

The Clinical and Economic Impact of Catheter-Related Bloodstream Infections: Is it a Public Health Problem?

NOVEMBER 2021

Clinical Discussions with:



Anil Agarwal, MD



**Krithika (Kitty)
Rajagopalan, BS, MD, PhD**



Dr. Anil Agarwal is chief of medicine at Veterans Administration Hospital in Fresno, California. He is a nephrologist trained at Ohio State University in Columbus, where he later established the interventional nephrology program. He also served as the director of clinical scholarship for Faculty Advancement, Mentoring and Engagement at OSU College of Medicine. He received his medical degree from Maharani

Laxmi Bai Medical College and has been in practice for four decades. He is experienced in general nephrology, acute renal failure, chronic kidney disease, interventional nephrology, and dialysis. He is currently the president of the American Society of Diagnostic and Interventional Nephrology and is also incoming chair of the Interventional Nephrology Workgroup of International Society of Nephrology. Dr. Agarwal also serves in multiple leadership roles locally, regionally, nationally, and internationally. He is a passionate educator, author, and mentor.



About Krithika (Kitty) Rajagopalan, BS, MD, PhD

Dr. Rajagopalan has over 25 years of operational experience in building and leading global and U.S. health economics, pricing, policy, and market access function across the drugs, devices, and biologics industry. Her expertise in the cross-therapeutic area of health economics and outcomes research (HEOR) spans a wide spectrum of diseases and

conditions including but not limited to psychiatry, neurology, oncology, cardiopulmonary, respiratory, autoimmune, and other rare diseases. She owns multiple copyrights for patient-reported outcomes instruments and has published over 80 manuscripts in peer-reviewed journals. She also has presented over 600 scientific papers, and is an invited speaker at DIA (Drug Information Association), ISPOR (International Society for Pharmacoeconomics and Outcomes Research), and other forums on healthcare topics as diverse and global as reimbursement, HEOR methodologies, patient-reported outcomes in clinical trials, public policy issues with the emergence of accountable care organizations, and expanded role of HEOR.

For patients with kidney failure, catheter-related bloodstream infections (CRBSIs) are a chief cause of both morbidity and mortality.¹ In addition to the clinical impact, these infections are a financial albatross on the healthcare system and represent an often-unaddressed public health problem.

Currently, approximately 80% of patients with incident kidney failure and up to 20% of patients with prevalent kidney failure in the United States receive dialysis via central venous catheters (CVCs).^{1,2} Establishing vascular access is often challenging for patients who require renal replacement therapy via hemodialysis (HD) for a bevy of reasons, including anatomic host factors, prolonged maturation time, and patient reluctance.¹ These factors have contributed to a stubbornly high rate of CVC use.¹ Despite significant efforts over the past 15 years to increase the number of patients initiating HD treatment via an arteriovenous (AV) fistula, CVCs remain the primary vascular access, and, while providing an immediate access method, are linked to a risk of CRBSIs.

Given that AV fistulas are often a better option for vascular access, why are CVCs still the most common access used for HD in patients with kidney failure initiating treatment? And why do up to 20% of patients remain on CVCs? “In an ideal world, everyone would start with permanent access. Unfortunately, that has not been possible for a number of issues,” says **Anil Agarwal, MD**, chief of medicine at the VA Central California Healthcare System

and professor at UCSF Fresno. “You can consider a lack of pre-dialysis care by the nephrologist. Generally, our patients are not referred to a nephrologist in the early stages of kidney disease so that they can educate the patients about the options at the time. Also, there is a lack of expertise on AV access placement. Many patients will suffer with catheters because there’s nobody to put AV fistulas in place. At the same time, not all patients are referred for AV fistula early. Even if they are referred, the process for patients with AV fistula has several hurdles.”

Dr. Agarwal noted that getting a referral to “an appropriate surgeon who has the skills, and then getting [the patient] on the surgical schedule” is one such hurdle. “Many patients have comorbidities [and] need clearance for surgery. That takes time,” he added. Patient preference must also be considered. “At times the patients do not know exactly which access to choose because they have not been educated about it.” In those cases, a catheter can seem like the easier procedure.

There are biological barriers, as well. A vein must reach maturity, both physically and functionally, prior to use for vascular access.³ The time required for fistula maturation varies among patients, but allowing the fistula to mature for 3 to 4 months prior to access may be ideal.³ “Even if you create an AV fistula in time, there’s still an issue with the maturation of AV fistula. We have been researching this but have not been able to find a uniform way of creating an AV fistula that will last for a long time,” Dr. Agarwal said.

Why CVCs Are Linked to Blood Stream Infections

Despite its prevalence, the Infectious Diseases Society of America (IDSA) only recognized CRBSIs in CVCs in recent years.¹ As it pertains to how CVCs are actually linked to CRBSIs, one culprit (along with other pathogens like fungal, viral, and parasitic infections) is bacteria, Dr. Agarwal explained. “A dialysis catheter actually hangs out of the body, [providing] connection to the external environment, directly into the heart where the catheter sits. There is some evidence that, as soon as these catheters are placed, bacterial contamination forms inside of them. These bacteria then lead to production of polysaccharides which turn into biofilms,” he said. “Biofilms provide a shelter for the bacteria where, even if these patients are treated with systemic antibiotics, they will not be able to reach the concentration required unless a very high concentration of antibiotic locks are used. The catheters are then, hopefully, placed with all the aseptic precautions. Still, these catheters are being manipulated three times a week in the United States when patients show up for dialysis.”

The Medical Challenge

CRBSIs can be arduous to treat and present a myriad challenges for clinicians, as well as a marked threat to patients’ quality of life. In a recent study of Medicare claims of HD patients, **Krithika (Kitty) Rajagopalan, MS, PhD**, and colleagues at Anlitiks (a health outcomes consulting firm) found that CRBSIs occurred in approximately one-third of patients that start HD using CVCs for vascular access. Dr. Rajagopalan believes that CRBSIs are a mounting public health problem both in the short-term and long-term. “CRBSIs occur relatively quickly among kidney failure patients requiring hemodialysis,” she said. “Over 50% happen in first three months after CVC insertion, and 80% occur within one year after CVC insertion. However, about one in five patients with CRBSIs have it in the long-term.” Based on her research, Dr. Rajagopalan also noted that, “on average, CRBSI patients have twice the number of hospitalizations and over four times the number of hospitalization days compared to those without CRBSIs.”³

Dr. Agarwal elucidated the challenges faced treating CRBSIs. “One [challenge] is on a broader level and the other is at the patient level,” said Dr. Agarwal. “Looking at the studies of catheter-related bacteremia, there is non-uniform reporting and comparison among these studies. We don’t have the clearest understanding of catheter-related bacteremia, how it is diagnosed, or how it is treated.”

“The management of outpatients, at least, is not standardized,” he said. “Patient management is difficult, and consequently, the patient goes into the hospital. Once

they’re in the hospital, they have a prolonged hospital stay that can lead to complications and possibly even death. This is echoed by the research conducted by Dr. Rajagopalan and her colleagues, as they found that CRBSIs augment the risk of endocarditis, congestive heart failure, stroke, and myocardial infarctions among others. “There are a number of issues, starting from diagnosis to management strategies to management tools,” she added. “We don’t have a perfect system and we have not standardized the way of managing CRBSIs.”

A Huge Financial Burden

Compounding the clinical burden of CRBSIs, the financial impact of CRBSIs and associated complications is not insignificant. Only 3.65% of ESRD patients on HD with CVC access are driving \$2.3 billion in annual direct medical expenses due to preventable CRBSIs.³ In short, these infections are extremely expensive – for payers and the healthcare system. “CRBSIs have a significant impact on patients’ lives and are burdensome to the healthcare system,” remarked Dr. Rajagopalan.

“Not including the costs and burden associated with reductions in quality of life, productivity losses when patients go into disability or step away from work, and premature mortality due to infections and real complications, direct cost of CRBSI may be as high as several billion dollars annually.”

—Krithika (Kitty) Rajagopalan, BS, MD, PhD

Dr. Rajagopalan and colleagues have conducted research using data from the United States Renal Data System linked with Medicare claims to estimate the potential annual costs of CRBSIs. “Not including the costs and burden associated with reductions in quality of life, productivity losses when patients go into disability or step

away from work, and premature mortality due to infections and real complications, direct cost of CRBSI may be as high as several billion dollars annually,” according to Dr. Rajagopalan’s research. Moreover, the monetary impact of these infections is not exclusive to patients. In the management of CRBSIs, dialysis providers also face revenue loss due to decreased dialysis sessions and incremental costs due to the increased use of erythropoietin and intravenous antibiotics.⁴⁻¹⁰

Potential Strategies to Attenuate Costs

Knowing the challenges that CRBSIs present, and the economic impact they have, the question becomes: What steps can be taken to attenuate the impact of CRBSIs on the healthcare system? “First of all, if you don’t want catheter infections, please do not put catheters in,” Dr. Agarwal stated. “So, catheter avoidance is probably the first strategy.”

“Considering that the cost of one hospitalization for CRBSI might be approximately \$45,000, we can reduce that to maybe \$10,000 for a very small investment. Spending a little bit of money on the prevention side can realize significant economic savings.”

—Krithika (Kitty) Rajagopalan, BS, MD, PhD

Dr. Agarwal opined that education is “a must.” “When I say ‘education,’ I mean that we need to also educate our primary care colleagues to refer patients early and collaborate because it’s a problem that affects

everybody,” he said. “We also need early referral by the nephrologist to the surgeons. We need to educate on AV fistula – the biological issues, expertise issues, lack of training among surgeons, and all those things.” Some of those challenges can be obviated with more time at hand. Dr. Agarwal offered the following example: “Scheduling delayed for a week would be fine if you are starting six months early. But, if you need to start dialysis in three weeks or four weeks or five weeks, having a week of delay can mean a lot. We need to have better early referral strategies.”

Dr. Rajagopalan concluded by saying: “Considering that the cost of one hospitalization for CRBSI might be approximately \$45,000, we can reduce that to maybe \$10,000 for a very small investment. Spending a little bit of money on the prevention side can realize significant economic savings. I like to say, ‘An ounce of prevention is better than a pound of cure.’ That’s where we are and that should help decrease the economic burden of CRBSIs on the healthcare system.”

References

1. Soi V, Moore CL, Kumbar L, Yee J. Prevention of catheter-related bloodstream infections in patients on hemodialysis: challenges and management strategies. *Int J Nephrol Renovasc Dis.* 2016;9:95-103. Published 2016 Apr 18. doi:10.2147/IJNRD.S76826
2. Farrington CA, Allon M. Management of the Hemodialysis Patient with Catheter-Related Bloodstream Infection. *Clin J Am Soc Nephrol.* 2019 Apr 5;14(4):611-613. doi: 10.2215/CJN.13171118. Epub 2019 Mar 5. PMID: 30837242; PMCID: PMC6450352.
3. Data on file.
4. Brunelli SM, Turenne W, Sibbel S, Hunt A, Pfaffle A. Clinical and economic burden of bloodstream infections in critical care patients with central venous catheters. *J Crit Care.* 2016 Oct;35:69-74. doi: 10.1016/j.jcrc.2016.04.035. Epub 2016 May 14. PMID: 27481738.
5. <https://adr.usrds.org/2020/end-stage-renal-disease/1-incidence-prevalence-patient-characteristics-and-treatment-modalities>
6. Zhang HH, Cortés-Penfield NW, Mandayam S, Niu J, Atmar RL, Wu E, Chen D, Zamani R, Shah MK. Dialysis Catheter-related Bloodstream Infections in Patients Receiving Hemodialysis on an Emergency-only Basis: A Retrospective Cohort Analysis. *Clin Infect Dis.* 2019 Mar 5;68(6):1011-1016. doi: 10.1093/cid/ciy555. PMID: 29986016; PMCID: PMC6399430.
7. Childers CP, Dworsky JQ, Kominski G, Maggard-Gibbons M. A Comparison of Payments to a For-profit Dialysis Firm From Government and Commercial Insurers. *JAMA Intern Med.* 2019;179(8):1136–1138. doi:10.1001/jamainternmed.2019.0431
8. BlueCross BlueShield of Texas, 2020 CPT/HCPCS Drug Fee Schedule
9. Pfizer Biosimilars (2018)
10. https://journals.lww.com/md-journal/_layouts/15/oaks.journals/ImageView.aspx?article=00021&i=T1&issue=05150&k=md-journal:2020:05150:00021&type=Fulltext&year=2020