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Risk factors for peripherally inserted central catheter line–related deep venous thrombosis in critically ill intensive care unit patients

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Abstract

Introduction: Central venous access using peripherally inserted central catheters is frequently used for patients receiving intravenous medications in the hospital or outpatients. Although there are several benefits of peripherally inserted central catheters, such as ease of insertion, low procedure-related risk and higher patient satisfaction, there are complications associated with peripherally inserted central catheter use. Despite some studies evaluating peripherally inserted central catheter line–related complications, the factors associated with peripherally inserted central catheter–related deep venous thrombosis in critically ill medical-surgical patients are poorly described. The objective of this case-control study was to identify the risk factors associated with peripherally inserted central catheter line–related deep venous thrombosis in critically ill medical-surgical intensive care unit patients in a community hospital.

Methods: We abstracted relevant clinical data from 21 cases with symptomatic peripherally inserted central catheter–related deep venous thrombosis and 42 controls with peripherally inserted central catheters but no deep venous thrombosis.

Results: Of the factors evaluated, female gender, the use of triple lumen peripherally inserted central catheters, larger outer diameter, and open (vs valve) peripherally inserted central catheters were associated with venous thrombosis. In this retrospective study, we did not identify any association of peripherally inserted central catheter–related deep venous thrombosis with a prior history of deep venous thrombosis, use of alteplase, antiplatelet therapy, prophylactic or therapeutic anticoagulation, international normalized ratio, platelet count and the use of peripherally inserted central catheters for total parenteral nutrition.

Conclusion: Our study indicates that the catheter size relative to the diameter of the vein could be an important risk factor for the development of peripherally inserted central catheter–related deep venous thrombosis. The study findings should be confirmed in a larger study designed to identify risk factors of peripherally inserted central catheter–related deep venous thrombosis. In the meantime, the peripherally inserted central catheter lines should be used judiciously in critically ill patients.

Keywords

Central venous catheters, peripherally inserted central catheter, deep venous thrombosis, thrombosis

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Introduction

Since its introduction in 1975, the peripherally inserted central catheter (PICC) has gained popularity for its simplicity of insertion and cost-effectiveness.[1,2] Indeed, PICC lines can be placed at the bedside by trained nurses.[3] They may be used for multiple indications such as frequent blood draws, drug administration, including irritants and vesicants; and total parenteral nutrition delivery. In addition, PICC lines are used to measure central venous pressure, although the merit of this indication is controversial. Furthermore, they are associated with higher patient satisfaction compared with peripheral intravenous catheters.[4]

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Despite several benefits, the complications associated with the use of PICC lines remains a concern. These complications could either be catheter-related, such as line malfunction, line fracture, infections, arteriovenous (AV) fistula, thrombophlebitis, venous stenosis, and thrombosis, or procedure-related, which includes mispositioning, bleeding, and brachial artery puncture.[5] PICCs are associated with up to 35% of all diagnosed upper extremity deep vein thrombosis (UEDVT).[6] A higher incidence of PICC-related UEDVT is linked to a variety of host factors, including severity of illness; malignancy[7]; a history of warfarin use; a prior history of venous thrombosis[8] or thromboembolism; high body mass index (BMI)[9]; trauma; renal failure; antibiotics infusion, especially vancomycin; the outer diameter of the PICC greater than 4F[6]; left-sided catheters; and basilic vein placement.[10] Some reports have indicated an up to 2.5 fold higher incidence of PICC line–related venous thrombosis in comparison to centrally inserted catheters (CIC).[11] Midline line catheters are now available as an alternate choice for intravenous access and the clinical practice for its use is evolving. One report identified a substantially higher risk of midline catheter-associated thrombosis when compared to PICCs.[12] Thus, a better understanding of the risk factors for PICC is needed to inform the choice of intravenous access between PICC, CIC, and midline catheters.

Although previous studies have linked PICCs to the development of thrombosis, these studies have not specifically investigated critically ill subjects in the intensive care unit (ICU). A recent study, however, reported a hazard ratio for 30-day venous thromboembolism (VTE) of 1.90 for PICC in critically ill patients.[13] The goal of our study was to identify the risk factors associated with PICC-related DVT in medical-surgical ICU patients in a community hospital. We did not include cases who had midline catheters in this study as midline catheters are considered as peripheral intravenous access at our institution, and the use of irritant of vesicant medications is not permitted in midline catheters.

Methods

The University of Minnesota Institutional Review Board approved this study. The bedside nursing staff and the intravenous access team personnel monitor the patients for the development of local symptoms or swelling, which prompts evaluation for DVT by a venous doppler ultrasound. All PICC line insertions and complications, such as DVT, are documented in the medical chart as well as separate records maintained by the intravenous access team. We used the records maintained by the intravenous access team to identify all cases with PICC placed over a 6-month period and those who had PICC line–related DVT between October 2011 and March 2012. The data obtained from the tracking sheets were then confirmed by reviewing the medical chart. The chart review was also used to abstract the relevant PICC line and patient-specific data to assess the risk factors for UEDVT. The patient data abstracted included age, gender, BMI, primary diagnosis for the hospital admission, any prior history of venous thromboembolic disease, past or concurrent malignancy, coagulation parameters such as international normalized ratio (INR), partial thromboplastin time (PTT), platelet count, and fibrinogen (done within a week of PICC line insertion). We also abstracted data about medications for the use of warfarin, enoxaparin, heparin, aspirin, and alteplase for in situ catheter clot lysis. The data relevant to the PICC line and its insertion included the side of PICC line placement (left vs right), insertion site (basilic vs cephalic vs brachial), external catheter diameter (F), number of lumens, and the catheter tip characteristics (open tip vs Groshong valve tip). In this study, we did not evaluate other characteristics that influence the risk of thrombosis such as the material used to make PICC, for example, silicone or polyurethane. For this case-control study, we collected data from 21 consecutive patients who developed symptomatic DVT during the 6 months of data reviewed. We collected data on twice the number of consecutive controls to determine the risk factors present in cases with venous thrombosis. For comparison of binary exposures between case-control groups, generally, a 1:1 case/control ratio is the most effective. For testing differences of quantitative measures between case-control groups, collecting more samples helps to improve the precision estimate. This observation has motivated us to double the control sample sizes in our study: a balance of resources needed for the study and the power.[14] The Medical Inpatients and Thrombosis Study used a similar strategy with a case to control ratio of 1:2[15] to identify risk factors for PICC-related thrombosis in patients with medical illnesses.

To determine whether meaningful differences exist, we used Fisher's exact test to compare the difference in proportions between the DVT and no DVT groups.[16] For comparison of continuous variables between the two groups, we used the two-sample Student t test. We used a standard threshold of p-valued $\leqslant 0.05$ to determine whether the differences were of meaningful significance.

Results

Of the 497 PICC line insertions during the study period, 21 patients were found to have symptomatic DVT confirmed with ultrasonography (Table 1). A total of 42 consecutive patients with PICC lines who did not develop DVT were selected as controls. The incidence of symptomatic UEDVT was 4.2% in this study. The mean age of the patients with PICC-related DVT was 65 ± 14.3 years. The mean duration from the placement of the PICC line to the development of thrombosis was 7.6 ± 4.7 days. A substantially increased incidence of PICC-associated UEDVT was seen in females, the use of triple lumen catheters, a larger external diameter of the catheter, and open catheter (compared to the valved Groshong catheters).

In this study, among PICC line groups with or without DVT, no difference was observed in age, BMI, INR, platelet

Table 1. Factors associated with PICC line–related thrombosis.

	DVT	No DVT	p-value[a]
Gender (%)			
Male	28.57	64.28	0.015
Female	71.43	35.72	
Number of lumens (%)			
One	–	28.57	0.005
Two	23.8	30.95	
Three	76.2	40.47	
External diameter (%)			
4F	4.76	28.57	0.045
5F	95.24	71.43	
Catheter tip characteristics (%)			
Open	76.19	47.61	0.035
Valved	23.81	52.39	

DVT: deep venous thrombosis; PICC: peripherally inserted central catheter.
[a]P-value: Fisher's exact test.

Table 2. Factors not associated with PICC line thrombosis.

	DVT	No DVT	p-value[a]
Past or concurrent cancer (%)	2/21 (9.5%)	11/42 (26.1%)	0.322
History of DVT	3/21 (14.2%)	7/42 (16.7%)	0.999
History of alteplase	5/21 (23.8%)	8/42 (19.05%)	0.755
Use of PICC line for TPN	4/21 (19.05)	5/42 (14.3%)	0.710
Use of antiplatelet/anticoagulation			
Aspirin	5/21 (23.8%)	5/42 (11.9%)	0.314
LMWH or IV/SQ heparin Coumadin[b]	14/21 (66%)	21/42 (50%)	0.518
INR[c]	1.4 ± 0.35	1.58 ± 1.14	0.412
Platelet count[c]	241.7 ± 148.7	207.4 ± 129.6	0.383

IV: intravenous; SQ: subcutaneous; PICC: peripherally inserted central catheter; DVT: deep venous thrombosis; TPN: total parenteral nutrition; LWMH: low-molecular-weight heparin; INR: international normalized ratio.
[a]Fisher's exact test for proportions, and two-sample t test for continuous variables.
[b]A case could be on more than one agent.
[c]Laboratory values not available on all case.

count, side or the venous insertion site of the PICC line. Similarly, no difference was seen in the two groups with respect to a prior or current history of cancer, previous DVT, the use of PICC line for total parenteral nutrition, the use of alteplase, and other medications such as aspirin, warfarin, heparin, and enoxaparin (Table 2).

Discussion

A major complication of PICC lines is UEDVT. In critically ill patients, PICC lines are associated with a higher incidence of UEDVT compared to CICs.[7,13] Thus, a better understanding of the risk factors for PICC line–related thrombosis is crucial to institute measures that will reduce this complication. A better understanding of risk factors also has the potential to inform health care providers about the choice of CIC vs PICC for a specific critically ill patient. Several risk factors are linked to catheter-associated DVT such as a diagnosis of cancer in the last 6 months,[17,18] catheter diameter,[18] a history of warfarin use, prior history of PICC-related venous thrombosis[8] or DVT,[19,20] a high BMI,[9] catheter tip location in proximal one-third of the distal superior vena cava (SVC),[21] insertion site for PICC placement (cephalic, basilic, or brachial),[22] and the agents infused in the PICC line, including chemotherapy[23] or amphotericin,[19] and we identified a substantially higher proportion of females among the DVT group, suggesting female sex to be associated with PICC line–related DVT, which was not demonstrated as a risk factor in prior studies.[17]

Our study showed a substantially higher incidence of PICC-related DVT in females. The potential explanations for this finding may include a hormonal mechanism, but this alone is not likely as the overall incidence of DVT in critically ill ICU patients is not different in males and females. An alternate explanation of the increased incidence in PICC-related thrombosis in females may be a smaller venous diameter in females relative to the size of the catheter, which leads to significantly lower blood flow and thus a higher incidence of thrombosis. This hypothesis is in line with our findings that catheter diameter matters, as discussed below. Sex as a major risk factor should be evaluated systematically in larger prospectively enrolled cohorts. If confirmed, this finding could have a major impact on the clinical practice and use of PICC in critically ill ICU patients.

Similar to previous studies, we identify the external catheter diameter as a risk factor for the development of thrombosis.[6,24,25] In this study, a catheter diameter of 5F was associated with a higher incidence of thrombosis. A larger diameter catheter could occlude or decrease blood flow in the smaller peripheral vein resulting in venous stasis. Venous stasis is a well-established mechanism that contributes to clot formation. Another potential mechanism for why larger and stiffer catheters could be associated with more venous thrombosis is the potential to cause more endothelial damage and dysfunction, which is also one of the risk factors in the Virchow's triad for venous thrombosis.[26] Moreover, if PICC lines are placed in patients prone to moving their upper extremities, PICCs may cause more intimal injury due to repeated mechanical stress, resulting in venous thrombosis.[27]

In our study, besides a larger catheter size, the number of lumens in the PICC line was also associated with more frequent DVT. Multi-lumen PICC lines are attractive for the critically ill ICU population as there is a need for the infusion of multiple antibiotics, pressors, sedatives, and other medications. However, with a larger number of lumens in the PICC line, the size of the individual lumen is smaller, which might contribute overall lower flow at the tip of the catheter and thus possible stasis that could initiate

thrombosis. The exact explanation or mechanism for this association remains to be established. However, it does not appear to be related to the size of the catheter as the outer diameter of the catheter was often the same in both double and triple lumen catheters. We also identified an increased incidence of thrombosis with open PICCs that do not have a valve, although a recent study showed no difference in the occlusion rates between open and valved PICC lines.[28] This observation could be related to the characteristic of the valve in the catheter, and improvements in valve design and antithrombotic coating in some catheters may influence the risk of thrombosis. A trend to use polyurethane catheters rather than silicone or other material could also impact the thrombotic potential. A larger sample size would be needed to validate our observation.

We acknowledge that in retrospective analysis, such as this study, a selection bias cannot be excluded. Given that asymptomatic cases might have been missed due to the lack of routine ultrasound screening, our study conclusions are only applicable to critically ill ICU cases with symptomatic DVT. However, symptomatic thrombosis is more likely to be clinically significant. We were unable to retrospectively obtain other data that may be collected prospectively to test alternative hypotheses. Furthermore, there is a possibility of a type 1 error, that is, rejection of a true null hypothesis, given the relatively small sample size in our study. Nonetheless, our study has important findings that, if validated in a larger cohort, would impact the care of critically ill ICU patients and warrant further investigations.

Conclusion

Our study suggests that the size and number of lumens increase the risk of thrombosis and that females have a higher risk. The clinical implication of these findings is that the incidence of PICC-related thrombosis in critically ill patients could be reduced by a conservative use of PICC line catheters in females and patients with small veins and by using smaller bore, and fewer lumen catheters when there is a need for PICC line use in critically ill patients. The use of ultrasonography to best match the size of the PICC to the size of an individual's veins offers promise, given an increasing availability of portable ultrasonography and a recent report that measurement of the catheter to vein ratio has the potential to decrease DVT in the ICU setting.[29] The findings of this small study will require confirmation in a larger prospective study.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

The retrospective chart review study was approved by University of Minnesota Institutional Review Board Protocol No. 1212M25661.

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Informed consent

As this was a minimal risk retrospective chart review study, waiver of Health Insurance Portability and Accountability Act (HIPAA) authorization was granted.

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References

1. Lam S, Scannell R, Roessler D, et al. Peripherally inserted central catheters in an acute-care hospital. *Arch Intern Med* 1994; 154(16): 1833–1837.
2. Ng PK, Ault MJ, Ellrodt AG, et al. Peripherally inserted central catheters in general medicine. *Mayo Clin Proc* 1997; 72(3): 225–233.
3. Barber JM, Booth DM, King JA, et al. A nurse led peripherally inserted central catheter line insertion service is effective with radiological support. *Clin Radiol* 2002; 57(5): 352–354.
4. Periard D, Monney P, Waeber G, et al. Randomized controlled trial of peripherally inserted central catheters vs. peripheral catheters for middle duration in-hospital intravenous therapy. *J Thromb Haemost* 2008; 6(8): 1281–1288.
5. Amerasekera SS, Jones CM, Patel R, et al. Imaging of the complications of peripherally inserted central venous catheters. *Clin Radiol* 2009; 64(8): 832–840.
6. Liem TK, Yanit KE, Moseley SE, et al. Peripherally inserted central catheter usage patterns and associated symptomatic upper extremity venous thrombosis. *J Vasc Surg* 2012; 55(3): 761–767.
7. Chopra V, Anand S, Hickner A, et al. Risk of venous thromboembolism associated with peripherally inserted central catheters: a systematic review and meta-analysis. *Lancet* 2013; 382(9889): 311–325.
8. Mermis JD, Strom JC, Greenwood JP, et al. Quality improvement initiative to reduce deep vein thrombosis associated with peripherally inserted central catheters in adults with cystic fibrosis. *Ann Am Thorac Soc* 2014; 11(9): 1404–1410.
9. Maneval RE and Clemence BJ. Risk factors associated with catheter-related upper extremity deep vein thrombosis in patients with peripherally inserted central venous catheters: a prospective observational cohort study: part 2. *J Infus Nurs* 2014; 37(4): 260–268.
10. Marnejon T, Angelo D, Abdou AA, et al. Risk factors for upper extremity venous thrombosis associated with peripherally inserted central venous catheters. *J Vasc Access* 2012; 13(2): 231–238.
11. Fallouh N, McGuirk HM, Flanders SA, et al. Peripherally inserted central catheter-associated deep vein thrombosis: a narrative review. *Am J Med* 2015; 128(7): 722–738.
12. Bahl A, Karabon P and Chu D. Comparison of venous thrombosis complications in midlines versus peripherally inserted central catheters: are midlines the safer option? *Clin Appl Thromb Hemost* 2019; 25: 9150.
13. White D, Woller SC, Stevens SM, et al. Comparative thrombosis risk of vascular access devices among critically ill medical patients. *Thromb Res* 2018; 172: 54–60.

14. Ørnulf Borgan NEB, Chatterjee N, Gail MH, et al. *Handbook of statistical methods for case-control studies*. Boca Raton, FL: CRC Press, 2018.
15. Winters JP, Callas PW, Cushman M, et al. Central venous catheters and upper extremity deep vein thrombosis in medical inpatients: the medical inpatients and thrombosis (MITH) study. *J Thromb Haemost* 2015; 13(12): 2155–2160.
16. Fisher RA. On the interpretation of χ^2 from contingency tables, and the calculation of P. *J Royal Stat Soc* 1922; 85(1): 87–94.
17. Clemence BJ and Maneval RE. Risk factors associated with catheter-related upper extremity deep vein thrombosis in patients with peripherally inserted central venous catheters: literature review: part 1. *J Infus Nurs* 2014; 37(3): 187–196.
18. Chopra V, Ratz D, Kuhn L, et al. Peripherally inserted central catheter-related deep vein thrombosis: contemporary patterns and predictors. *J Thromb Haemost* 2014; 12: 847–854.
19. Chemaly RF, de Parres JB, Rehm SJ, et al. Venous thrombosis associated with peripherally inserted central catheters: a retrospective analysis of the Cleveland clinic experience. *Clin Infect Dis* 2002; 34(9): 1179–1183.
20. Lobo BL, Vaidean G, Broyles J, et al. Risk of venous thromboembolism in hospitalized patients with peripherally inserted central catheters. *J Hosp Med* 2009; 4(7): 417–422.
21. Hansson PO, Sorbo J and Eriksson H. Recurrent venous thromboembolism after deep vein thrombosis: incidence and risk factors. *Arch Intern Med* 2000; 160(6): 769–774.
22. Allen AW, Megargell JL, Brown DB, et al. Venous thrombosis associated with the placement of peripherally inserted central catheters. *J Vasc Interv Radiol* 2000; 11(10): 1309–1314.
23. Grove JR and Pevec WC. Venous thrombosis related to peripherally inserted central catheters. *J Vasc Interv Radiol* 2000; 11(7): 837–840.
24. O'Brien J, Paquet F, Lindsay R, et al. Insertion of PICCs with minimum number of lumens reduces complications and costs. *J Am Coll Radiol* 2013; 10(11): 864–868.
25. Evans RS, Sharp JH, Linford LH, et al. Reduction of peripherally inserted central catheter-associated DVT. *Chest* 2013; 143(3): 627–633.
26. Nifong TP and McDevitt TJ. The effect of catheter to vein ratio on blood flow rates in a simulated model of peripherally inserted central venous catheters. *Chest* 2011; 140(1): 48–53.
27. Har-Noy O and Meltzer E. Upper-extremity deep-vein thrombosis in an elderly man. *CMAJ* 2007; 176(8): 1078–1079.
28. Johnston AJ, Streater CT, Noorani R, et al. The effect of peripherally inserted central catheter (PICC) valve technology on catheter occlusion rates–the 'ELeCTRiC' study. *J Vasc Access* 2012; 13(4): 421–425.
29. Sharp R, Cummings M, Fielder A, et al. The catheter to vein ratio and rates of symptomatic venous thromboembolism in patients with a peripherally inserted central catheter (PICC): a prospective cohort study. *Int J Nurs Stud* 2015; 52(3): 677–685.