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Peripherally Inserted Central Catheters and Other Intravascular Devices: How Safe Are They for Hemodialysis Patients?

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The growing emphasis on the use of arteriovenous fistulas (AVF) in hemodialysis patients during the past few years has led to a systematic exploration of the myriad barriers to achieving this goal^{1, 2}. Clearly, maintaining the integrity of the vasculature is one critical element in optimizing AVF maturation and patency. The burgeoning use of intra-vascular devices may promote vascular injury, stenosis, and thrombosis, thereby jeopardizing the success of AVF use in these patients (Table). Peripherally inserted central venous catheters (PICCs) are a common intra-vascular device with growing popularity since the late 1970s and are deemed a safer and simpler alternative to central venous lines. Over a million PICCs are placed each year in the US alone³. The major advantages of PICCs include greater patient comfort, simpler catheter care, and, possibly, long-term dwell time. The most common indication for a PICC is the need for long-term antibiotic administration, particularly in the outpatient setting. In fact, the guidelines for the prevention of intravascular catheter-related infections promulgated by the Infectious Diseases Society of America recommend using PICC lines for antibiotic administration lasting longer than 6 weeks⁴.

More recently, there has been enhanced recognition of PICC lines' potential to produce venous injury and thrombosis. Symptomatic venous thrombosis occurs in fewer than 10% of patients with PICC lines⁵⁻⁷, but the overall rate of thrombosis, including both symptomatic and asymptomatic, reaches an astounding 38%⁸. The risk of venous thrombosis associated with PICC lines is two-fold higher in patients with chronic kidney disease (CKD) as compared to those with normal kidney function⁹. PICC lines are inserted in the cephalic or basilic vein in the antecubital fossa, with the tip in the subclavian vein or right atrium.

Given the deleterious effects of PICC lines on the veins that are used to create an AVF, it is likely that PICC placement affects the subsequent ability to create successful AVFs in patients with CKD. This possibility prompted the NKF-KDOQI (National Kidney

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Foundation's Kidney Disease Outcomes Quality Initiative) guidelines on vascular access to caution against the use of PICC in patients with CKD¹⁰, but, to date, these recommendations have been based on anecdotal evidence. The case control study by El Ters *et al* reported in the current issue of *AJKD* provides compelling evidence for an association between the prior placement of a PICC and a lower subsequent frequency of AVF use in hemodialysis patients¹¹. The authors compared the frequency of prior PICC use in 120 patients dialyzing with a central venous dialysis catheter or an arteriovenous graft ("cases") to that observed in 162 patients dialyzing with an AVF ("controls"). The frequency of prior PICC use was substantially higher in the cases (44 vs 20%), and the association between lack of a functioning AVF and prior PICC use was highly significant (odds ratio, 3.2; $p < 0.001$) even after adjusting for patient sex, artery and vein diameters, and prior history of a central venous catheters.

As the authors acknowledge, this study has several limitations. Most importantly, this was an observational study. As such, it can only demonstrate an association between prior PICC line and absence of a functioning fistula, but cannot prove causality. Notwithstanding the authors' attempt to adjust statistically for potential confounders, it is still possible that those patients with prior PICC lines had vessels of inferior quality that were not identified by preoperative vascular mapping. Nevertheless, given the propensity of PICC to promote thrombosis of veins required for the vascular anastomosis, it would be unethical to conduct a randomized clinical trial in which CKD patients were allocated to receive a PICC prior to AVF creation. Second, the authors did not differentiate between primary AVF failure (AVF non-maturation) and late AVF failure (AVF failure after successful cannulation). This distinction is important in understanding the link between PICC use and AVF failure and designing strategies to maximize AVF survival. AVF non-maturation may be attributed to a draining vein that has been exposed to a PICC and became sclerotic, thereby failing to dilate appropriately under increased shear stress, as often happens with mobilized veins^{12, 13}. In contrast, AVF failure subsequent to successful use for dialysis usually indicates a new outflow problem in the proximal draining vein or the central vein^{14, 15}. Unfortunately, El Ters *et al* did not provide sufficient information to evaluate whether the deleterious effect of PICCs is due to primary or late AVF failure.

If any of the three upper arm veins (brachial, basilic or cephalic) are exposed to and damaged by a PICC, the other two veins remain intact (Figure). However, the axillary, subclavian, and brachiocephalic veins, which serve as the common entry route for a PICC into the superior vena cava, are always exposed to the proximal end of a PICC. Two studies examining the incidence of central vein stenosis (CVS) in association with PICC lines reported a 3% rate of subclavian vein stenosis⁸ and a 7% rate of overall CVS¹⁶. Patient selection in both studies was limited to those undergoing serial extremity venography, which may have led to underestimation of the true incidence of PICC-associated CVS. Development of CVS is not unique to PICC lines. Pacemakers that are usually inserted via the left subclavian vein are also associated with an incidence of CVS ranging from 10 to 64%^{17, 18}. Central venous catheters inserted via the internal jugular vein are reported to be associated with alarming 41% CVS prevalence¹⁹ and a history of a prior dialysis catheter has been implicated in higher subsequent AVF failure rate²⁰. Finally, recent data from our

institution suggests that a history of a prior dialysis catheter ipsilateral to the AVF is associated with a shorter cumulative survival of the AVF²¹.

Direct analysis of the relationship between catheter caliber and the diameter of the vein used for PICC placement was not possible in the El Ters study, as they lacked detailed findings of the preoperative vascular mapping as it related to the ipsilateral PICC. However, at least one prior study reported a higher rate of vein thrombosis with the use of larger PICCs²² and there is a report of higher rate of internal jugular vein thrombosis (28%) compared to brachiocephalic vein and superior vena cava thromboses (14 and 2%, respectively)²³. This leads to a hypothesis that thrombosis is more likely if greater cross-sectional area of the vessel is occupied by a foreign object, resulting in greater stasis and denudation from greater contact surface area, which is consistent with two of Virchow's postulates.

Three additional observations in the El Ters study are notable. First, 30% of the hemodialysis patients in this study had a history of prior PICC use, a frequency comparable to that observed at another medical center²⁴. Second, among this group, 54% had their PICC placed after initiating dialysis. Finally, 56% of the PICCs placed were intended specifically to administer intravenous antibiotics. Given the consensus guidelines that discourage PICC lines in patients with CKD, how can we account for these alarming statistics? The authors note that the decision to place PICC lines in these patients was determined by non-nephrologists (presumably without consultation with nephrologists). This is a case in which the recommendations from medical societies of two different subspecialists (infectious diseases and nephrology) are in conflict. Whereas the infectious disease guidelines encourage PICC lines for management of long-term intravenous antibiotics, the nephrology guidelines discourage their use in patients with CKD. The overriding incentive for the non-nephrologist treating the hospitalized patient is to accelerate hospital discharge by placing a PICC line that permits safe and convenient outpatient intravenous antibiotics. The long-term consequence of inducing venous thrombosis and jeopardizing the success of a future AVF is either not recognized or considered to be of secondary importance.

Educational efforts might reduce the use of PICC in CKD patients, but one such an initiative at a medical center has been reported to be unsuccessful²⁴. One option to resolve this dilemma would be to implement a hospital policy that mandates a nephrology consultation in any hemodialysis patient prior to scheduling PICC placement. The vast majority of systemic infections in hemodialysis patients can be treated with appropriate intravenous antibiotics administered thrice weekly on dialysis days using the hemodialysis access without requiring a separate vascular device²⁵, and routinely involving nephrologists in the decision process would likely eliminate most PICC lines in hemodialysis patients. The optimal approach in CKD patients who have not yet initiated dialysis is more challenging, as these patients lack a suitable vascular access for outpatient administration of antibiotics. If there is no alternative to using a PICC in a CKD patient, there are two available measures that may reduce the potential harm. First, using a smaller diameter PICC may reduce the risk of venous injury. Second, preferential use of the brachial vein may minimize the injury to the target vessel, as most AVFs are created using the cephalic or basilic veins. Another potential alternative is to place a small-caliber tunneled catheter in the right internal jugular vein in lieu of a PICC, as the diameter of the internal jugular vein is greater than that of the

subclavian vein and no arm veins are disrupted. Prospective clinical trials are needed to determine whether any of these alternative approaches would decrease the likelihood of prolonged hemodialysis catheter dependence in such patients.

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Figure 1.

Veins commonly used for intravascular device placement. PICC lines are inserted in the cephalic, basilic, or brachial vein above the antecubital fossa, with the proximal tip positioned in the superior vena cava or right atrium.

Table 1

Studies exploring complications of intravascular devices.

Reference	Study design	Major findings
<u>Peripherally-inserted central catheters</u>		
Grove ²² (2000)	Cross-sectional	Stepwise increase in PICC-associated thrombosis rate with increasing catheter diameter (1% for 4-F, 6.6% for 5-F, and 9.8% for 6-F)
Allen ⁸ (2000)	Retrospective review	38% overall PICC-associated thrombosis rate, with 57% found in cephalic, 14% in basilic, and 10% in brachial veins
Gonsalves ¹⁶ (2003)	Retrospective review	7% incidence of PICC-associated CVS
Marnejon ⁹ (2011)	Retrospective case control	PICC-associated venous thrombosis associated with decreased kidney function, left-sided placement, and use of basilic vein
El Ters ¹¹ (2012)	Retrospective case control	3.2-fold higher rate of lack of functioning AVF in patients with PICC history
<u>Dialysis catheters</u>		
Schillinger ²⁶ (1991)	Prospective cohort	32% higher incidence of CVS in patients with subclavian vs internal jugular dialysis catheters
Rayner ²⁰ (2003)	Prospective cohort	1.8-fold higher risk of AVF failure with a history of temporary dialysis catheter use
MacRae ¹⁹ (2005)	Cross-sectional	Higher prevalence of CVS with longer catheter dwell time and number of cannulations
Shingarev ²¹ (In Press)	Retrospective case control	2.5-fold higher rate of AVF failure with history of ipsilateral vs contralateral dialysis catheter
<u>Pacemakers/Defibrillators</u>		
Da Costa ¹⁸ (2002)	Prospective cohort study	21% incidence of >70% venous stenosis 6 months after the last pacemaker placement
Korkeila ¹⁷ (2007)	Prospective cohort study	14% incidence of new >50% venous stenosis 6 months after pacemaker placement
Drew ²⁷ (2011)	Retrospective case control	Higher frequency of CVS and catheterdependence in patients with ipsilateral transvenous cardiac device
Borsato ²⁸ (2012)	Prospective cohort study	50% primary patency rates of central veins with pacemaker lead-induced stenosis at 120 days post angioplasty

Abbreviation: CVS, central vein stenosis; AVF, arteriovenous fistula; PICC, peripherally inserted central venous catheter