Peripherally Inserted Central Catheters (PICCs) in CKD: PICC'ing the Best Access for Kidney Disease Patients

Commentary on Greene MT, Flanders SA, Woller SC, Bernstein SJ, Chopra V. The association between PICC use and venous thromboembolism in upper and lower extremities. Am J Med. 2015;128(9):986-993.

The use of peripherally inserted central venous catheters (PICCs) has increased significantly in recent years,[1,2] in part due to perceived advantages over other forms of venous access, particularly among patients with difficult-to-obtain intravenous access. It is generally accepted that PICCs are safe and effective while having the benefits of ease of placement, a lower rate of procedure-related complications, and the potential for lower costs in comparison to other forms of venous access.[3,4] Most importantly, PICCs are viewed as highly convenient for both patients and physicians because they are often inserted by nurse-led teams, can be used for phlebotomy, can substitute for nontunneled central lines that have greater insertion-associated risk, and can remain in place following discharge, allowing for home rather than hospital administration of medications, including antibiotics (Table 1). Despite what is seen as a favorable safety profile, significant complications related to PICC placement are now increasingly recognized.[1]

Patients with chronic kidney disease (CKD), including those receiving dialysis, may disproportionately receive PICCs.[5,6] Patients with CKD, including those with additional comorbid conditions such as diabetes, heart failure, and vascular disease, have high rates of hospitalization and require frequent administration of intravenous therapies, such as antibiotics to treat infections. Given often extensive histories of medical encounters, they may also have limited veins for peripheral intravenous access. Accordingly, PICCs are more likely to be placed in patients with acute kidney injury and CKD.[7] With prior research showing that PICCS are associated with a high rate of upper-extremity venous thrombosis and residual central venous stenosis,[5] this may have future implications for these patients, including impacts on future hemodialysis vascular access creation and longevity.[8]

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WHAT DOES THIS IMPORTANT STUDY SHOW?

A recent study by Greene et al[9] published in the *American Journal of Medicine* assessed the association between PICC placement and venous thromboembolism among more than 76,000 patients admitted to 48 Michigan hospitals between January 2011 and March 2014. Eligible patients included only those admitted to a medicine service for acute care for 2 days or longer, excluding patients admitted directly to an intensive care unit and those hospitalized for surgery. Additional exclusions were known venous thromboembolism within 6 months and admission for presumed thromboembolism. Using medical record review and telephone follow-up 90 days postdischarge, investigators ascertained outcomes of interest, specifically symptomatic image-confirmed deep venous thrombosis of the upper or lower extremity, as well as pulmonary embolism. Medical record review was completed in 100% of participants, whereas telephone contact occurred in 58%.

Among 76,242 eligible participants, 3,790 (5%) had a PICC either at hospital admission (n = 898) or during the hospital stay (n = 2,892). Those with a PICC had more comorbid conditions, including more frequent hospitalizations during the prior year, with a higher proportion with cancer, recent surgery, immobility, and sepsis. Data for kidney measures are not reported. In analyses adjusting for potential venous thrombosis–related risk factors such as older age, immobility, cancer, and recent surgery, as well as other factors, PICC use was independently associated with a 3 times greater hazard of all-cause thromboembolism (hazard ratio [HR], 3.16 [95% confidence interval (CI), 2.59-3.85]). This finding was driven by upper-extremity deep venous thrombosis, with a 10-fold greater hazard for those with PICCs (HR, 10.49; 95% CI, 9.79-14.11). PICC use was also associated with a 1.5–fold greater hazard of lower-extremity deep venous thrombosis (HR, 1.48; 95% CI, 1.02-2.15), but was not associated with pulmonary embolism. No change was seen in study results when the study authors included the use of deep venous thrombosis prophylaxis.

Although the association between PICC use and upper-extremity thrombosis is intuitive, the significant albeit lower magnitude association with lower-extremity thrombosis is less clear. The authors

Table 1. Types of Venous Access and Application in CKD

Access Type	Description	Uses	Special Risks in Patients With CKD	Other Risks
Peripheral intravenous catheter	Short-term (days) venous access inserted typically into a superficial vein in the arm	Usable for most medications; usually insufficient for phlebotomy	May affect peripheral veins that could be used for arteriovenous fistulas in the future depending on site; no known effects on central veins	Rare peripheral thrombophlebitis
Nontunneled CVC	Short- and moderate-term (days to week) venous access inserted into larger caliber veins, typically 15-25 cm in length, most often placed in the internal jugular, subclavian, or femoral sites and, for jugular and subclavian lines, terminating in the superior vena cava or right atrium	Usable for central hemodynamic monitoring, phlebotomy, and administration of nearly all medications	Potentially longer term effects on central vein patency, particularly with subclavian vein placement	Catheter-related bacteremia
Tunneled CVC, large and small bore	Similar to nontunneled CVCs, but the exit site and site of ultimate venipuncture are physically separated; tunneled CVCs may be cuffed, with a polyethylene or silicone flange that anchors the catheter within the subcutaneous tissue and limits bacteria entry	Usable for central hemodynamic monitoring, phlebotomy, and administration of nearly all medications; may be used for long weeks to months	Most common catheter used for dialysis access; concerns exist with subclavian placement and potentially left internal jugular, resulting in damage to the smaller central veins; this may be lower with small-bore catheters and placement in the right internal jugular vein	Catheter-related bacteremia
Peripherally inserted central catheter	Long vascular access device (>45 cm) inserted into a peripheral upper-arm vein and advanced until terminating in the superior vena cava or right atrium	Similar to CVCs, providing access to the central circulation, but with lower insertion risks; may also be used for weeks to months	May cause local trauma to peripheral and central veins, including the subclavian and brachiocephalic veins	Deep venous thrombosis, infection, dislodgement
Midline catheter	7.5- to 25-cm long catheter most often inserted in veins above the antecubital fossa, typically transiting the basilic or cephalic vein and terminating just peripheral to the subclavian vein	Similar to peripheral catheters, but may be more amenable to blood draw; cannot accommodate irritant or vesicant infusions; may be used for weeks to months	May cause local trauma to peripheral and, depending on where it terminates, central veins	Venous thrombosis, infection, dislodgement

Abbreviations: CKD, chronic kidney disease; CVC, central venous catheter.

posit 3 factors: (1) ascertainment bias, (2) PICCs may trigger a systemic prothrombic milieu, and (3) there may be additional unmeasured confounding factors associated with increased thrombosis risk regardless of the PICC. Supporting the third possible factor, those with PICCs in place are clearly sicker patients with higher risk for thromboembolism. Potentially, the authors could have attempted to better account for unmeasured factors using alternative statistical methods, such as inverse probability treatment weighting or propensity score–based matching.[10] Despite this shortcoming, it is remarkable how high the risk for upper-extremity clots is with PICCs, even if this "baseline" thrombosis risk represented by lower-extremity thrombosis is considered.

One strength of the study is the use of a detailed database of hospital admissions that includes one of the largest cohorts of patients with PICCs. The authors have also separated thromboembolic events into 3 different distinct outcomes of upper deep venous thrombosis, lower deep venous thrombosis, and pulmonary embolism, allowing a more accurate rate of upper-extremity deep venous thrombosis to be determined. A major weakness is the use of retrospective design, which may bias toward more deep venous thrombosis events in the PICC group

due to increased scrutiny for deep venous thrombosis in those with catheters.

HOW DOES THIS STUDY COMPARE WITH PRIOR STUDIES?

Multiple previous studies have demonstrated higher risk for deep venous thrombosis in patients with PICCs. A meta-analysis by Chopra et al[11] published in 2013 attempted to include the existing literature published on PICCs and thromboembolic events. The majority of published articles included in this analysis had small numbers of patients, did not discriminate between upper and lower deep venous thrombosis, and did not adjust for thromboembolic risk factors. Overall, PICCs were found to be strongly associated with deep venous thrombosis, but not with pulmonary embolism, similar to the finding by Greene et al. Subgroup analyses showed that prospective studies and those using asymptomatic surveillance had higher rates of thromboembolism, suggesting that this retrospective study may have underestimated the true incidence of thromboembolic events.

WHAT SHOULD CLINICIANS AND RESEARCHERS DO?

This study raises concerns about the safety of PICCs, almost certainly underestimating total upper-extremity thrombosis due to potentially asymptomatic cases, as well as not identifying vein trauma that may lead to stenosis and predispose to future vein failure. Supporting this pathophysiology, a case-control study of hemodialysis patients by El Ters et al[8] showed a strong independent association between PICC use and lack of a functioning arteriovenous fistula. Similarly, a retrospective study of hemodialysis patients also showed that the presence of transvenous cardiac device wires was associated with more radiologic central vein stenosis and a higher likelihood of being catheter dependent.[12]

Reflecting potential concerns about PICC overuse, a recently published guide in the *Annals of Internal Medicine* addressed scenarios in which PICC use could be considered acceptable,[13] positing that PICC use was acceptable only when the duration of use was longer than 6 days unless non–peripherally compatible infusions were needed (eg, sclerosing antibiotics or chemotherapy). Among patients with CKD stage 3b or higher (estimated glomerular filtration rate < 45 mL/min/1.73 m^2), PICC use was almost always considered unacceptable, largely due to the high likelihood of peripheral and central venous complications (including thrombosis) interrupting future hemodialysis access. This guide urged nephrology input prior to PICC placement in these individuals to facilitate assessment of risk versus benefit and argued strongly for using PICCs only in cases of clinical necessity, pushing back against the now common use of PICCs for patient and provider convenience.

A comprehensive guide outlining PICC indications is a step in the right direction, but this is unlikely to be sufficient to change clinical practice on its own. Nephrologists need to remain vigilant in preventing PICC placement in patients with CKD. Protocols that require nephrology consultation for any PICC request in patients with reduced kidney function (including acute kidney injury) are a good starting point and may be facilitated with electronic alerts or stops triggered in electronic order entry systems. Such policies have the benefit of involving a nephrologist in decision making before potentially harmful decisions are made. Importantly, non-nephrologist clinicians need to become more familiar with vein protection strategies aimed at preserving future hemodialysis access. All providers should be aware that any foreign object that sits within a blood vessel, whether a catheter or device wire/lead, has the potential to cause vascular damage, leading to diminished prospects for future hemodialysis access. Finally, patients with CKD need to be informed about the potential risks of PICCs so they can make a fully informed decision about their health care.

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