referral for access decisions and vessel protection as recommended by the guideline needs to percolate down to general practice physicians, endocrinologists, and other specialists who treat patients with kidney disease—something that the local nephrology communities and health systems should prioritize.

Training of personnel to provide the guideline-recommended care needs to be prioritized. In the first instance, the focus should be on the basics: timely referral, vessel protection, correct use of fistulae and catheters, regular access surveillance, and implementation of quality improvement programs. Given the difficulty in providing care to a patient with a failed access, a core tenet of access care in LMICs is to ensure that the first access is optimal and stays healthy.

Developing a cadre of vascular access experts—physicians, surgeons, radiologists, and nurses—is not easy. In the absence of local expertise, overseas help is required. Many countries, like the United States, do not allow hands-on training to overseas doctors not licensed to practice locally. Exchange programs, such as the International Society of Nephrology Education Ambassador and Sister Center programs (7) in which experts (both medical and allied health professionals) travel to LMIC centers and provide training along with help with setting up the program, are of value. Simulation-based training and videos are being increasingly used.

The guideline lays down an extensive research agenda, to which we should add the need for collection of high-quality data about dialysis that includes information about vascular access use and outcomes in sufficient granularity, health economic studies to help with priority-setting in LMICs, and implementation studies that can test interventions appropriate for local settings.

To maximize the returns on investment from public funding, LMICs should set up centers of excellence. In addition to service provision, these centers should be charged

Continued on page 16 >

KDOQI Vascular Access Guideline

Continued from page 15

with setting up training programs, starting from broad-based expertise in surveillance and the correct use of vascular access and scaling up as needed, using the KDOQI vascular access guidelines as the driver. This process should be driven by local data and will need assessment. Large countries will need several such centers; small countries may come together to develop a regional center that could serve the population in the region.

In conclusion, this document lays out an excellent set of standards that countries can use as an aspirational document and develop their own tiered but resource-sensitive guidelines. ■

Vivekanand Jha, MBBS, MD, DM, PhD, is executive director of the George Institute for Global Health, India; professor of nephrology, University of Oxford; conjoint professor of medicine, University of New South Wales, Sydney; and president of the International Society of Nephrology.

References

1. Trerotola SO. KDOQI Clinical Practice Guideline for Vascular Access 2019 Update: Kinder, gentler, and more important than ever. *J Vasc Interv Radiol* 2020; 31:1156–1157. doi: 10.1016/j.jvir.2020.04.005
2. Jha V. End-stage renal care in developing countries: The India experience. *Ren Fail* 2004; 26:201–208. doi: 10.1081/jdi-120039516
3. Bansal D, et al. Haemodialysis vascular access: Current practices amongst Indian nephrologists. *J Vasc Access* 2018; 19:172–176. doi: 10.5301/jva.5000817
4. Shaikh M, et al. Utilization, costs, and outcomes for patients receiving publicly funded hemodialysis in India. *Kidney Int* 2018; 94:440–445. doi: 10.1016/j.kint.2018.03.028
5. Ashuntantang G, et al. Outcomes in adults and children with end-stage kidney disease requiring dialysis in sub-Saharan Africa: A systematic review. *Lancet Glob Health* 2017; 5:e408–e417. doi: 10.1016/S2214-109X(17)30057-8
6. Parameswaran S, et al. Referral pattern of patients with end-stage renal disease at a public sector hospital and its impact on outcome. *Natl Med J India* 2011; 24:208–213. PMID: 22208139
7. International Society of Nephrology. Education, Training and Research. Available at: https://www.theisn.org/programs. Accessed July 17, 2020.

Hemodialysis Access 101

By Mukesh Sharma and Vandana Dua Niyyar

Hemodialysis vascular access remains both the lifeline and an Achilles heel for patients receiving hemodialysis (HD). Vascular access management was revolutionized by the Fistula First initiative, which led to a robust increase in arteriovenous fistula (AVF) placement in prevalent hemodialysis patients in the United States. However, >80% of dialysis patients still start HD with a central venous catheter (1).

An ideal hemodialysis access would provide long-term, consistent, reliable, adequate dialysis with minimal complications. Unfortunately, the ideal access does not yet exist. Rather, each access must be optimized for each individual patient. The updated Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines recommend a patient-centered approach and the development of an ESKD life plan that considers patients' needs and preferences (2).

Types of arteriovenous access

Arteriovenous fistula

An AVF is created by surgical or endovascular connection of an artery to a vein (Endovascular AVF are discussed in detail elsewhere in this issue). AVF are typically created at the forearm (radial artery), upper arm (brachial artery or proximal radial artery) and occasionally lower extremity (femoral artery). Once mature, fistulae require minimal interventions to maintain patency and are associated with lower infection rates as compared to other AV access. However, AVF have high non-maturation rates, may need additional interventions prior to maturation, and require a long time between surgery and successful use for dialysis (1, 3, 4).

Arteriovenous graft

For patients with inadequate veins for an AVF, an arteriovenous graft (AVG) is an acceptable alternative. In addition to an AVG created by using the same upper extremity vessels as mentioned above for AVF, lower-extremity femoral grafts are also commonly used. Patients with limited options can also receive AVGs in exotic locations, such as chest wall "necklace" grafts by use of the axillary artery. The Hemodialysis Reliable Outflow (HeRO) graft is a subcutaneous hybrid device that combines an upper extremity AVG with a venous outflow catheter component through a titanium connector and can be used in patients with central stenosis. Grafts typically require fewer interventions than AVF before successful cannulation but have higher rates of infections and thrombosis, and they require more interventions to maintain long-term patency (1, 3, 4).

Catheters

HD catheters are usually placed into large central veins draining into the superior vena cava (SVC) or the inferior vena cava (IVC). Nontunneled HD catheters provide emergent access for HD, and tunneled catheters serve as a bridge to permanent AV access. However, catheters are associated with the highest rate of infections among all AV access, frequent dysfunction, and central venous stenosis (1, 3, 4).

Determining the best AV access for your patient

The key to establishing an optimal access is the adoption of a multidisciplinary approach to establish a long-term life plan for each patient and to individualize the access for each patient. The needs of a young, relatively healthy patient with minimal comorbidities vary vastly from those of an elderly patient with multiple comorbidities and a limited life expectancy; the dialysis access should be tailored accordingly. Table 1 summarizes a five-step approach to devising such a plan for HD access.

Preoperative evaluation

Patients with advanced chronic kidney disease may have comorbidities like diabetes, obesity, and peripheral vascular disease and often require frequent hospitalizations (increased phlebotomies and intravenous line placements) that may negatively affect the vasculature. The updated KDOQI guidelines recommend a greater emphasis on preoperative clinical examination to assess patients and their vessels before the placement of vascular access (2). Preoperative vascular mapping is akin to preparing a blueprint before surgery to help select the best suitable vein and artery to maximize the success of AV access placement.

Physical examination, ultrasonography, and/or venography may be used individually or in conjunction with each other (3–6). The chest wall should be examined for the presence of any collateral veins, scars from previous central line or catheter placements, implantable cardioverter-defibrillators, or other features that may indicate underlying central vein stenosis. Evaluation of the arterial system includes comparing bilateral extremity pulses, differential BP measurements in both arms, and Allen's test. Duplex ultrasonography is useful in assessing both anatomy and function of the vasculature, especially calcifications in arterial walls, patency of the palmar arch, and identification of suitable veins for anastomosis, including perforating veins required for the creation of percutaneous AVF. The veins are evaluated for patency, compressibility, diameter, and depth. Venography provides additional information about central vein patency and can be done with the use of iodinated contrast material or CO_2 angiography. Several studies have shown improvement in AVF placement and successful use when preoperative vascular mapping was used to guide AVF surgery (7, 8). An individualized approach to vascular mapping should be taken, with careful consideration of the patient's risk factors for access type and failure, and the advantages and disadvantages of each mapping technique (Table 2).

Postoperative evaluation

The benefits of AVF are not realized until it can be successfully used for dialysis. An AVF must mature to the point at which it is easily palpable and superficial (for cannulation by the dialysis staff), it has a large enough diameter (for cannulation with large-bore dialysis needles), and has adequate blood flow (to sustain the pull from the blood pump). Physical examination of AV access is an easy, cost-effective technique that can help predict maturation correctly in 70% to 80% of patients (9), but experience varies greatly among dialysis centers and staff. Postoperative ultrasonography measuring three variables—AVF diameter, depth, and blood flow—has been shown to be useful in predicting the likelihood of AVF maturation (10). AVF ultrasonography can also help detect inflow stenosis or accessory veins that may contribute to immaturity.

Maintenance of HD access

Once AV access is successfully used for dialysis, regular monitoring and surveillance are necessary to maintain access patency. Physical examination can be used to detect early access dysfunction. The main components of physical examination are inspection (look for arm swelling, presence of collateral veins, skin overlying the aneurysm(s), signs of distal ischemia), palpation (feel for thrill—a strong bounding thrill or hyperpulsatility may denote an outflow stenosis), and auscultation (listen for a bruit—a normal low-pitched continuous systolic-diastolic bruit vs. a high-pitched monosystolic bruit or whistle due to stenosis). In addition, two

simple tests—arm elevation (AVF collapse rules out significant outflow stenosis) and augmentation (strong augmentation of thrill on manual occlusion of mid AVF rules out significant inflow stenosis)—yield important information and can be performed in under a minute.

Point-of-care ultrasonography (POCUS) is currently underused in dialysis units. Dialysis staff can easily be trained to use POCUS (11) to guide cannulation, assess maturity, and minimize infiltrations. In one study, ultrasonography-guided cannulations allowed for earlier cannulations (35 vs. 63 days) and decreased catheter dependence (68 vs. 98 days) (12). POCUS can also help with bedside evaluation of aneurysms and identify alternative sites for cannulation. Aneurysms with rapid increase in size, overlying skin erosion, or both are at risk for spontaneous rupture and should be referred for surgical intervention.

Endovascular interventions may help to maintain AV access patency and generally require an angiogram, followed by balloon angioplasty, stent placement, or both as needed. Thrombosed accesses can be salvaged by endovascular or surgical thrombectomies.

Conclusion

All members of a dialysis care team should have a basic understanding of dialysis access, and nephrologists should be the leaders in a multidisciplinary collaboration to develop and implement an individualized vascular access plan for each of their patients. ■

Mukesh Sharma, MD, FASN, FASDIN, is a physician with Sierra Nevada Nephrology Consultants. Vandana Dua Niyyar, MD, FASN, FASDIN, is professor of medicine with the division of nephrology, department of medicine, Emory University.

Table 1. Plan for hemodialysis vascular access

5 STEPS TO A LIFE TERM VASCULAR ACCESS PLAN		
I	**PLAN** *Determine the best AV access for the patient*	• AVF vs. AVG vs. PD vs. Long term Catheter for patients (with limited life expectancy or special medical circumstances)
II	**GROUNDWORK** *Preparing a Blue Print for AV access creation* *- where, by whom, when ?*	• Educate patient on vein preservation (Vascular real estate planning: lab draws on dialysis; venipuncture on dorsum hand veins, avoiding PICC lines/mid-lines) • Schedule for vascular mapping – both vein and arterial evaluation • Ultrasound vein mapping vs. venogram
III	**SURGERY** *Open Surgery* *Percutaneous AVF*	• Provide feedback and recommendations to the surgeon for the best possible site and type of AV access based on patient's vein mapping/venogram • Coordinate access surgery with an experienced vascular access surgeon/interventionist
IV	**SUCCESSFUL AND CONTINUED USE** *Close Follow-Up Post-surgery*	• Rule of 6's (6mm diameter; <6mm deep; >600cc/min blood flow) for maturation • Devise a cannulation protocol – start with small needles, tourniquet, step ladder technique vs. buttonholes • Experienced 'Star cannulators' in each HD unit for new AVF/G's • Use POCUS if available for cannulations
	Monitoring/Surveillance of AV access	• Periodic physical exam of AV access: One minute access exam (Look, Feel, Hear) • Arm elevation test, Augmentation test
V	**CONTINGENCY/ FUTURE PLANNING** *Plan early for next AV access – where, by whom, when ?*	• Early referral to vascular access center if problems with the access • Don't wait until the current AV access fails

Table 2. Comparison of different vascular mapping techniques

Vascular Mapping Technique	Advantages	Disadvantages
Physical examination	• Cost- and time-effective • Noninvasive • Convenient	• Obesity / deep veins poorly evaluated
Ultrasound	• Noninvasive • Direct visualization of both veins and arteries • Provides information on both structure and function	• Dependent on operator skill level • Provides indirect assessment of central veins
Venogram	• Direct visualization of veins, including accessory veins and collaterals • Best option to evaluate central veins	• Invasive (though minimally) • IV contrast exposure in small amount (unless Co_2 used) • Arteries are not directly visualized

References

1. *USRDS Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States*, Bethesda, MD, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, 2010, 2017.
2. Lok CE, et al. KDOQI Clinical Practice Guideline for Vascular Access: 2019 update. *Am J Kidney Dis* 2020; 75:S1–S164. doi: https://doi.org/10.1053/j.ajkd.2019.12.001
3. Niyyar VD, Work J. Interventional nephrology: Core curriculum in nephrology. *Am J Kidney Dis* 2009; 54:169–182. doi: 10.1053/j.ajkd.2009.03.011
4. Maya I, Allon M. Vascular access: Core curriculum in nephrology. *Am J Kidney Dis* 2008; 51:702–708. doi: 10.1053/j.ajkd.2007.10.046
5. Niyyar VD, Wasse H. Vessel mapping for dialysis access planning. *Semin Dial* 2017; 30:305–308. doi: 10.1111/sdi.12594
6. Salman L, Beathard G. Interventional nephrology: Physical examination as a tool for surveillance for the hemodialysis arteriovenous access. *Clin J Am Soc Nephrol* 2013; 8:1220–1227. doi: 10.2215/CJN.00740113
7. Allon M, et al. Effect of preoperative sonographic mapping on vascular access outcomes in hemodialysis patients. *Kidney Int* 2001; 60:2013–2020. doi: 10.1046/j.1523-1755.2001.00031.x
8. Silva MB Jr, et al. A strategy for increasing use of autogenous hemodialysis access procedures: Impact of preoperative noninvasive evaluation. *J Vasc Surg* 1998; 27:302–307. doi: 10.1016/s0741-5214(98)70360-x
9. Ferring M, Henderson J, Wilmink T. Accuracy of early postoperative clinical and ultrasound examination of arteriovenous fistulae to predict dialysis use. *J Vasc Access* 2014; 15:291–297. doi: 10.5301/jva.5000210
10. Robbin ML, et al. Prediction of arteriovenous fistula clinical maturation from postoperative ultrasound measurements: Findings from the hemodialysis fistula maturation study. *J Am Soc Nephrol* 2018; 29:2735–2744. doi: 10.1681/ASN.2017111225
11. Niyyar VD. Ultrasound-based simulation for cannulation in outpatient hemodialysis units: an educational protocol [published online ahead of print Nov 29, 2019]. *J Vasc Access* doi: 10.1177/1129729819891530
12. Coritsidis GN, et al. Point-of-care ultrasound for assessing arteriovenous fistula maturity in outpatient hemodialysis [published online ahead of print Apr 23, 2020]. *J Vasc Access* doi: 10.1177/1129729820913437 Accessed on July 1, 2020

Arteriovenous Access by Nephrologists
Percutaneous Creation of Arteriovenous Fistula

By Umar Waheed

Autologous arteriovenous fistulae (AVF), compared with prosthetic arteriovenous grafts and central vein catheters, are the most effective hemodialysis vascular access option for patients who require renal replacement therapy because of ESKD (1). The effects of autologous AVF include lower thrombosis and infection rates, fewer hospital admissions for access revision, significantly lower mortality rates, increased life expectancy, and lower healthcare-related costs (2, 3).

However, there are many challenges to the successful use of an autologous AVF. One hindrance is the relatively high early thrombosis and failure to mature rate. Surgically created AVF failure rates are high, and primary/secondary patency rates are low (4). Thus, an important logistic challenge is the well-timed placement and maturation of a functional AVF. Unfortunately, early loss of patency leads to high central venous catheter use, lengthy catheter contact time, additional procedures to maintain catheter patency, and attempts at AVF maturation and salvage. These additional procedures adversely affect fistula patency and lead to further frequent interventions (5).

Percutaneous creation of AVF (pAVF) for hemodialysis access in patients with kidney disease now allows for AVF creation in the outpatient setting. This provides nephrologists the opportunity to create an AVF in dialysis access centers in a safe and effective manner. Inasmuch as these procedures are entirely percutaneous, the advantages include quicker initiation of hemodialysis, quicker maturation times, and reduced costs and complications. Two devices are currently available to create pAVF.

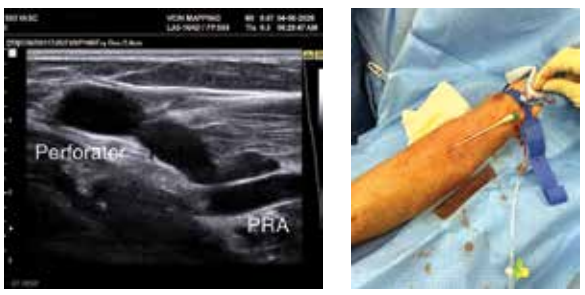
Ellipsys Vascular Access System

The Ellipsys percutaneous arteriovenous fistula device (Avenu Medical, Inc., San Juan Capistrano, CA) (Figure 1) is a single venous catheter vascular access system that uses thermal resistance energy to create an arteriovenous anastomosis with fusion of the arterial and venous walls between the proximal radial artery and the perforating vein in the proximal part of the forearm (6). Overall, it has demonstrated good cumulative patency rates for as long as 2 years (7).

Figure 1. Top, Ellipsys catheter. Bottom, Ellipsys power controller.

The procedure is straightforward. First, with continuous ultrasound guidance, a retrograde venous puncture is made into the median cephalic or median basilic vein. The needle is advanced over a micropuncture guidewire to the perforating vein (Figure 2).

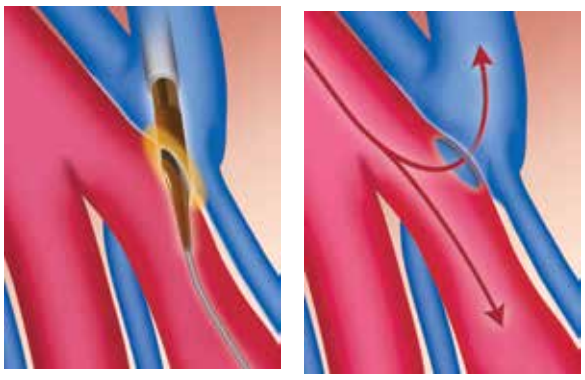
Figure 2. Procedure for percutaneous arteriovenous vascular access



Left, perforator anatomy. Right, access.

Then, the needle is advanced into the adjacent proximal radial artery (PRA). Next, a 6-Fr Glidesheath Slender (Terumo Interventional Systems) is inserted through the perforating vein into the PRA. The Ellipsys catheter is now introduced. The sheath is retracted to the more superficial part of the perforating vein, and gentle traction is applied to the Ellipsys catheter until the tip of the device engages the anterior wall of the PRA. This provides tactile resistance to further traction. Next, the catheter is closed, which captures the arterial and venous walls between the tip and the base (Figure 3). To confirm proper positioning of the device, a display on the power controller can verify correct tissue capture. Next, the device is activated with thermal energy, and a side-to-side elliptical anastomosis is formed between the perforating vein and the PRA.

Figure 3. Wall capture, application of thermal energy, and anastomosis creation



After the device is removed, immediate improvement of flow and acceleration of maturation is induced by angioplasty balloon dilatation of the anastomosis with a 4- × 20-mm or a 5- × 20-mm monorail balloon catheter (Boston Scientific Corporation) (Figure 4). This may reduce the postanastomotic stenosis observed in earlier studies (Figure 5).

Figure 4. Left, Anastomotic narrowing. Right, creation of percutaneous transluminal angioplasty showing balloon waist

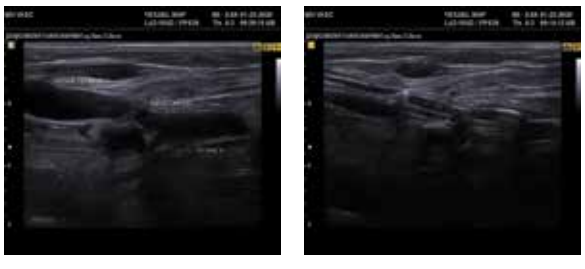
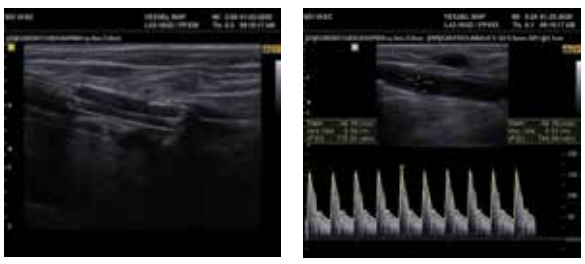


Figure 5. Left, complete balloon effacement. Right, flow of 770 mL/min after percutaneous transluminal angioplasty

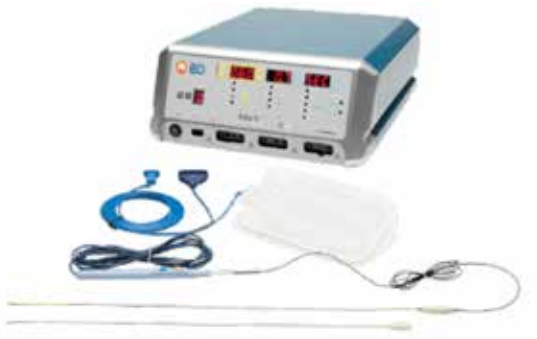


With a single entry into a low-pressure venous system and short procedure times (most cases require 10 to 20 minutes, and several have been performed in under 10 minutes), the procedure is highly effective. The use of real-time ultrasound guidance eliminates radiation exposure for both the physician and the patient. In addition, the pAVF in the setting of advanced chronic kidney disease eliminates the risk of radiocontrast nephropathy.

Wavelinq EndoAVF System

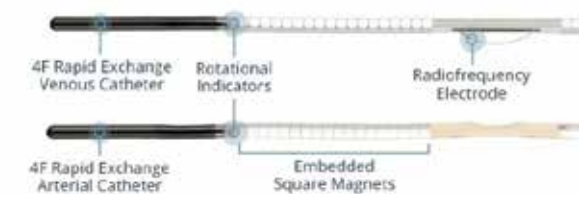
The WavelinQ endoAVF system (Figure 6) consists of a 4-Fr venous catheter, a 4-Fr arterial catheter, and an electrosurgical generator (Becton Dickinson, Franklin Lakes, NJ). The catheters are lined with square magnets and have rotational indicators that help with alignment during AV access creation (Figure 7).

Figure 6. Wavelinq EndoAVF system



Under ultrasound guidance, the selected vein and artery are accessed. Next, under fluoroscopy, the arterial catheter is placed into the creation site in the proximal forearm over a 0.014-inch guidewire through an introducer sheath. The venous catheter is then similarly placed.

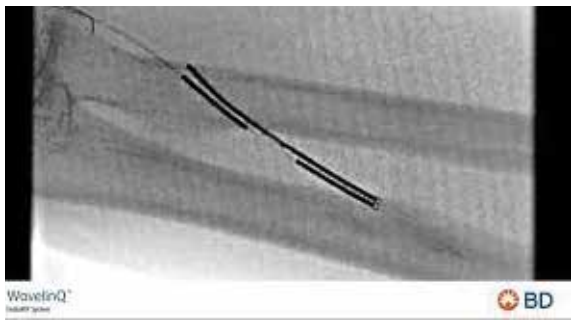
Figure 7. Arterial and venous catheters, Wavelinq EndoAVF



The anastomosis site will vary on the basis of the patient's anatomy but is typically a proximal ulnar–ulnar or proximal radial–radial anastomosis. As both catheters traverse their respective vessels to reach the creation site, they are rotationally aligned so that the electrode and ceramic backstop are facing each other (Figure 8). Once they reach

the creation site, confirmation of placement is made by the operator with the help of the rotational indicators.

Figure 8. Arterial and venous catheters aligned



The magnets attract, coapting the catheters together. The device is then activated to deliver 60 W of radiofrequency energy for 0.7 seconds through the venous electrode to cut a precise channel to the arterial backstop. The devices are removed, and a fistulogram is performed to confirm successful endoAVF creation. When feasible, a deep brachial vein may be embolized to divert arterialized flow to the more superficial cephalic, median cubital, and basilic veins to enhance maturation.

Advantages of pAVF

The side-to-side anastomosis configuration of pAVF leads to a modest flow to various outflow veins. This is excellent because it leads to lower access pressure and may contribute to fewer complications such as aneurysm formation, steal syndrome, recurrent access stenosis, and the resultant need for frequent reintervention. The perforating vein flows from the deep veins of the forearm to the superficial venous system, which allows for vessel maturation. Multiple outflow veins can potentially be developed for cannulation, including the cephalic vein, medial cubital vein, median basilic vein, and basilic vein. Thus, different cannulation options may be available for accessing the pAVF to provide dialysis.

The path forward for patients requiring creation of a traditional AV access with open surgery is one of many complexities and potential delays. Several steps can negatively affect the timeline to a functional AVF, including vessel mapping, referral to surgery, surgical consultation along with additional anesthetic and associated investigations, surgical time in the operating room, surgical follow-up, and return referral for maturation evaluation and access cannulation. However, pAVF creation significantly reduces the time from recognition of the need for AV access creation to the creation of a pAVF. Additionally, it gives the nephrologist more control over the access process. Ultimately, this technique has demonstrated its success by allowing nephrologists to create an AV access within 1 to 2 days after patient referral. In some cases, the achievement of ultrasound maturation criteria and use has occurred as early as 2 weeks after pAVF creation (8).

In brief, pAVF technology is a useful tool for dialysis access creation because it allows for more direct involvement by the nephrologist and lower-cost procedures in the outpatient setting. It has many advantages over traditional surgical AVF creation and is a feasible alternative to open surgical AVF creation for patients with favorable vascular anatomy. ■

Umar Waheed, MD, specializes in nephrology and vascular surgery and is affiliated with Banner University Medical Center, Phoenix.

References

1. Almasri J, et al. Outcomes of vascular access for hemodialysis: A systematic review and meta-analysis. *J Vasc Surg* 2016; 64:236–243. doi: 10.1016/j.jvs.2016.01.053
2. Leermakers JJ, et al. Cost-effectiveness of vascular access for haemodialysis: arteriovenous fistulas versus arteriovenous grafts. *Eur J Vasc Endovasc Surg* 2013; 45:84–92. doi: 10.1016/j.ejvs.2012.10.012
3. Hicks CW, et al. Mortality benefits of different hemodialysis access types are age dependent. *J Vasc Surg* 2015; 61:449–456. doi: 10.1016/j.jvs.2014.07.091
4. Al-Jaishi AA, et al. Patency rates of the arteriovenous fistula for hemodialysis: A systematic review and meta-analysis. *Am J Kidney Dis* 2014; 63:464–478. doi: 10.1053/j.ajkd.2013.08.023
5. Lee T, et al. Long-term outcomes of arteriovenous fistulas with unassisted versus assisted maturation: A retrospective national hemodialysis cohort study. *J Am Soc Nephrol* 2019; 30:2209–2218. doi: 10.1681/ASN.2019030318
6. Hull JE, et al. The pivotal multicenter trial of ultrasound guided percutaneous arteriovenous fistula creation for hemodialysis access. *J Vasc Interv Radiol* 2018; 29:149–158. doi: 10.1016/j.jvir.2017.10.015
7. Beathard GA, Litchfield T, Jennings WC. Two-year cumulative patency of endovascular arteriovenous fistula. *J Vasc Access* 2020; 21:350–356. doi: 10.1177/1129729819877780
8. Mallios A, et al. Early cannulation of percutaneously created arteriovenous hemodialysis fistulae. *J Vasc Access* 2019, in press. doi: 10.1177/1129729819892796

The Relevance of High Flow Arteriovenous Access for the Nephrologist

By Bhavnish Bucktowarsing

Forty percent of end stage kidney disease (ESKD) patients have a history of heart failure, and 39% have a history of ischemic disease at baseline [Hemodialysis (HEMO) study]. An arteriovenous (AV) access is the preferred access for dialysis, as it reduces risks of infections and hospitalizations and need for interventions. It is well documented that the creation of AV access can cause or aggravate heart failure (1). Typically, this occurs when an AV access turns into a high flow circuit, with resultant high output cardiac failure. In this article, we explore how the recommended access of choice for dialysis can sometimes be detrimental to a patient's cardio-pulmonary health.

Coming to a definition for high flow AV access

High output cardiac failure is associated with AV access that has blood flows >1.5 L/min (2–4). When access flow (Qa) exceeds 30% of cardiac output (CO), the risk of developing high output heart failure increases. A Qa/CO ratio of >0.30 should be used as a screening tool to perform further cardiac testing. Another criterion that can be used includes AV fistula (AVF) flow ≥1.5 L/min. It is to be noted that upper-arm AVF are at higher risk (5).

How does an AV access turn into a high flow circuit?

After creation of an AV access, the vascular endothelium undergoes structural and functional changes due to release of nitric oxide following the increase in blood flow through the newly created low resistance circuit (6). There is a series of adaptations and sometimes maladaptations in cardio-pulmonary physiology. Left ventricular (LV) mass increases (7). The increase in LV mass can occur over a period of 3 months (8). When blood flows through an AV access, it bypasses the capillary beds and essentially shunts blood back to the heart with nonphysiologic pressures and velocities. The resultant higher filling pressures cause significant atrial stretch, which, per Starling's Laws, results in a higher CO.

Why is it important to remain vigilant about high flow AV access?

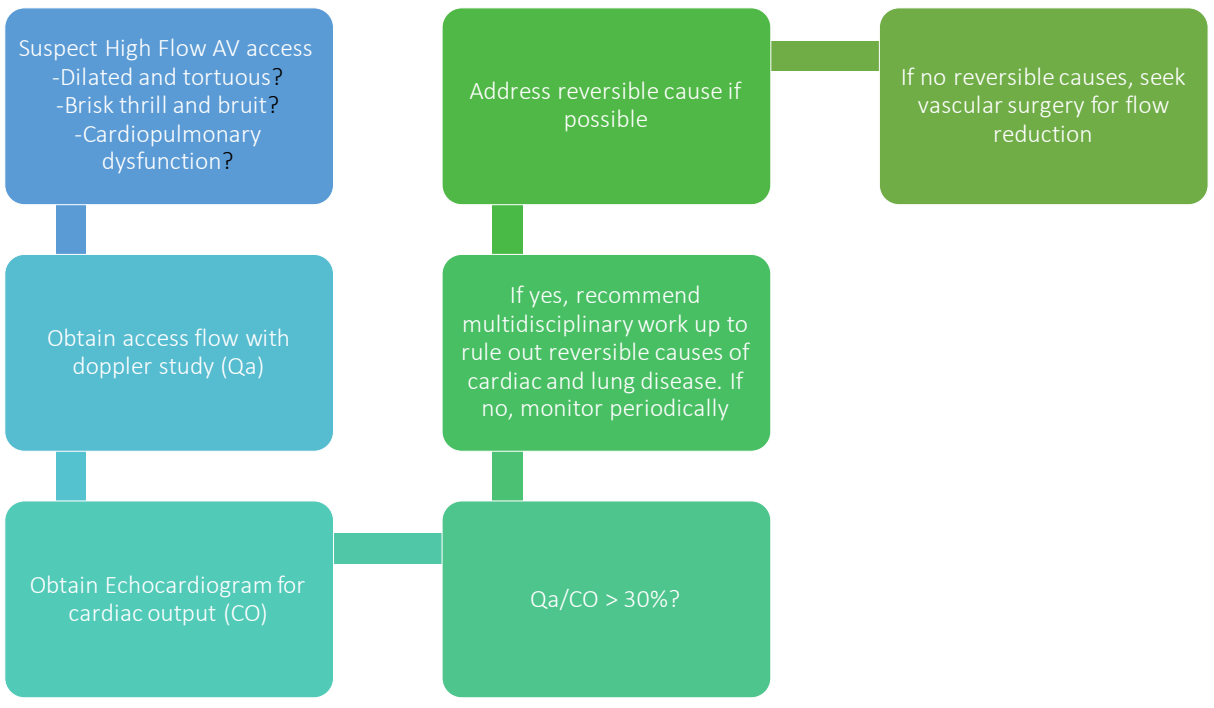
Common scenarios encountered in clinical nephrology include patients with recurrent hospitalizations for volume overload, acute-on-chronic hypoxic respiratory failure, and decompensated heart failure, despite compliance to outpatient dialysis and dietary restrictions. One should always inspect the fistula and proceed with further investigations if clinical suspicion for high flow AVF arises (Figure 1).

During dialysis, there are significant enough hemodynamic changes, such that a high flow AV access can become a life-threatening condition for ESKD patients. A study entitled "Characteristics of sudden death in hemodialysis patients," by Bleyer et al. (9), postulated that 35% of sudden deaths occur within the first 12 hours after dialysis due to critically low levels of cardiac index (<2 L/min/m^2). End organ perfusion can be fatally impaired if a high flow AVF is present and "steals" much of the already-compromised CO.

What should be done once a high flow AV access is confirmed?

Once a Qa/CO > 30% is confirmed (mainly through dialysis Qa measurement and echocardiogram to determine CO), a multidisciplinary approach is recommended. Reversible causes of cardiac dysfunction, as well as a primary pulmonary disease, need to be ruled out (e.g., worsening ischemic cardiomyopathy, valvular diseases, chronic obstructive pulmonary disease, restrictive lung disease, infectious process, malignancy). If no other explanation exists for declining cardio-pulmonary status, then the expertise of a vascular surgeon needs to be sought to consider access banding for flow reduction. ■

Figure 1. High flow AV access flowchart



Bhavnish Bucktowarsing, is a board-certified general and interventional nephrologist at Kidney & Hypertension Consultants Inc, in Canton, Ohio.

References

1. Reddy YNV, et al. Long-term cardiovascular changes following creation of arteriovenous fistula in patients with end stage renal disease. *Eur Heart J* 2017; 38:1913–1923. doi: 10.1093/eurheartj/ehx045
2. Martínez-Gallardo R, et al. Congestive heart failure in patients with advanced chronic kidney disease: association with pre-emptive vascular access placement. *Nefrologia* 2012; 32:206–212. doi: 10.3265/Nefrologia.pre2011
3. Locatelli F, et al. Cardiovascular disease in chronic renal failure: the challenge continues. Registro Lombardo Dialisi e Trapianto. *Nephrol Dial Transplant* 2000; 15:69–80. doi: 10.1093/ndt/15.suppl_5.69 (Transonic Reference #HD9643R)
4. MacRae JM. Vascular access and cardiac disease: is there a relationship? *Curr Opin Nephrol Hypertens* 2006; 15:577–582. doi: 10.1097/01.mnh.0000247506.79538.3e (Transonic Reference #HD7382A)
5. MacRae JM, et al. Arteriovenous fistula-associated high-output cardiac failure: a review of mechanisms. *Am J Kidney Dis* 2004; 43:17–22. doi: 10.1053/j.ajkd.2004.01.016 (Transonic Reference #HD408A)
6. Basile C, et al. The relationship between the flow of arteriovenous fistula and cardiac output in haemodialysis patients. *Nephrol Dial Transplant* 2008; 23:282–287. doi: 10.1093/ndt/gfm549 (Transonic Reference #HD7542A)
7. Agarwal AK. Systemic effects of hemodialysis access. *Adv Chronic Kidney Dis* 2015; 22:459–465. doi: 10.1053/j.ackd.2015.07.003
8. Ahearn DJ, Maher JF. Heart failure as a complication of hemodialysis arteriovenous fistula. *Ann Intern Med* 1972; 77:201–204. doi: 10.7326/0003-4819-77-2-201
9. Bleyer AJ, et al. Characteristics of sudden death in hemodialysis patients. *Kidney Int* 2006; 69:2268–2273. doi: 10.1038/sj.ki.5000446
10. Ori Y, et al. The contribution of an arteriovenous access for hemodialysis to left ventricular hypertrophy. *Am J Kidney Dis* 2002; 40:745–752. doi: 10.1053/ajkd.2002.35685

The Age of Point-of-Care Ultrasonography
A Nephrologist's Perspective

By Daniel W. Ross, MD, MPH

"Good morning, Dr. Ross!" the emergency medicine resident said. "Thank you for consulting on this case of acute kidney injury. We performed a sonogram of his lungs, heart, kidneys, and bladder. We've determined that he is volume depleted and has no signs of urinary obstruction."

"Good evening, Dr. Ross!" the critical care fellow said. "We need to pull fluid on bed 12; he's got B lines on lung ultrasonography."

As a nephrologist, I must be able to contribute to conversations about the etiology of acute kidney injury and volume status. In this rapidly evolving medical landscape, nephrologists need to be ultrasound savvy. We are in the dawning of the age of point-of-care ultrasonography (POCUS) in medicine, and the nephrology community has an opportunity to forge ahead.

One of the most important applications of POCUS in nephrology (also known as POCUN) is in assisting with the diagnosis of acute kidney injury. A nephrologist rounding with an ultrasound machine in his or her pocket can rapidly diagnose obstructive uropathy and avoid the lag in diagnosis associated with ordering a formal ultrasound. Moving beyond the kidney, POCUS has been shown to be a valuable tool in managing volume status. The same probe that is used to acquire images of the kidneys can also be used to look at the lungs and heart. Lung ultrasonography can help nephrologists evaluate extravascular lung water and pleural effusions. Nephrologists can also perform limited echocardiography to evaluate cardiac contractility and inferior vena cava (IVC) size. Both lung ultrasonography and limited cardiac echocardiography are useful in tailoring ultrafiltration prescriptions in hemodialysis patients (1, 2). There is also mounting evidence that nephrologists can use POCUS to assess venous congestion by looking at the IVC, hepatic, portal, and renal veins (3).

The wave of POCUS is sweeping through American medical schools and internal medicine residency programs (4, 5). Twenty-eight percent of American medical schools have a POCUS curriculum (4). Before long, many of our nephrology trainees will be entering fellowships with the ability to use an ultrasound probe to acquire images of the heart, lungs, kidneys, and bladder. Whether by design or by time, POCUS is coming to nephrology.

At Emory University, ultrasound has been part of the nephrology fellowship curriculum since 1994 (6). Dr. W. Charles O'Neill has trained a generation of nephrologists from across the country in diagnostic kidney ultrasound at his weekend course and mini fellowship. Now, in the last decade, nephrologists have begun to look beyond the kidney and vascular access and are using ultrasound to assess volume status and hemodynamics. In 2016, I, along with a few other nephrologists and critical care physicians, taught the first POCUS for nephrologists course at the National Kidney Foundation (NKF) Spring Clinical Meetings. At that meeting, there was palpable excitement about learning ultrasonography of not just the kidneys but also of the lungs and the heart. Yet, many attendees had no access to an ultrasound machine, and others had never even touched an ultrasound probe. Fast forward to NKF 2019, where most attendees were coming to the course with a working knowledge of POCUS, and many had access to portable ultrasound machines.

Figure 1 shows that academic interest in POCUN has gained popularity in the past decade. A rudimentary PubMed search for "point of care ultrasound kidney" shows that there has been an increase in the number of publications on the subject each year. Interest in POCUN, however, goes beyond building medical literature. There has been a concerted effort by members of the nephrology community to offer hands-on training in POCUN. Short courses are offered annually where nephrologists can learn about heart, lung, and kidney ultrasound (Table 1). There is now a one-year ultrasound fellowship for internists at the University of Pennsylvania, and nephrologists are eligible to apply.

Much of the momentum for POCUN has come from social media and web-based platforms. A number of Twitter-savvy nephrologists regularly post educational vignettes and images. One website (https://nephropocus.com/) can serve as a "one-stop shop" for all things POCUN. Another website (https://www.sononephrology.com/) has a section on POCUN literature and offers guidance on where to find training and certification. The website https://www.renalfellow.org/ has an image gallery as well as an education series, entitled "Focus on POCUN."

There is evidence that nephrologists can become proficient in POCUS with appropriate training (7). Nephrologists can learn to image the IVC just as well as cardiologists (8). Lung ultrasonography can be effectively taught to nephrologists in a short session (9). Enthusiasm for POCUN is high, and we know that ultrasound skills can be effectively taught to nephrologists. The question that lingers is "How do we get to a point where POCUN is an established and required part of our clinical practice?" The Accreditation Council for Graduate Medical Education (ACGME) includes proficiency in POCUS for other medical specialties, such as pulmonary and critical care. Figure 2 shows a roadmap of how to incorporate ultrasound into nephrology training so that it might, one day, be an ACGME requirement. This roadmap is based on the experiences of other medical specialties that have all relied on a concerted effort by professional societies.

The next time an emergency medicine resident or critical care fellow approaches a nephrologist with his or her interpretation of a POCUS exam, the nephrologist should be able to verify and, when necessary, challenge those findings. We are at a crossroads. If we move forward now, then we have a chance to be innovative and ahead of the POCUS learning curve. If we delay, we risk being the only doctors in town without the modern stethoscope. ■

Daniel W. Ross, MD, MPH, is an academic nephrologist at the Donald and Barbara Zucker School of Medicine at Hofstra-Northwell in Long Island, New York. He has been using point-of-care ultrasonography to treat patients with kidney disease for the past five years.

References

1. Zoccali C, et al. Pulmonary congestion predicts cardiac events and mortality in ESRD. *J Am Soc Nephrol* 2013; 24:639–646. doi: 10.1681/ASN.2012100990
2. Kaptein MJ, et al. Changes in cardiac output with hemodialysis relate to net volume balance and to inferior vena cava ultrasound collapsibility in critically ill patients. *Ren Fail* 2020; 42:179–192. doi: 10.1080/0886022X.2020.1726384
3. Beaubien-Souligny W, et al. Quantifying systemic congestion with point-of-care ultrasound: development of the venous excess ultrasound grading system. *Ultrasound J* 2020; 12:16. doi: 10.1186/s13089-020-00163-w
4. Dinh VA, et al. Integration of ultrasound in medical education at United States medical schools: a national survey of directors' experiences. *J Ultrasound Med* 2016; 35:413–419. doi: 10.7863/ultra.15.05073
5. LoPresti CM, et al. A road map for point-of-care ultrasound training in internal medicine residency.

Table 1. Short courses in point-of-care ultrasound in nephrology and what they teach

National Kidney Foundation Spring Clinical Meetings
Kidney and Bladder
Lung
Inferior Vena Cava
KIDNEYCon
Lung
Inferior Vena Cava
Focused Cardiac Ultrasound
Mini Fellowship in Renal Sonography
Kidney and Bladder
Cardiorenal University
Kidney and Bladder
Lung
Inferior Vena Cava
Focused Cardiac Ultrasound
Vascular Access
American Society of Diagnostic and Interventional Nephrology—Scientific Meeting
Lung
Inferior Vena Cava
Vascular Access

Continued on page 22 >

Point-of-Care Ultrasonography

Continued from page 21

Ultrasound J 2019; 11:10. doi: 10.1186/s13089-019-0124-9

6. O'Neill WC. *Atlas of Renal Ultrasonography*. W.B. Saunders Company, 2001.
7. Koratala A, et al. Integrating point-of-care ultrasonography into nephrology fellowship training: a model curriculum. *Am J Kidney Dis* 2019; 74:1–5. doi: 10.1053/j.ajkd.2019.02.002
8. Pazeli JM, et al. Can nephrologists use ultrasound to evaluate the inferior vena cava? A cross-sectional study of the agreement between a nephrologist and a cardiologist. *Nephron Extra* 2014; 4:82–88. doi: 10.1159/000362170
9. Gargani L, et al. Efficacy of a remote web-based lung ultrasound training for nephrologists and cardiologists: a LUST trial sub-project. *Nephrol Dial Transplant* 2016; 31:1982–1988. doi: 10.1093/ndt/gfw329

Figure 1. Number of publications by year

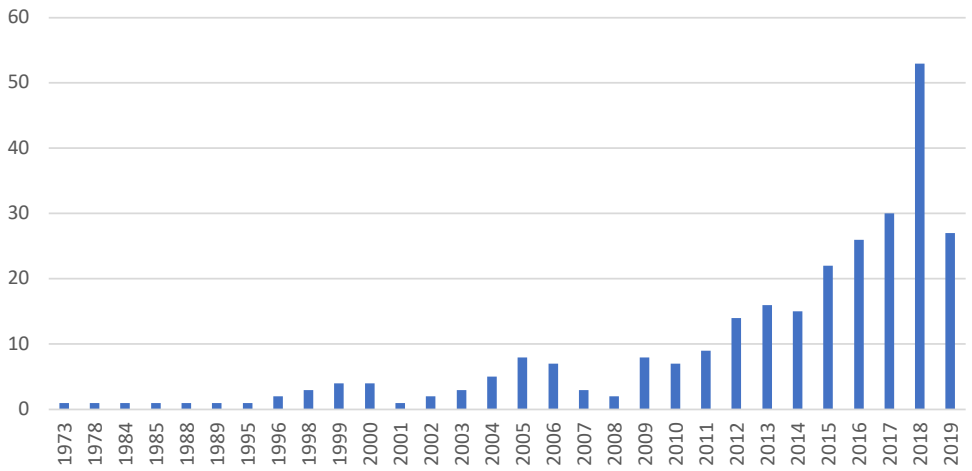


Figure 2. Roadmap to incorporate ultrasound into nephrology training

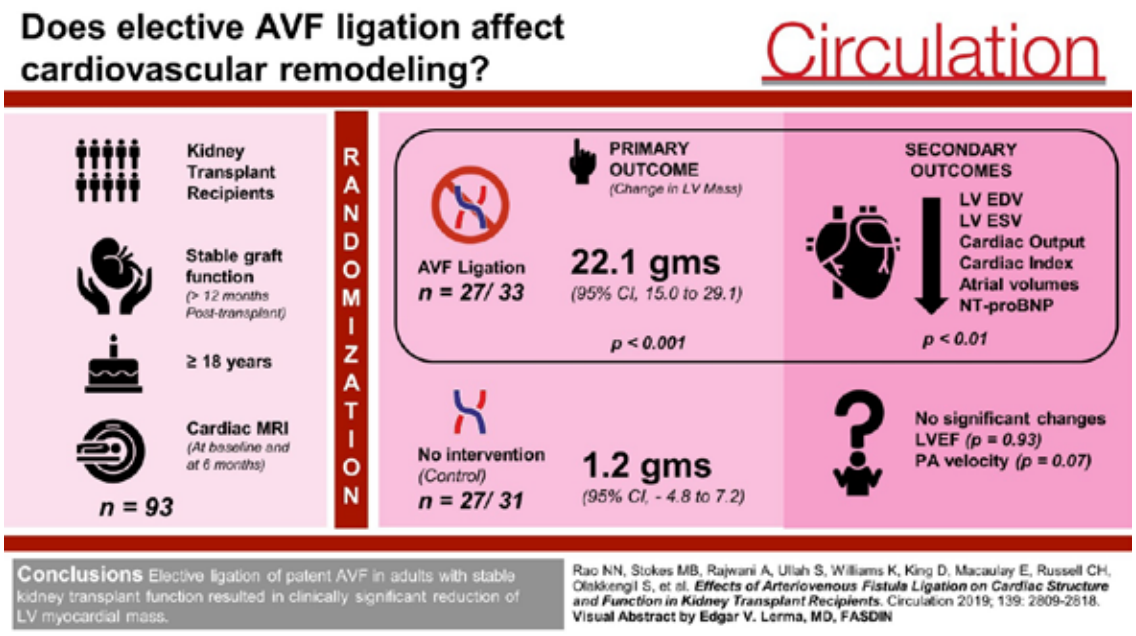
Kidney Controversy
TO LIGATE OR NOT LIGATE

By Edgar Lerma

In 2019, a randomized controlled trial to evaluate the effect of arteriovenous fistula (AVF) ligation on cardiac structure and function in stable kidney transplant recipients was published in *Circulation*.

Kidney transplant recipients (>12 months post-transplantation) with stable allograft function were randomized to AVF ligation versus no intervention (control). The primary outcome was the change in left ventricular (LV) mass [obtained by performing cardiac magnetic resonance imaging (MRI) at baseline and at 6 months], whereas secondary outcomes included changes in LV volumes, left and right atrial areas, LV ejection fraction (LVEF), N-terminal pro-hormone B-type natriuretic peptide (NT-proBNP) levels, cardiac output/index, brachial flows (ipsilateral to AVF), and pulmonary artery (PA) velocity.

Sixty-four of 93 screened patients were randomized to the AVF ligation (n = 33) versus no intervention/control (n = 31) groups. A mean decrease of 22.1 g [95% confidence interval (CI), 15.0–29.1] was observed in LV mass in the AVF ligation group versus an increase of 1.2 g (95% CI, –4.8 to 7.2) in the control group ($p < 0.001$). In addition, decreases in LV end-diastolic volumes (LVEDVs), LV end-systolic volumes (LVESVs), cardiac output (CO), cardiac index, atrial volumes, and NT-proBNP were also demonstrated in the AVF ligation group ($p < 0.01$).



The authors of this study concluded that "Elective ligation of patent AVF in adults with stable kidney transplant function resulted in clinically significant reduction of LV myocardial mass."

In this set of articles, Dr. Aisha Shaikh and Dr. Loay Salman discuss the clinical and practical implications of these findings to everyday practice. ■

Edgar V. Lerma, MD, FASN, FASDIN, is clinical professor of medicine in the section of nephrology at the University of Illinois at Chicago College of Medicine, and is affiliated with Associates in Nephrology, SC, in Chicago, IL.

Controversy
To Ligate or Not Ligate Arteriovenous Accesses: PRO

By Aisha Shaikh, MD

Arteriovenous fistula (AVF) is the preferred vascular access in hemodialysis patients because of its superior long-term patency and low risk of infection (1). The impact of AVF on the cardiovascular (CV) system has been an area of interest to the scientific community for decades, from the time soldiers sustained traumatic AVF in the battlefield to the first description of AVF use in dialysis patients in 1966 (2).

The creation of an AVF between an artery and a vein diverts the blood from the high-resistance capillary system to the low-resistance venous system. The shunting of blood causes an immediate decline in peripheral vascular resistance, increases the venous return to the heart, and increases the cardiac output. These hemodynamic changes lead to an increase in left ventricular (LV) filling pressure and can cause LV hypertrophy (LVH) as a result of cardiac remodeling (3). In some patients, the cardiac remodeling can become maladaptive and result in high-output heart failure. In a prospective study, Basile et al. (4) demonstrated that patients with AVF flow rate of ≥2 L/min have a higher risk for the development of high-output heart failure.

LVH is highly prevalent among ESKD patients, and it is associated with increased risk of heart failure and death. Several factors contribute to the development of LVH in ESKD, including hypertension, volume overload, anemia, and the presence of an AVF. A study by Dundon et al. (5) showed a 12.7% increase in LV mass within 6 months of AVF creation.

It is important to note that observational studies have shown that AVF use is associated with better CV outcomes compared with central venous catheter use in ESKD patients (6). It should be noted, however, that the observational data are riddled with selection bias, and the superior patient outcomes associated with AVF use are at least partly due to patient-related factors rather than solely to the type of vascular access (7). In summary, on one hand the AVF can have an adverse impact on the cardiac structure and function in some patients, but on the other hand AVF use is associated with better clinical outcomes in the majority of ESKD patients. Hence, AVF is the vascular access of choice in hemodialysis patients unless a contraindication to AVF creation exists, such as heart failure, severe vascular disease, advanced age, or poor life expectancy.

Kidney transplantation is the preferred treatment for ESKD. CV disease remains the leading cause of death in ESKD patients even after kidney transplantation. Several factors contribute to the higher prevalence of CV disease in kidney transplant recipients, and many of these CV risk factors are acquired before the kidney transplantation. LVH is common in kidney transplant recipients and is associated with increased CV morbidity and mortality. Although LVH improves after kidney transplantation, it does not completely reverse (8). Therefore, the impact of a functioning AVF on cardiac structure and function becomes relevant in kidney transplant recipients with a stable allograft function. Several nonrandomized observational studies have demonstrated that AVF ligation in kidney

Continued on page 24

Controversy: To Ligate or Not to Ligate Arteriovenous Accesses: PRO

Continued from page 23

transplant recipients leads to a decrease in LV mass, but until recently no randomized controlled study had been conducted to show the impact of AVF ligation on LV mass in kidney transplant recipients (9, 10).

In 2019, Rao et al. (11) conducted a randomized controlled trial in which kidney transplant recipients with stable kidney allograft function were randomized to AVF ligation or no AVF ligation 1 year after kidney transplantation. The baseline characteristics were well matched in the two groups. All patients underwent cardiac magnetic resonance imaging (MRI) at baseline and at 6 months to assess the change in LV mass. AVF flow rates were not reported in this study, and both groups had the same proportion of forearm and upper arm AVF. The follow-up cardiac MRI showed that the AVF ligation group (n = 27) had a 15% reduction in the LV mass, whereas no significant change in LV mass was observed in the control group (n = 27). The study provides clear evidence that regression in LV mass index occurs after AVF ligation in kidney transplant recipients, but the question that remains unanswered is whether the decrease in LV mass index translates into better CV and overall outcomes.

Currently, no guidelines exist to determine the fate of the AVF after kidney transplantation.

The advantage of having a functional AVF after kidney transplantation is that it can be used for future dialysis if the kidney allograft fails. AVFs have a high primary failure rate, and a functional AVF is a precious commodity. Therefore, abandoning a functional AVF is not a straightforward decision.

The long-term kidney allograft outcomes have improved, and the decision to ligate an AVF after kidney transplantation should be based on several patient-related and AVF-related factors. The goal should not be to merely preserve an AVF at all costs. Several factors must be taken into account when making the decision regarding the fate of the AVF after kidney transplantation, such as the likelihood of kidney allograft failure, AVF flow rate and its impact on cardiac structure and function, local effects of the AVF (e.g., aneurysms), and patient preference (cosmetic, functionality of the arm). Clinicians must also be familiar with AVF flow reduction procedures that may help preserve a functional AVF while potentially addressing the complications resulting from the high flow AVF (12).

The approach to AVF ligation after kidney transplantation must be patient-centered, and a one-size-fits-all approach must be avoided. The recent study by Rao et al. (11) offers a clear insight into the impact of AVF ligation on cardiac structure. We look forward to future studies to learn whether these structural cardiac changes translate into better outcomes. Until then we must continue to individualize the decision regarding AVF ligation in kidney transplant patients. ■

Aisha Shaikh, MD, is affiliated with the James J. Peters Veterans Affairs Medical Center in New York City.

References

1. Lok CE, et al. Cumulative patency of contemporary fistulas versus grafts (2000-2010). *Clin J Am Soc Nephrol* 2013; 8:810–818. doi: 10.2215/CJN.00730112
2. Cohen SM, et al. Cardiac output and peripheral blood flow in arteriovenous aneurysm. *Clin Sci* 1948; 7:35–47. PMID: 18871742
3. Guyton AC, Sagawa K. Compensations of cardiac output and other circulatory functions in areflex dogs with large A-V fistulas. *Am J Physiol* 1961; 200:1157–1163. doi: 10.1152/ajplegacy.1961.200.6.1157
4. Basile C, et al. The relationship between the flow of arteriovenous fistula and cardiac output in haemodialysis patients. *Nephrol Dial Transplant* 2008; 23:282–287. doi: 10.1093/ndt/gfm549
5. Dundon BK, et al. The deleterious effects of arteriovenous fistula-creation on the cardiovascular system: A longitudinal magnetic resonance imaging study. *Int J Nephrol Renovasc Dis* 2014; 7:337–345. doi: 10.2147/IJNRD.S66390
6. Ravani P, et al. Associations between hemodialysis access type and clinical outcomes: A systematic review. *J Am Soc Nephrol* 2013; 24:465–473. doi: 10.1681/ASN.2012070643
7. Brown RS, et al. The survival benefit of "fistula first, catheter last" in hemodialysis is primarily due to patient factors. *J Am Soc Nephrol* 2017; 28:645–652. doi: 10.1681/ASN.2016010019
8. Rigatto C, et al. Long-term changes in left ventricular hypertrophy after renal transplantation. *Transplantation* 2000; 70:570–575. doi: 10.1097/00007890-200008270-00006
9. van Duijnhoven EC, et al. Effect of closure of the arteriovenous fistula on left ventricular dimensions in renal transplant patients. *Nephrol Dial Transplant* 2001; 16:368–372. doi: 10.1093/ndt/16.2.368
10. Unger P, et al. Reduction of left ventricular diameter and mass after surgical arteriovenous fistula closure in renal transplant recipients. *Transplantation* 2002; 74:73–79. doi: 10.1097/00007890-200207150-00013
11. Rao NN, et al. Effects of arteriovenous fistula ligation on cardiac structure and function in kidney transplant recipients. *Circulation* 2019; 139:2809–2818. doi: 10.1161/CIRCULATIONAHA.118.038505
12. Bourquelot P. Access flow reduction for cardiac failure. *J Vasc Access* 2016; 17[Suppl 1]:S60–S63. doi: 10.5301/jva.5000517

Controversy
To Ligate or not Ligate Arteriovenous Accesses: CON

By Loay Salman

Kidney transplantation remains the best treatment option for patients with end stage kidney disease (ESKD). However, a dilemma faces healthcare providers when they care for ESKD patients: whether to ligate the patient's arteriovenous (AV) access after kidney transplantation or leave it patent and maintain it. There is still considerable disagreement among providers on the best course of action when dealing with an AV access after kidney transplantation (1). In this article, I will discuss the disadvantages of ligating an AV access after kidney transplantation.

The 1-year and 5-year kidney graft survival rates range between 87% and 95% and 65% and 83%, respectively, based on a donor's status (2). Therefore, significant numbers of kidney transplant recipients will end up receiving dialysis again in the future. And this means that these patients will need AV access when reinitiating dialysis. Creating a new AV access, if the original access was ligated, carries its own challenges and risks. They include not only the risk of the procedure itself, the lead time to maturation, the primary failure rate, the failure rate of related procedures, and the need for tunneled hemodialysis catheters (TDC) but also the difficulty of finding a suitable artery and vein that meet the criteria for AV access creation (3). Two-thirds of patients with a failed kidney transplant start hemodialysis with a TDC (4). Using a TDC by itself adds significant morbidity and mortality to patients with an already higher morbidity and mortality risk than their peers (5).

There is no proven benefit to patient mortality of an access ligation after kidney transplantation. Hicks et al. (6) used the United States Renal Data System to look at 16,845 patients with AV access who received kidney transplants between January 2011 and December 2013. Access ligation occurred in 4.6% of these patients. There was no statistically significant difference between the two groups in all-cause mortality and post-transplantation allograft failure. This study highlighted that the current practice pattern in the United States is to ligate problematic AV accesses only, hence the low rate of access ligation. At the same time, Maresca et al. (7) evaluated six hemodialysis patients and four transplant patients with high AVF blood flow (>1.5 L/min per 1.73 m^2) coupled with symptoms of heart failure. The patients underwent an AVF flow reduction procedure. The flow reduction rate was approximately 58.4%. The results showed that 80% of patients had an improvement in heart failure symptoms. Improvement in systolic pulmonary artery pressure was also noted. However, there is an increased risk of recurrence of high blood flow after flow reduction procedures. Vaes et al. (8) have shown that AV access high flow (>2 L/min) recurred in 52% of patients during the observation period (1 year) among patients who underwent flow reduction procedures.

It is also important to mention that studies have shown some conflicting results of the effect of AV access ligation on cardiac parameters. Rao et al. (9) conducted a randomized controlled trial among kidney transplant recipients (>12 months after transplantation with stable kidney graft function) comparing AVF ligation with no ligation. They randomized 64 patients and used cardiac magnetic resonance imaging at baseline and at 6 months after ligation. AVF ligation resulted in a significant reduction in left ventricular (LV) mass as compared with an increase in the control group but with no significant changes in LV ejection fraction. In other work, Laranjinha et al. (10) conducted a study on 17 patients after kidney transplan-

tation with functioning AV accesses. The team looked at transplanted kidney resistive indices before and after 30 seconds of compression on the AV access and while the AV access was still blocked. They found that 82.4% of patients had a significant decrease in their resistive indices and an increase in their mean arterial blood pressure during compression. All patients had a decrease in heart rate. These are interesting findings; however, more research is needed to investigate the clinical impact of these practices. Nonetheless, Cortesi et al. (11) performed a retrospective study evaluating patients with established LV hypertrophy who underwent AVF banding. The patients underwent two-dimensional echocardiography before and after the procedure. The study authors found that AV access ligation did not result in significant changes in LV mass index. These results contradicted previous findings of the effects of AV access ligation on cardiac parameters.

Although there is enough evidence to suggest that AV access ligation leads to a reduction in LV mass (9), it is important to mention that not all studies have shown this benefit of AV access ligation on LV mass (11, 12). Additionally, it will be important to correlate various AV access blood flow rates with LV mass and cardiac parameters.

Patients with a stable kidney transplant and patent AV access who experience AV access–related complications such as hand ischemia, arm edema, or other changes should receive a careful assessment weighing the benefit of treating these complications versus AV access ligation. However, there is no evidence to suggest that mortality improves by the ligation of an AV access without AV access–related complications among patients with kidney transplants. Additionally, although evidence suggests the benefit of AV access ligation on LV mass, some evidence has shown no benefit. With these conflicting results, the practice should continue to keep and maintain nonproblematic AV accesses after kidney transplantation. There is a need for well-designed and well-powered studies to investigate whether ligating a noncomplicated AV access reduces morbidity and mortality after kidney transplantation (1).

Loay Salman, MD, MBA, is chief of the division of nephrology and hypertension, the Thomas Ordway Distinguished Professor of Medicine at Albany Medical College, and the medical director of Dialysis Clinic, Inc., Albany.

References

1. Voorzaat BM, et al. No consensus on physicians' preferences on vascular access management after kidney transplantation: Results of a multi-national survey. *J Vasc Access* 2019; 20:52–59. doi: 10.1177/1129729818776905
2. Hart A, et al. OPTN/SRTR 2018 Annual Data Report: Kidney. *Am J Transplan*t 2020; 20:20–130. doi: 10.1111/ajt.15672
3. Vachharajani TJ, Agarwal AK, Asif A. Vascular access of last resort. *Kidney Int* 2018; 93:797–802. doi: 10.1016/j.kint.2017.10.030
4. Chan MR, et al. Initial vascular access type in patients with a failed renal transplant. *Clin J Am Soc Nephrol* 2014; 9:1225–1231. doi: 10.2215/CJN.12461213
5. Rao PS, et al. Survival on dialysis post-kidney transplant failure: Results from the Scientific Registry of Transplant Recipients. *Am J Kidney Dis* 2007; 49:294–300. doi: 10.1053/j.ajkd.2006.11.022
6. Hicks CW, et al. Practice patterns in arteriovenous fistula ligation among kidney transplant recipients in the United States Renal Data Systems. *J Vasc Surg* 2019; 70:842–852.e841. doi: 10.1016/j.jvs.2018.11.048
7. Maresca B, et al. Early echocardiographic modifications after flow reduction by proximal radial artery ligation in patients with high-output heart failure due to high-flow forearm arteriovenous fistula [published online ahead of print Feb 20, 2020]. *J Vasc Access* doi: 10.1177/1129729820907249
8. Vaes RH, et al. Effectiveness of surgical banding for high flow in brachial artery-based hemodialysis vascular access. *J Vasc Sur*g 2015; 61:762–766. doi: 10.1016/j.jvs.2014.09.034
9. Rao NN, et al. Effects of arteriovenous fistula ligation on cardiac structure and function in kidney transplant recipients. *Circulation* 2019; 139:2809–2818. doi: 10.1161/CIRCULATIONAHA.118.038505
10. Laranjinha I, et al. The impact of functioning hemodialysis arteriovenous accesses on renal graft perfusion: Results of a pilot study. *J Vasc Access* 2019; 20:482–487. doi: 10.1177/1129729818817248
11. Cortesi C, et al. Assessment of left ventricular mass changes after arteriovenous fistula surgical banding in end-stage renal disease. *Saudi J Kidney Dis Transplant* 2018; 29:1280–1289. doi: 10.4103/1319-2442.248299
12. Duque JC, et al. The impact of arteriovenous fistulae on the myocardium: The impact of creation and ligation in the transplant era. *Semin Dialysis* 2015; 28:305–310. doi: 10.1111/sdi.12313

Are You Still Getting Called Regarding Peripherally Inserted Central Catheters?

By Ammar Almehmi and Sloan E. Almehmi

Peripherally inserted central catheters (PICC) are increasingly used in modern clinical practice, especially among critically ill patients (1). The main attraction to the use of PICCs in clinical practice is likely driven by their perceived safety, low procedural complication rate, ability to facilitate care transition, low cost, and ease of insertion (2, 3).

PICCs are used for several indications, including extended antibiotic therapy, difficult venous access, total parenteral nutrition, chemotherapy, and occasionally central venous monitoring. They are usually single-lumen or dual-lumen catheters that are inserted under ultrasound guidance by a nurse-led team. Above-the-elbow basilic, brachial, or cephalic veins are commonly used for PICC insertion, with the catheter tip being in the central venous system (superior vena cava, subclavian vein, or brachiocephalic vein). Because more than 50% of critically ill patients require venous access, the use of PICCs is seen as a marker for a high burden of morbidity.

Patients with chronic kidney disease (CKD) and those using dialysis have a high burden of comorbidities related to a cluster of risk factors, both traditional (such as diabetes, hypertension, peripheral arterial disease, and heart failure) and nontraditional (abnormal mineral metabolism, left ventricular hypertrophy, and anemia). This profile of comorbidities places CKD patients at a higher risk for hospitalization, which usually requires venous access and intravenous therapies (4), leading to a high exposure to PICCs.

It is well acknowledged that PICC placement is associated with significant morbidity and mortality. In a comprehensive review and meta-analysis of approximately 30,000 patients, PICCs were associated with an increased risk of deep vein thrombosis and residual central venous stenosis (5). Furthermore, PICCs are associated with three times the risk of all-cause thromboembolism (4). Moreover, other complications of these catheters include thrombophlebitis and catheter-associated bacteremia with subsequent sepsis, endocarditis, and osteomyelitis (6).

The PICC-related complications have deleterious effects on vein quality and are associated with a lower frequency of functional arteriovenous (AV) fistulas in the CKD population (2). In a case control study, El Ters et al. (2) compared the PICC exposure in 120 patients receiving dialysis through a dialysis tunneled catheter or an AV graft with the exposure to 162 patients receiving dialysis through an AV fistula. They found that the frequency of previous PICC exposure was higher among AV fistula patients (44% vs. 20%), and this exposure was associated with fewer functioning AV fistulas ($p < 0.001$).

By contrast, in a dialysis population, McGill et al. (7) used the US Renal Data System to anlayze 34,000 patients who started dialysis by central venous catheter and found that 12.6% of them had previously used PICCs. Furthermore, PICCs placed before or after dialysis initiation were independently associated with a low likelihood of transition to AV fistula or graft. The presence of these catheters within the vein lumen for prolonged times is associated with repetitive trauma and subsequent thrombosis and stenosis (8).

Accordingly, the American Society of Nephrology, as part of the American Board of Internal Medicine's "Choosing Wisely" campaign, recommended consulting nephrologists before inserting PICCs in patients with CKD stage 3 to 5 (9). Moreover, the National Kidney Foundation Kidney Disease Outcomes Quality Initiative guidelines for vascular access recommended preservation of the forearm and upper arm veins, which are suitable for fistula creation, in patients with CKD stage 4 or 5. These veins should not be used for venipuncture or the placement of PICCs (5).

Now, with all these practice guidelines in place that discourage the use of PICCs in the CKD population, why are we still getting called or consulted regarding PICCs? With the increased risk of vein depletion of the upper extremity caused by healthcare-related venipuncture, how are we, as nephrologists, performing as the gatekeeprs of the venous real estate for our CKD patients?

The honest answer is that despite the available guidelines and the known disastrous effects of PICCs, a substantial number of dialysis patients continue to receive PICCs under the watch of their nephrologists (3).

Whereas some programs have already developed institutional protocols in which PICC insertion orders in patients with CKD stage 3 to 5 trigger the need for a nephrology consultation, most community hospitals lack such processes and protocols. Furthermore, despite these efforts and guidelines to avoid PICCs in patients with advanced CKD, 33.1% of short-term PICCs (dwell time <5 days) were seen in patients with GFR <60 mL/

Continued on page 26

Are You Still Getting Called Regarding Peripherally Inserted Central Catheters?

Continued from page 25

min (10).

All in all, the expanding use of PICCs is associated with vascular injury and subsequent venous thrombosis and stenosis. Morover, even with the current guidelines from different societies, there is a tendency to choose the PICC mostly for convenience and for a short dwelling time. In view of this reality, we are far from winning the battle for preserving the patient's venous real estate. To overcome the PICC tide, more coordinated collaborative efforts are required among different disciplines and specialties, mainly interventionists, nephrologists, hospitalists, and oncologists. In addition, PICCs should be inserted for valid indications, not out of convenience. Finally, more efforts by the stakeholders, mainly nephrologists, at the grassroots level are needed. One such effort is to advocate the use of small-bore (4-Fr or 5-Fr) rather than the current (6-Fr) central venous catheters as good alternatives to the current use of PICCs in patients with advanced CKD.

Ammar Almehmi, MD, is with the department of medicine and radiology and Sloan E. Almehmi, BS, MA, is with the department of biology, University of Alabama at Birmingham.

References

1. Govindan S, et al. Peripherally inserted central catheters in the ICU: A retrospective study of adult medical patients in 52 hospitals. *Crit Care Med* 2018; 46:e1136–e1144. doi: 10.1097/CCM.0000000000003423
2. El Ters M, et al. Association between prior peripherally inserted central catheters and lack of functioning arteriovenous fistulas: A case-control study in hemodialysis patients. *Am J Kidney Dis* 2012; 60:601–608. doi: 10.1053/j.ajkd.2012.05.007
3. Kalloo S, Wish JB. Nephrologists versus peripherally inserted central catheters: Are the PICCs winning? *Clin J Am Soc Nephrol* 2016; 11:1333–1334. doi: 10.2215/CJN.05750516
4. Drew DA, Weiner DE. Peripherally inserted central catheters (PICCs) in CKD: PICC'ing the best access for kidney disease patients. *Am J Kidney Dis* 2016; 67:724–727. doi: 10.1053/j.ajkd.2016.01.013
5. Chopra V, et al. Risk of venous thromboembolism associated with peripherally inserted central catheters: A systematic review and meta-analysis. *Lancet* 2013; 382:311–325. doi: 10.1016/S0140-6736(13)60592-9
6. Chopra V, et al. Bloodstream infection, venous thrombosis, and peripherally inserted central catheters: Reappraising the evidence. *Am J Med* 2012; 125:733–741. doi: 10.1016/j.amjmed.2012.04.0**10**
7. McGill RL, et al. Peripherally inserted central catheters and hemodialysis outcomes. *Clin J Am Soc Nephrol* 2016; 11:1434–1440. doi: 10.2215/CJN.01980216
8. Shingarev R, Allon M. Peripherally inserted central catheters and other intravascular devices: How safe are they for hemodialysis patients? *Am J Kidney Dis* 2012; 60:510–513. doi: 10.1053/j.ajkd.2012.07.003
9. Williams AW, et al. Critical and honest conversations: The evidence behind the "Choosing Wisely" campaign recommendations by the American Society of Nephrology. *Clin J Am Soc Nephrol* 2012; 7:1664–1672. doi: 10.2215/CJN.04970512
10. Paje D, et al. Patterns and predictors of short-term peripherally inserted central catheter use: A multicenter prospective cohort study. *J Hosp Med* 2018; 13:76–82. doi: 10.12788/jhm.2847

Fellows Corner

Impact of a Hurricane on Dialysis Patients: A Case Study

By A. Oussama Rifai and Harini Bejjanki

Harini Bejjanki

A. Oussama Rifai

Hurricane Michael made landfall as an unprecedented category 5 hurricane in the Florida panhandle, with maximum sustained wind speeds of 155 mph at 1 p.m. on October 10, 2018. Along the Florida panhandle, the cities of Mexico Beach and Panama City suffered the worst of Michael, with catastrophic damage reported (1).

According to US Renal Data System 2015 data, a total of 468,000 patients were receiving dialysis in the United States (2). Of those patients, 26,382 were in Florida, and about 350 patients were in Bay County. Dialysis patients are a very vulnerable group, and it is necessary to plan how to care for them in special circumstances, such as anticipated natural disasters. Hurricane Michael gave 5 days of warning.

Hurricane Michael brought with it a significant decline in quality of life; loss of infrastructure, including electricity, phones, and the internet; evacuation of medical personnel; a severe shortage of medicines; unavailability of pharmacies; lack of essential supplies; and an increased risk of infectious diseases and mortality in the Panama City area for weeks after it landed. All hospitals in Bay County were severely damaged and were no longer able to provide inpatient care. The only functioning facility was an emergency department, which transferred all patients who needed admission. Inpatient dialysis services were suspended as well.

Accurate figures are lacking, and most of the information in this article is based on observations by the authors—Dr. Oussama Rifai, MD, a practicing nephrologist in the Panama City area, and Dr. Harini Bejjanki, MD, a renal fellow at the University of Florida, Gainesville—who were involved in the care of dialysis patients from Panama City admitted to the University of Florida, Gainesville. Our direct observations revealed that the care of dialysis patients was severely compromised because of a lack of access to outpatient dialysis units, electricity outages, lack of medications and equipment, destruction of healthcare infrastructure, and shortage of medical care providers, including dialysis technicians, patient care technicians, and dialysis nurses.

Lessons learned after Hurricane Michael: how did we handle it and what can we do better?

Predisaster emotional dialysis

There are five dialysis centers in the Panama City area, serving 350 patients. Hurricane Michael made landfall on a Wednesday. Knowledge of this information ahead of time led to "emotional dialysis," whereby we provided 2-hour or 3-hour dialysis sessions to all the patients on Tuesday, a day before landfall. In retrospect, we propose that dialysis not be provided to everyone for the best use of resources. We suggest making phone calls to all dialysis patients to find out who will evacuate, using resources for those who stay back, and providing them 4 hours of dialysis instead of 2 hours, in anticipation of missed dialysis sessions during the hurricane after the landfall. We also suggest administering dialysis only to patients who plan to evacuate and describe symptoms of volume overload, and providing information on where patients may go for future dialysis sessions depending on the location to which they are evacuating.

Hemodialysis companies and the need for disaster relief teams

Day T-1 should be the day when the dialysis centers provide dialysis for all patients who have decided to stay and not evacuate, a full treatment being given by both the Monday-Wednesday-Friday and the Tuesday-Thursday-Saturday shifts.

The team of nurses and technicians providing this dialysis treatment should consist of seasoned patient care technicians, nurses, and volunteers brought in from outside the projected affected area. They arrive on day T-2 to a staging safe area, then get a bus and work all of day T-1, possibly in two 16-hour shifts, and depart before the hurricane makes landfall, when it is still safe to leave.

This allows the local team members to attend to their personal lives if they decide to stay and places them in a better position to emerge and care for patients during the days after day T+1 onward. Our staff in Bay County and the surrounding counties did not have time to care for their families, homes, and personal lives before the hurricane. The disaster team members will have more energy by working in teams of two (disaster shifts) during these situations, providing efficient services.

Large dialysis organizations should send disaster response

teams for assessment and rebuilding. The teams should be on standby to ensure continuity of service for this vulnerable group of patients. Fresenius mentions on its website that it routinely conducts mock disaster training sessions to make sure teams know their roles and responsibilities so that disaster operations will run as smoothly as possible.

A contingency plan

During times of disaster, people, communities, and organizations often come together. It is important to have a contingency plan with other dialysis units in the surrounding areas and to have patients receive dialysis at these surrounding facilities. Although dialysis units must have emergency generators and water tanks, we had some unpredictable challenges. A contingency plan to provide patients access to surrounding hemodialysis centers should have been prearranged because most units were nonfunctional after Hurricane Michael, owing to destruction of the infrastructure and lack of utilities.

Four hours away in Gainesville, at the University of Florida, patients presented to the emergency department with shortness of breath, volume overload, and life-threatening hyperkalemia requiring urgent dialysis. The other problem we noticed was an increase in the length of stay because these patients could not be discharged to their skilled nursing facilities. A successful contingency plan was implemented in Puerto Rico after Hurricane Maria because of previously established agreements with surrounding hospitals; consequently, the entire team, including nurses and nephrologists, were able to move to the new location, which made the transition easier (3). At least four of our dialysis patients died during the hurricane because of their inability to communicate and reach a hospital.

Providing an emergency hurricane packet

Hurricane packets should be available at the dialysis facility to be provided to patients. Each patient's hurricane packet should at the minimum include the dialysis prescription, laboratory results from the prior month, a prescription for monthly dialysis laboratory tests, hepatitis B status, any other needs for isolation, results of a recent history and physical examination, prescription for medications, and names, locations, and phone numbers of backup dialysis units and hospitals in the area and surrounding areas. Many people in Panama City had catastrophic damage. While they were swimming in their own homes trying to get out, looking for the hurricane package would have been the last thing on their mind. Hence, there should be an online repository with each patient's pertinent information that can be easily accessed by patients or family members and by receiving dialysis facilities.

Hyperkalemia

Availability of a point-of-care or iSTAT portable clinical analyzer in the dialysis clinic is essential and could be lifesaving. In our case, all local hospitals were damaged, and there were no inpatient dialysis services. Outpatient laboratory services were shut down as well. The long lines in the emergency department made checking potassium levels a major undertaking. When all food and local restaurants were not able to support the communities, patients used meals-ready-to-eat provided by the Department of Defense; these meals tend to be rich in sodium, calories, and potassium.

We had samples of patiromer (Veltassa) in our office, and we provided patients with 1 week of patiromer packets according to the following sliding scale, based on the monthly laboratory results:

For K 5.0 to 5.5 mEq/L, patiromer 8.4 g daily
For K 5.5 to 6.0 mEq/L, patiromer 16.8 g daily
For K over 6 mEq/L, we recommended patiromer 25.2 g daily

Patiromer should be available at the dialysis clinic before the hurricane, in the evacuation package with the patients, and after the hurricane in the dialysis clinics. A laminated instruction manual should be added to include directions on the use of patiromer. We preferentially used patiromer rather than sodium polystyrene sulfonate (Kayexalate) because it is low-sodium resin, which is a consideration especially when sodium is an additional risk with meals-ready-to-eat and when lack of regular dialysis is possible.

Peritoneal dialysis

This has not yet been a problem. Most of our peritoneal dialysis patients evacuated with 1 months' worth of supplies. We recommend including in the emergency medication pack a 5-day supply of the antibiotic for peritonitis in line with recommendations in the National Kidney Foundation's disaster brochure (4). If a disaster occurs, it may be difficult to maintain a clean environment, and the risk of peritonitis may be higher. Almost all the peritoneal dialysis patients evacuated. By default, peritoneal dialysis is a modality of freedom, so patients can easily evacuate and can take the cycler with them or do manual exchanges.

It is important to have a contingency plan with other dialysis units in the surrounding areas and to have patients receive dialysis at these surrounding facilities.

Clotted access

It was observed that dialysis accesses had more frequent clotting. Formal data are lacking, but according to our observations of emotional dialysis for 2 hours the day before and the ensuing days after, more cannulation than usual and different techniques with pressures on the access to expedite diaylsyis for the next patients might have contributed to this anecdotally observed phenomenon.

Increased mortality

This observation was also reported in local newspapers after examining the medical records of deceased patients (5).

Postdisaster dialysis

Day T+1 should be the day to dialyze patients and provide full treatments, if possible. Transportation, gasoline, roadblocks, and curfews lead to difficulty in reaching the dialysis centers, so 2-hour "emotional dialysis" should be avoided if possible. This can be achieved by proper screening and continued dialogue with each patient. A patient accounts liaison person should update contact information and plans for each patient.

Encourage patients to have a 1-month supply of all medications and to have all prescriptions with at least a few months of refill instructions.

Emotional dialysis

We do not recommend 2-hour short runs, before and after a hurricane. Adequacy of twice-a-week dialysis with patiromer in between should be considered, especially for patients with residual kidney function. Telemedicine infrastructure should be available in the dialysis center for dialysis patients, with nephrology providers on the other side, along with another channel for clinical staff supported by seasoned nurses and technicians on the other side.

During the Syrian political and humanitarian crisis, "The standard of care regarding the frequency of dialysis was one per week and sometimes two but very rare to have a dialysis schedule of three times a week," and this did not seem to result in adverse outcomes as of 2014 (6). ■

A. Oussama Rifai has been a practicing nephrologist for more than 20 years in the Panama City, Florida, area, and is affiliated with Hypertension Kidney & Dialysis Specialists. Harini Bejjanki MD, FACP, is an onconephrology fellow at the University of Texas MD Anderson Cancer Center.

References

1. Hurricane Michael – October 2018. www.weather.gov/mob/michael.
2. Kidney Disease Statistics of the United States: https://www.niddk.nih.gov/health-information/health-statistics/kidney-disease
3. Bonilla-Félix M, Suárez-Rivera M. Disaster management in a nephrology service: Lessons learned from hurricane Maria. *Blood Purif* 2019; 47:199–204. doi: 10.1159/000494580
4. National Kidney Foundation. Planning for Emergencies: A Guide for People with Chronic Kidney Disease. https://www.kidney.org/sites/default/files/docs/disaster-brochure.pdf
5. Dion E. *Panama City News Herald*. Remembering Hurricane Michael's Panhandle victims (PHOTOS). https://www.nwfdailynews.com/news/20181120/remembering-hurricane-michaels-panhandle-victims-photos
6. Al-Makki A, et al. The Syrian National Kidney Foundation: Response for the need of kidney patients during the crisis. *Avicenna J Med* 2014; 4:54–57. doi: 10.4103/2231-0770.133331

Recommendations for dialysis during hurricane season

1. Screen every patient regarding evacuation plans and encourage them to maintain a 1-month supply of all medication prescriptions.
2. Have disaster relief team arrive on day T-1 to dialyze all patients staying behind for a complete treatment, to support the local staff.
3. Use a cloud-based repository for evacuation packages.
4. Use point-of-care or iSTAT devices for laboratory results, especially for potassium and patiromer availability in dialysis clinics.
5. After the hurricane, consider twice-a-week dialysis for a few weeks for patients with residual renal function (complete treatment) until normal conditions return. Use patiromer in between dialysis sessions to control hyperkalemia.
6. Establish collaboration protocols with nearby centers outside the danger zone with access centers and dialysis clinics.
7. Use social media for updates, and form groups with WhatsApp and Facebook.

Give yourself the best nephrology board examination prep.

World-class preparation available with ASN's Board Review Course & Update (BRCU) Online.

ASN's BRCU Online combines the convenience of distance learning, a complete curriculum, and world-renowned faculty in one program. BRCU Online 2019 with CME and MOC has been extended through July 2021. This activity provides the best online preparation course for board examinations (certification and recertification) in nephrology.

The complete program includes:

- Up to 65.25 CME Credits and MOC Points by passing the Post Test
- Practice Exam with 300+ case-based questions
- Five, one-hour, pre-recorded webinars on specific core topics

Purchase the full resource or select topics in the ASN Learning Center.

Learn more at ASN-online.org/BRCU

AMERICAN SOCIETY OF NEPHROLOGY · ASN ·

BRCU
Board Review
Course & Update

Metabolic Acidosis
Insights®

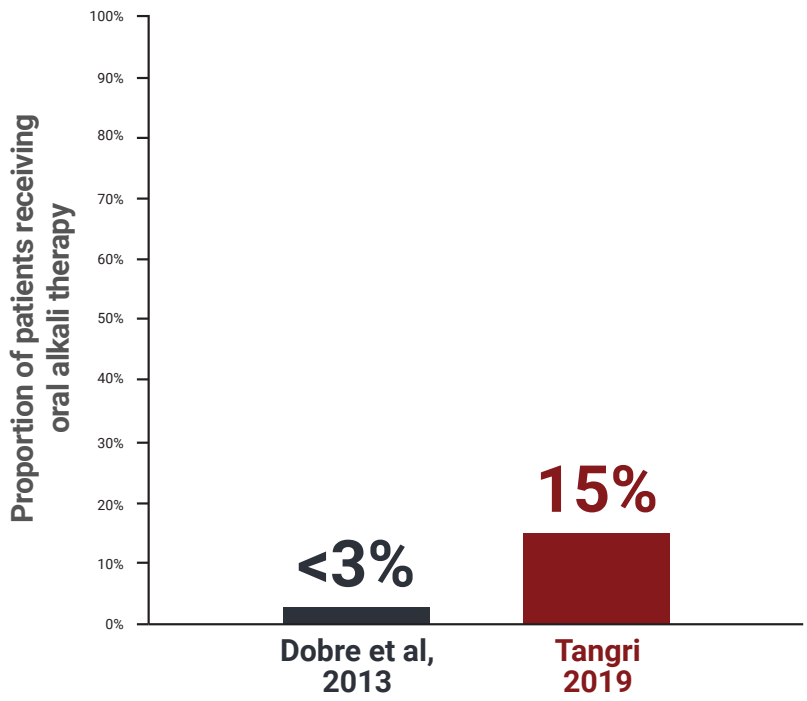
CHRONIC METABOLIC ACIDOSIS IS **UNDERTREATED**[1,2]

A growing body of evidence shows that metabolic acidosis is undertreated in patients with chronic kidney disease (CKD)[1,2]

- An analysis of claims and prescription data from a cohort of over 80,000 patients with laboratory data indicative of unequivocal Stage 3-5 CKD and chronic metabolic acidosis showed:
  - Metabolic acidosis was treated in 15.3% of the cohort[1]

- In the Chronic Renal Insufficiency Cohort (CRIC) study, a longitudinal study of over 1000 patients with Stage 2-4 CKD and metabolic acidosis:
  - Less than 3% of the cohort were treated with oral alkali therapy[2]

PATIENTS TREATED FOR METABOLIC ACIDOSIS[1,2]



Learn more at **MetabolicAcidosisInsights.com**

References: 1. Tangri N. Metabolic acidosis is underdiagnosed and undertreated in patients with chronic kidney disease. Poster presented at: American Society of Nephrology Kidney Week 2019; November 5-10, 2019; Washington, DC. **2.** Dobre M, Yang W, Chen J, et al. Association of serum bicarbonate with risk of renal and cardiovascular outcomes in CKD: a report from the Chronic Renal Insufficiency Cohort (CRIC) study. *Am J Kidney Dis*. 2013;62(4):670-678.

TRICIDA

Are you a fellow and have a tip or idea you'd like to share with your fellow peers and the broader kidney community?

Send your idea to the Kidney News Fellows Corner column at kidneynews@asn-online.org

KidneyNews Free Subscriber Service Request Card

☐ I wish to start/renew a FREE* subscription to Kidney News

7-digit number label (Required for change of name/address only)

Name

Address

City State Zip

Telephone Fax

Email Address

Signature Date

Title/Position
- ☐ Physician
- ☐ Researcher
- ☐ RN, CNN, NM, LPN, APN, PA
- ☐ Dialysis Center Director
- ☐ Administration
- ☐ Clinic Manager/Coordinator
- ☐ Social Work
- ☐ Other

Specialty Area
- ☐ General Nephrology
- ☐ Transplantation
- ☐ Dialysis
- ☐ Laboratory
- ☐ Other

Institution
- ☐ Hospital <100 beds
- ☐ Hospital 100-250 beds
- ☐ Hospital 251-500 beds
- ☐ Hospital > 500 beds
- ☐ Dialysis Center
- ☐ Clinical Lab
- ☐ Other

Please Circle Degree:
MD MD/PhD DO
PhD MBA RN MS
BS Other_____

ASN American Society of Nephrology

Return the completed form to:
Bob Henkel, 1401 H Street NW, #900, Washington, DC 20005
or Fax: 202-403-3615 or Email: bhenkel@asn-online.org

Index to Advertisers

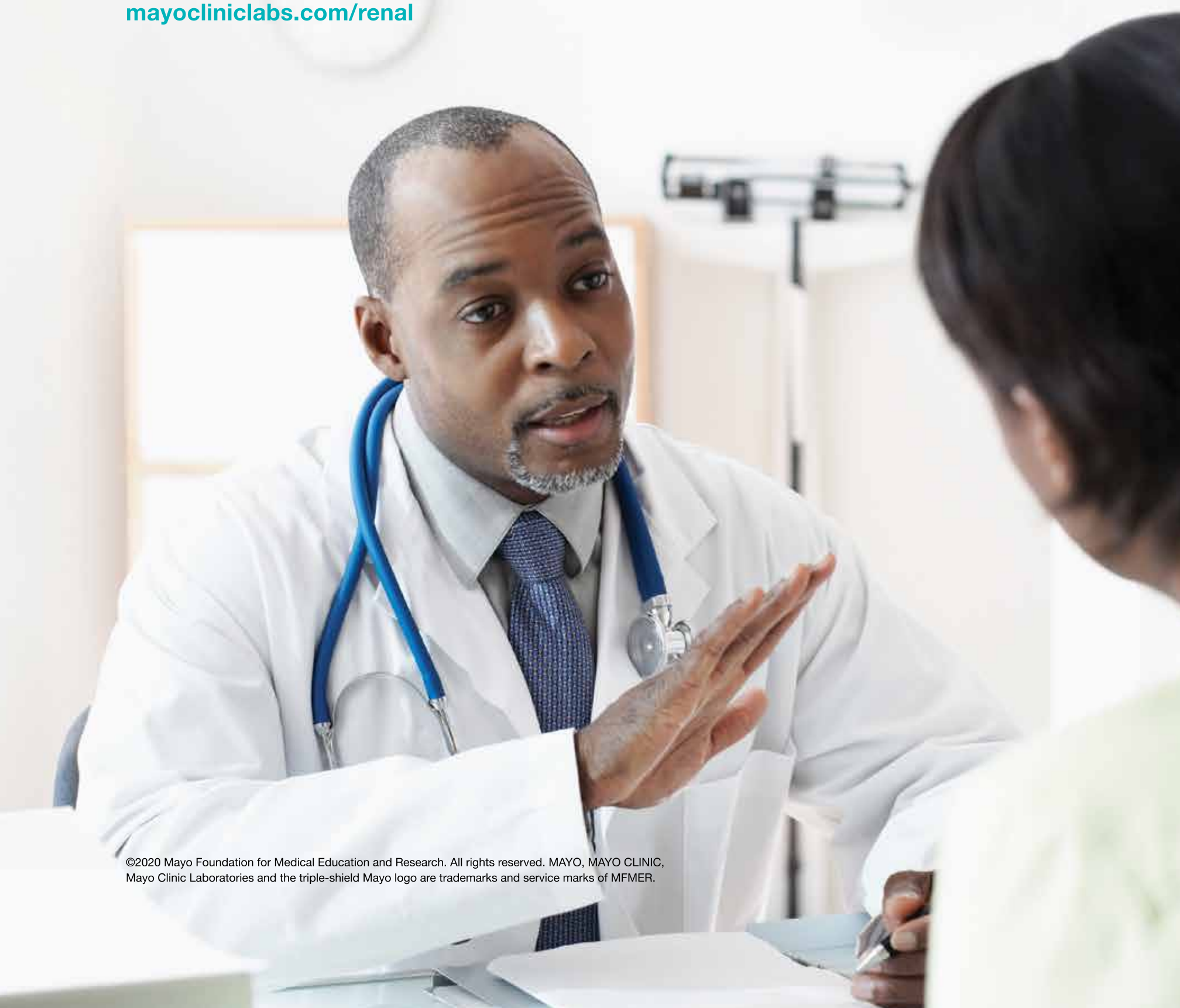
MAYO CLINIC
LABORATORIES

EFFECTIVELY
DIAGNOSE AND TREAT.

Partner with a single diagnostic source to strengthen your practice and keep care local.
Our 200+ renal tests deliver more accurate diagnoses and improve patient outcomes.

Helping you be the hero your patients need.

mayocliniclabs.com/renal



AlloSure®

CareDx®
Your Partner in Transplant Care

Derek F., kidney transplant recipient

It's time for innovation

DETECT TRANSPLANT REJECTION EARLIER

AlloSure is the first clinically and analytically validated, non-invasive test that assesses kidney health by directly measuring allograft injury.

PROVEN EXPERIENCE IN TRANSPLANT SPECIFIC cfDNA

>60K
Patient Results Served

>160
Centers Actively Using AlloSure

14
Center Prospective Validation Trial

Learn more at: **caredx.com/allosure**