Interventional Nephrology

Interventional nephrology has become a growing and distinct discipline within nephrology. The first two articles in this special section deal with everyday issues that practicing nephrologists, dialysis nurses, and technicians encounter.

In "The PICC Conundrum: Vein Preservation and Venous Access," Dr. Pflederer provides background on the increasing use of PICC lines and how their use impacts CKD patients who will require vascular access. Indeed, Dr. Pflederer's article may serve as a resource for developing a PICC line use policy.

Dr. Besarab outlines the enormous impact that the all too frequent use of central venous dialysis catheters has on the morbidity and mortality of patients. He describes the three scourges of dialysis central venous catheters: maintaining patency, catheter-related infection, and central vein stenosis. The frequent use of central venous dialysis catheters has led to what many describe as an epidemic of central venous stenosis. Unfortunately, there are no durable endovascular or surgical strategies once central vein stenosis develops, often leading to permanent vascular access loss.

Dr. Agarwal describes multiple factors favoring peritoneal dialysis. The alignment of benefits to patients (for example, better initial survival, which may be related to not using a central venous dialysis catheter) and now financial benefits derived from the changes in reimbursement may lead to an increase in peritoneal dialysis in the United States. Perhaps these changes will lead to a "PD First" approach as a corollary to "Fistula First."

Next, Drs. Rahbari-Oskoui and O'Neill outline the utility of ultrasonography when used by nephrologists. Several medical specialties have incorporated ultrasonography as part of their practice. Rahbari-Oskoui and O'Neill successfully argue that nephrologists can improve patient care by doing so. In many ways, ultrasound is supplanting the stethoscope.

In the final two articles in this issue, Dr. Dwyer discusses the development of interventional nephrology and Dr. Roy-Chaudhury discusses research opportunities in interventional nephrology.

Interventional nephrology, born in the private practice sector, has now evolved and matured with the development of formal training programs in academic medical centers. ASN has recognized the importance of these developments by establishing the Interventional Nephrology Advisory Group (INAG), which informs the ASN Council and Board of Advisors about issues of importance to the society.

Most recently, INAG has developed a comprehensive curriculum for academic-based nephrology training programs. As described by Dr. Roy-Chaudhury, INAG has also worked with other societies to recommend to the National Institute of Diabetes and Digestive and Kidney Diseases research initiatives germane to improving the care of kidney patients. This focus on research in dialysis vascular access should lead to improved patient care.

I hope that this special edition of *Kidney News* stimulates you, the reader, to learn more about interventional nephrology.

—Jack Work, MD, chair of the ASN Interventional Nephrology Advisory Group, edited this special section for ASN Kidney News, *along with* KN *editorial board member Edgar Lerma.*

The PICC Conundrum:
Vein Preservation and Venous Access

By Timothy A. Pflederer

Peripherally inserted central venous catheters (PICC lines) are being used with increasing frequency in the hospital and outpatient settings for patients who require venous access. Originally intended as a less invasive way to obtain long-term central venous access, PICC lines are now being used for a growing number of indications. Patients who require an extended course of antibiotics or other medications were often chosen to have a PICC line placed after treatment was begun with a peripheral intravenous (IV) catheter. However, PICC lines are now often chosen as the first-line access option in patients with difficult venous access regardless of the duration of therapy required.

Hospitalized patients are older and more chronically ill than in the past. Many of these patients have poor peripheral veins caused by underlying disease, repeated phlebotomy, and IV catheters. Maintaining peripheral IV access can be challenging and time consuming for hospital staff. PICC lines obviate these frustrations and have therefore become staff's preferred venous access device, often placed even when venous access may not truly be required for very much longer. Because of an increasing body of evidence that PICC lines interfere with future arteriovenous fistula placement for dialysis access, the rapid rise in the use of PICC lines has become of great concern.

PICC lines are single-lumen or dual-lumen catheters designed to be placed in a peripheral vein with the tip advanced into a central vein—typically the subclavian vein, brachiocephalic vein, or superior vena cava. They can be placed in the cephalic, median cubital, or basilic veins of the upper arm.

Ultrasound is commonly used to facilitate accurate placement, especially in the more deeply located basilic vein. PICC lines provide convenient, long-term venous access with low rates of failure from thrombosis or infection. They last longer and require less maintenance than peripheral IV catheters. And because they are placed in larger veins at the elbow or above, they can usually be successfully placed even in the most challenging patient. Hospital nursing staff can be trained to place the lines, and this often allows PICC placement to be readily available day or night. These advantages of PICC lines have led to a dramatic rise in their use, especially in the hospital setting.

Unfortunately, this increasing use of PICC lines has come with a cost for patients with chronic kidney disease who go on to require dialysis. PICC lines are associated with a 23–57 percent incidence of thrombosis of the vein in which they are inserted (1). Additionally, 7.5 percent of patients experience central venous abnormalities after the use of PICC lines (2). Loss of peripheral and central venous patency may preclude the successful placement of arteriovenous fistula access when that is necessary. This is a grave concern for these patients, in whom arteriovenous access options have a profound impact on morbidity and mortality during dialysis.

But the problem with prior venous access devices limiting future dialysis access options is not unique to PICC lines. Repeated venipuncture, peripheral IV catheters, and central venous catheters are associated with phlebitis, venous sclerosis, stenosis, and thrombosis. Central venous catheters cause endothelial denudation, smooth muscle proliferation, and pericatheter thrombus even with relatively short-term use (3,4). Not all central venous access sites are the same. Various studies have shown that central venous catheters placed in the subclavian vein are associated with a 13–42 percent incidence of venous stenosis or occlusion, whereas internal jugular catheters are associated with only a 0.3–3 percent incidence (5–7). Tunneled small-diameter catheters placed in the internal or external jugular veins may be associated with an even lower risk of catheter-related central venous complications and do not cause direct damage to peripheral veins (8).

So what are we to do to preserve the veins of patients with chronic kidney disease who may progress to a need for dialysis? PICC lines certainly have a high risk of interfering with future arteriovenous fistula placement by causing stenosis and thrombosis of both peripheral and central veins. But peripheral IV catheters and central venous catheters also carry significant risk. Several organizations have established guidelines and position statements that can be helpful in considering this issue. The Fistula First Coalition (9), the National Kidney Foundation (10), and the American Society of Diagnostic and Interventional Nephrology (11) all have provided useful direction. The Renal Network Inc. (NW 4, 9, 10) has developed a tool kit to aid in implementing a vein preservation strategy (12).

Based on these sources, several recommendations can be made. First, the actual need for venous access should be assessed carefully in all patients. Reducing the frequency of venipuncture and choosing oral medication therapy when possible can significantly reduce venous injury. When venous access is required, patients who are at risk for requiring dialysis in the future should be identified. This requires a review of their history and prior laboratory values. Patients with stage 3–5 chronic kidney disease, patients currently receiving dialysis, and patients with functioning kidney transplants should be identified before venous access is obtained. Venous access in these patients should occur with the following priority:

1. The dorsal veins of the hand are the preferred location for phlebotomy and peripheral venous access.
2. The internal jugular veins are the preferred location for central venous access.
3. The external jugular veins are an acceptable alternative for venous access.
4. The subclavian veins should not be used for central venous access.
5. Placement of a PICC should be avoided.
6. Tunneled small-bore catheters in the internal or external jugular location should be used as an alternative to PICC lines and nontunneled internal jugular central venous catheters.

For these recommendations to be implemented, processes will have to be established within the hospital to ensure that estimated GFR is determined and medical history is obtained in every patient being considered for central venous access, including a PICC line. In most instances, when the patient is at risk for future kidney failure, PICC lines should not be used. Protocols should be in place to guide decisions regarding the appropriate venous access when the patient fits one of the above categories at risk for requiring future dialysis. Finally, physicians must be available with expertise to guide these decisions and place the tunneled small-bore

Continued on page 6

The PICC Conundrum:

Continued from page 5

catheters. Careful attention to venous access decisions should be effective in reducing venous catheter–associated complications and in preserving the veins of patients at risk for needing dialysis in the future so that successful arteriovenous fistulae can be constructed.

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The Scourges of the **Hemodialysis Catheter**

By Anatole Besarab

Hemodialysis (HD) sustains life for those with ESRD. Currently, nearly 400,000 individuals in the United States receive HD as management of ESRD (1). Sustainable vascular access that provides high-volume blood flow rates (Qb) above 300 mL/min is essential, whether through arteriovenous autologous fistulas, synthetic grafts, or tunneled dialysis catheters (TDCs) (2). Unfortunately, the overwhelming majority of incident patients begin HD treatments with a TDC: 82 percent, according to the most recent data from the U.S. Renal Data System (1). More than 20 percent of prevalent patients become or remain dependent on long-term TDC use, spanning months to years (3–5). Other nations, such as Brazil and some in Europe and the Far East, appear to be able to reduce their use of TDCs more quickly and to reduce dependence on long-term TDC use to less than 5–10 percent.

Because of the widespread use of TDCs, research efforts are focused on identifying strategies to prevent and minimize the risk of the most common catheter-related complications—thrombotic occlusion, infection, and central vein occlusion—the three catheter scourges. Proper catheter management to preserve patency and maintain high blood flow rates, reduce the risk of infection, and avoid stenosis is vital in improving patient outcomes.

The first scourge: maintaining patency

The standard procedure for maintaining patency between dialysis treatments, the instillation of heparin into the lumens in a volume sufficient to fill to the lumen tip (the lock) is being replaced by the substitution of a trisodium citrate (TSC) 4 percent lock at many centers. One large Canadian study (6) showed a lower rate of TDC exchange and tissue plasminogen activator (tPA) use without a change in hospitalization for TSC 4 percent versus heparin. On the basis of available evidence, the American Society of Diagnostic and Interventional Nephrology Clinical Practice Committee (7) recommends using a locking solution of heparin 1000 U/mL or TSC 4 percent to maintain TDC patency.

Although a larger-bore catheter design allows an initial rate of blood flow above 400 mL/min to be achieved, virtually all catheters show eventual flow dysfunction manifested as progressive blood flow reductions at prepump pressures considered safe: 200–250 mm Hg.

Prospective monitoring for blood flow dysfunction through systematic monitoring of blood flow and prepump negative arterial pressure (Pa) during HD should be a routine part of the management of patients using TDCs (8) but in many centers it is not. Most large-gauge catheters have a conductance (Qb/Pa) of 2 mL/min/mm Hg. When prescribed blood flow rate (e.g., 350–400 mL/min) is examined serially over time, an increasing negative prepump pressure over time to achieve the prescribed flow reflects alterations in inlet orifice and suggests impending access dysfunction, which may warrant intervention.

Dysfunction manifests as thrombus formation within or at the tip of an HD catheter or by its entrapment within a fibrin sleeve. Systemic anticoagulants and antiplatelet agents have proved to be ineffective in preventing such dysfunction while adding a risk of bleeding. Noninvasive pharmacotherapy with thrombolytic agents has proved to be effective in restoring catheter patency over the short term. All too often, however, adequate flow function can be restored only by catheter replacement with balloon disruption of the fibrin sheath (9), an invasive and costly procedure.

Various protocols for thrombolytic dwells are used by dialysis centers to restore TDC blood flow, usually when the situation is urgent. I favor the slow advancement of the thrombolytic by the injection of saline solution 0.2 mL/lumen behind it every 10–15 minutes to advance the lytic to the catheter tip during a 1-hour dwell, because this strategy decreases the need for repeat lytic dwells by 81 percent (10). Two alternative strategies attempt to improve flow before the development of an "emergency" TDC flow problem: so-called preemptive postdialysis thrombolytic lock or intradialysis lytic infusions. I favor the use of a thrombolytic agent as a prolonged lock of 44–68 hours, both to restore flow and to prevent flow dysfunction. Regular once-weekly use of a tPA agent as a catheter lock solution may be the most effective technique to reduce the risk of vessel occlusion between HD sessions, avoid bleeding risk, and may incur the additional benefit of lower catheter-related bloodstream infection (CRBSI) (11). However, there have been no comparative efficacy or cost studies of the various strategies.

The second scourge: CBRSI

TDCs are responsible for almost half of all infections in HD patients. The infection rates of TDC are 15- and 25-fold higher than those for grafts and native fistulas, respectively. Infection is the leading cause of catheter removal, and CRBSI is a major reason for the loss of anatomic sites for vascular access. CRBSI is associated with substantial morbidity, including metastatic infection. One can estimate from the U.S. Renal Data System and Medicare reimbursement data that there are approximately 100,000 episodes of CRBSI per year in the United States at an average cost of $22,000 per episode (1). CRBSI usually requires catheter removal and 3 weeks of appropriate antibiotics. In some circumstances, catheter removal may be avoided by adding an antibiotic lock to the systemic antibiotic therapy.

Several approaches have been used to decrease the incidence of CRBSI: the use of intravenous antibiotics around the time of catheter implantation; the use of exit-site antimicrobial agents such as honey, mupirocin, and povidone-iodine combined with nasal mupirocin; and the use of antimicrobial-impregnated catheters and antimicrobial locks (AMLs) instilled into the catheter lumen.

Of these, only AMLs and exit-site antimicrobial agents significantly reduce the risk and rate of catheter-related infection and the risk of catheter loss from any complication (12). In a metaanalysis, the use of AMLs resulted in a 75 percent reduction in the risk of CRBSI (12) and only one published study showed the emergence of resistant organisms. Despite the demonstrated effectiveness of AMLs in reducing CRBSI, there is obvious reluctance to their use because of the potential for the development of bacterial drug resistance. Given that the U.S. Food and Drug Administration is unlikely to approve an antibiotic lock, current research focuses on the use of antimicrobial agents, usually combinations of several agents that prevent biofilm formation (13).

The third scourge: central vein stenosis and occlusion

The insertion of a large-bore catheter into a central vein is all too frequently associated with the development of stenosis within that vein. Central vein stenosis is catastrophic when it develops on the side of an established or maturing permanent access, graft, or native fistula, and it all too often precludes the placement of permanent access in the ipsilateral upper extremity. When such catheters are placed in the inferior vena cava, stenosis of the iliac vein can compromise the placement of a kidney graft. Strategies considered to reduce such stenosis include self-centering catheters and catheters configured to support themselves at opposite points of the superior vena cava. Inasmuch as longer catheter dwell times increase the development of central vein abnormalities, and catheter-related infection appears to promote stenosis, it is imperative to keep a TDC as short as possible and prevent infection.

Although catheters offer several advantages in the acute setting, acting as a bridge to more permanent vascular access, continued improvement in the design and performance of catheters is needed. Future studies should focus on better defining the prophylactic use of thrombolytic agents as locking solutions and the appropriate use of AMLs. Clearly, we need improvements in the process of care to reduce the fraction of patients in whom HD is begun with a TDC.

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