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Is Peripherally Inserted Central Catheter–Related Thrombosis Associated With ABO Blood Group? A Case–Control Pilot Study

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Abstract

Peripherally inserted central catheter (PICC) use is associated with many complications including line-related thrombosis. Several studies and meta-analyses confirmed the increased risk to develop venous thromboembolism in non-O blood group individuals. Our pilot study aimed to examine whether PICC-related thrombosis is influenced by ABO blood group. We identified patients admitted to Hurley Medical Center between March 2012 and March 2016 who had PICC placed during their admission, had their ABO blood group identified in their medical record, and had upper extremity venous Doppler ultrasound performed on the same side of PICC. We excluded pregnant women, patients on anticoagulation initiated before PICC insertion, and patients with active cancer. Data of 227 patients who met our criteria were analyzed. Of these patients, 140 (61.7%) patients had PICC-related thrombosis (cases) and 86 (37.9%) patients had O blood group. Controls were patients who had PICC and did not develop PICC-related thrombosis. Multivariate logistic regression revealed no association between PICC-related thrombosis and ABO blood group (adjusted odds ratio: 1.1; 95% confidence interval: 0.6-2.0; $P = .733$). Therefore, our data suggest that non-O blood group does not increase the odds of having PICC-related thrombosis.

Keywords

PICC, thrombosis, ABO blood group, hemostasis

Introduction

Peripherally inserted central catheters (PICCs) have been increasingly used, given the fact that they are easily inserted and provide safe, multipurpose vascular access.[1] Peripherally inserted central catheters also carry less catheter-related infections and conjugate mechanical injuries when compared to centrally inserted venous catheters. Although PICC has a preferable profile, PICC-related venous thrombosis is a prominent complication.[2] A wide range of line-related thrombosis incidence (3%-20%) is reported based on patient- and catheter-related factors.[3,4]

Factors that contribute to PICC-related thrombosis formation have been assessed by numerous studies. Although ABO blood group is a known factor that influences hemostasis, it has not been studied as a contributing factor for the development of PICC-related thrombosis. Several studies and meta-analyses showed that non-O blood group individuals have higher risk to develop venous thromboembolism compared to O blood group.[5-7] Individuals with blood group O have approximately 25% lower plasma levels of von Willebrand factor and factor VIII; thus, they have a lower incidence of venous thromboembolism.[8,9]

Methods

After obtaining institutional review board approval, we conducted a case–control study using electronic medical records at Hurley Medical Center, a community-based teaching hospital with 418 beds. We identified patients admitted to the hospital between March 2012 and March 2016, 18 to 65 years old, who had PICC inserted by the radiology department and intravenous (IV) registered nurses team during their hospital stay and have

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their ABO blood group identified in their medical record. We excluded pregnant patients, patients with active cancer, patients on oral or IV anticoagulation initiated any time before PICC thrombosis was diagnosed, and patients who did not undergo venous Doppler ultrasound on the same side of PICC during their stay.

We reviewed patients' records who underwent venous Doppler ultrasound on the same side of PICC insertion. We classified patients into cases and controls based on their ultrasound results after reading the full radiology report. Cases were identified as patients who developed PICC-related thrombosis and were further classified based on the site of thrombosis into superficial, deep, or both. Superficial veins include the cephalic, basilic, median cubital, and accessory cephalic veins, while deep veins include the subclavian axillary, brachial, radial, and ulnar. Controls were patients who had PICC and did not develop PICC-related thrombosis confirmed by negative ultrasound results. If a patient had more than one episode of PICC-related thrombosis, we only included the first event. In contrast, if a patient had more than one negative venous Doppler ultrasound, we included the most recent encounter.

The primary outcome was the identification of an ultrasound-confirmed episode of PICC-related thrombosis. We then determined the odds of having PICC-related thrombosis for O blood group versus non-O blood groups. Other secondary aims were to evaluate selected explanatory variables that could affect the odds of experiencing PICC-related thrombosis including age, sex, number of lumens of the PICC, history of deep vein thrombosis (DVT), history of malignancy, smoking status, body mass index (BMI), and whether the patient was on pharmacological DVT prophylaxis or not.

We performed bivariate analysis using either Fisher exact tests or independent Student *t* tests to determine any associations between the study explanatory variables (ie, ABO blood group, age, sex, number of lumens of the PICC, history of DVT, history of malignancy, smoking status, BMI, and whether the patient was on pharmacological DVT prophylaxis or not) and the presence of an episode of PICC-related thrombosis. Multivariate logistic regression analysis was conducted to examine the relationship between the main study explanatory variable (ie, ABO blood group) and the main study outcome (ie, the presence of an episode of PICC-related thrombosis) after controlling for clinically suspected confounders. All analyses were done using Stata statistical software package (Stata Corporation, College Station, Texas). The usual 0.05 type I error threshold for statistical significance was used for all analyses.

For sample size calculation, we assumed the risk of PICC line thrombosis around 10% and the odds of having PICC line thrombosis around 1.8 in the non-O blood group compared to O blood group individuals as shown in the previous literature.[5] We need at least 430 individuals in each group to obtain a statistically significant result using a power of 80% with an α level of .5. However, after reviewing all individuals who had an ultrasound at the site of PICC line in our institution, we could not reach the required sample size. Therefore, our protocol was changed to run a small pilot study to assess that association.

Table 1. Comparison of Patients Without Versus Those With Ultrasound Confirmed Venous Thrombosis (Superficial, Deep, or Both).

	Total (N = 227)	Negative Ultrasound (n = 87)	Positive Ultrasound (140)	*P* Value
Age, mean (SD)	57.3 (18.5)	55.9 (17.6)	58.2 (19.0)	.363
Sex, %				
Female	145 (63.8)	59 (67.8)	86 (61.4)	.394
ABO blood group, %				
O	86 (37.9)	35 (40.2)	51 (36.4)	.391
A	85 (37.4)	36 (41.4)	49 (35.0)	
B	44 (19.4)	13 (14.9)	31 (22.1)	
AB	12 (5.3)	3 (3.5)	9 (6.4)	
Smoking status, %				
Never	7 (3.1)	5 (5.8)	3 (1.4)	.176
Current	158 (69.6)	57 (65.5)	100 (72.1)	
Former	62 (27.3)	25 (28.7)	37 (26.4)	
Number of lumens, %				
1	5 (2.2)	2 (2.3)	3 (2.1)	.393
2	196 (86.3)	72 (82.8)	124 (88.6)	
3	26 (11.5)	13 (14.9)	13 (9.3)	
Malignancy history, %				
Yes	35 (15.4)	10 (11.5)	25 (17.9)	.257
DVT history, %				
Yes	180 (7.9)	7 (8.1)	11 (7.9)	>.999
DVT prophylaxis, %				
Yes	128 (56.4)	57 (65.5)	71 (50.7)	.039
BMI (kg/m^2), mean (SD)	30.4 (10.0)	29.8 (9.4)	30.8 (10.3)	.456

Abbreviations: BMI, body mass index; DVT, deep vein thrombosis; SD, standard deviation.

Results

During the period of March 2012 and March 2016, in our institution, 2414 PICCs were inserted on admitted patients aged above 18 and 65 years. Of these, 1549 patients had their ABO blood group identified in the medical record and only 240 patients had venous Doppler ultrasound performed on the same side of PICC insertion due to suspected PICC-related complications. After reviewing the medical records to identify patients who met our exclusion criteria (ie, being on anticoagulation, having active cancer, and being pregnant), the number was further reduced to 227 patients, the final study sample.

There were 140 (61.7%) cases of PICC-related thrombosis divided as deep (77), superficial (28), or both (35). The distribution of ABO blood groups was 86 (37.9%) with O, 85 (37.4%) with A, 44 (19.4%) with B, and 12 (5.3%) with AB blood groups. The mean age for our study population was 57.3 (18.5) years and 63.8% were females. Table 1 shows the characteristics of the study population by the presence or absence of DVT.

Multivariate logistic regression revealed no association between PICC-related thrombosis and ABO blood group (adjusted odds ratio [OR]: 1.1; 95% confidence interval [CI]:

Table 2. Adjusted[a] Odds Ratios for the Presence of Ultrasound-Confirmed Venous Thrombosis (Superficial, Deep, or Both).

	Adjusted Odds Ratio (95% CI)	*P* Value
O Group		
Yes (reference)	-	.733
No	1.1 (0.6-2.0)	
Age	1.01 (0.99-1.02)	.444
Sex		
Male (reference)	-	.153
Female	0.6 (0.4-1.2)	
Smoking status		
Never (reference)	-	.080
Current	4.6 (0.8-25.3)	.166
Former	3.5 (0.6-20.0)	
BMI	1.0 (1.0-1.1)	.198
DVT prophylaxis		
No (reference)	-	.016
Yes	0.5 (0.3-0.9)	

Abbreviations: BMI, body mass index; CI, confidence interval; DVT, deep vein thrombosis.
[a]Adjusted for all other variables in the table.

0.6-2.0; $P = .733$). Further analysis did not reveal any association between PICC-related thrombosis and other clinically suspected factors. However, patients who received pharmacological DVT prophylaxis had about 50% less chance of developing PICC-related thrombosis compared to those who did not (adjusted OR: 0.5; 95% CI: 0.3-0.9; $P = .016$). Table 2 summarizes the results of our logistic regression analysis.

In the subgroup that had an ultrasound confirmed DVT only, and in comparison, with those who did not have either superficial or DVT. The odds of having DVT were not different between O and non-O blood groups. On the other hand, patients who received pharmacological DVT prophylaxis were less likely to develop DVT thrombosis compared to those who did not, with an OR of 0.4 and 95% CI of 0.2 to 0.4, as illustrated in Tables 3 and 4.

Discussion

The main finding of this case–control study was the association between ABO blood group and PICC-related thrombosis, which was not significant, despite the fact that ABO blood group has been known to influence the thromboembolic hemostasis.[10] A large body of evidence from clinical studies and meta-analyses reported the link between the ABO blood group and hemostasis. A recent study by Vasan et al conducted on 1.5 million blood donors also confirmed this evidence with thromboembolic risk approaching 2-fold in non-O blood group.[11]

When other clinical confounders were taken into consideration, they did not alter the results. Yet, a multivariate analysis showed that patients who received pharmacological DVT prophylaxis (ie, patients received at least 1 dose of prophylactic dose of low-molecular-weight heparin or unfractionated heparin) had an odds of 40% of having PICC line–related DVT

Table 3. Adjusted[a] Odds Ratios for the Presence of Ultrasound-Confirmed Venous Thrombosis (Deep Only) Compared to Those With No PICC Line Thrombosis.

	Total (N = 199)	Negative Ultrasound (n = 87)	Positive Ultrasound (112)	*P* Value
Age, means (SD)	57.3 (18.4)	55.9 (17.6)	58.4 (19.0)	.340
Sex, %				
Female	63.8 (127)	67.8 (59)	60.7 (68)	.372
ABO blood group, %				
O	36.2 (72)	40.2 (35)	33.0 (37)	.477
A	40.2 (80)	41.4 (36)	39.3 (44)	
B	18.6 (37)	14.9 (13)	22.4 (25)	
AB	5.0 (10)	3.5 (3)	6.3 (6)	
Smoking status, %				
Never	3.0 (6)	5.8 (5)	0.9 (10)	.151
Current	68.3 (136)	65.5 (57)	70.5 (79)	
Former	28.6 (57)	28.7 (25)	28.6 (23)	
Number of lumens, %				
1	1.0 (2)	2.3 (2)	0.0	.093
2	87.4 (174)	82.8 (72)	91.1 (102)	
3	11.6 (23)	14.9 (13)	8.9 (10)	
Malignancy history, %				
Yes	15.6 (31)	11.5 (10)	18.8 (21)	.174
DVT history, %				
Yes	7.5 (15)	8.1 (7)	7.1 (8)	>.999
DVT prophylaxis, %				
Yes	55.3 (110)	65.5 (57)	47.3 (53)	.014
BMI (kg/m^2), mean (SD)	30.4 (9.2)	29.8 (9.4)	30.1 (9.0)	.823

Abbreviations: BMI, body mass index; DVT, deep vein thrombosis; SD, standard deviation; PICC, peripherally inserted central catheter.

Table 4. Adjusted[a] Odds Ratios for the Presence of Ultrasound-Confirmed PICC-Related Thrombosis (Deep DVT Only).

	Unadjusted OR (95% CI)	*P* Value	Adjusted OR (95% CI)	*P* Value
O group				
Yes (reference)	–	.295	–	.417
No	1.4 (0.8-2.4)		1.3 (0.7-2.4)	
Age			1.01 (0.99-1.02)	.544
Sex				
Male (reference)			–	.157
Female			0.6 (0.3-1.2)	
Smoking status				
Never (reference)			–	.076
Current			7.4 (0.8-68.1)	.117
Former			6.1 (0.6-59.0)	
BMI			1.0 (1.0-1.0)	.560
DVT prophylaxis				
No (reference)			–	.006
Yes			0.4 (0.2-0.8)	

Abbreviations: BMI, body mass index; CI, confidence interval; DVT, deep vein thrombosis; PICC, peripherally inserted central catheter; SD, standard deviation.
[a]Adjusted for all other variables in the table.

and 50% odds of having either superficial or DVT at the site of PICC line insertion compared to those who did not receive any pharmacological prophylaxis. Several studies have evaluated the use of thromboprophylaxis to prevent catheter-related thrombosis, especially in patients with malignancy and critical illness.[12,13] A definitive clinical benefit for thromboprophylaxis use has yet to be proven. Our study suggests a protective effect of using prophylactic doses of heparin, but adverse events were not assessed.

In our study, we focused on classifying cases and controls by an objective method. We only included patients who had venous Doppler ultrasound performed on the same side of PICC insertion. Thus, the control groups had no thrombosis confirmed by negative ultrasound results rather than clinically not observing signs of thrombosis. On the other hand, cases had an ultrasound-confirmed PICC-related thrombosis. We believe that this is an important approach of our study that eliminates false-positive and false-negative diagnoses, especially in the latter for asymptomatic cases who could account for up to 13% of the total cohort as shown in other studies,[14] but at the same time, it limited our sample size as we excluded 1309 patients who did not have an ultrasound performed, which decreased the power for the main outcome of interest. However, the incidence of different ABO blood groups in our cohort was similar among those who had and those who had not have PICC line thrombosis, which makes the selection bias—which could have occurred due to small sample size in our cohort—unlikely contributing to the negative finding for the effect of ABO blood group in PICC line-related thrombosis.

This study was conducted in a single center with a limited number of patients, which might have decreased the chance to reach statistical significance for some of the OR estimates. Further studies with larger numbers are needed to establish such association related to PICC. Also, additional confounders should be studied such as the duration of PICC placement, time from PICC line insertion until PICC line thrombosis, appropriate placement of the catheter tip, and type of the infused medications. Moreover, our study did not assess the outcomes after either removing the PICC line or starting anticoagulation for those who had developed PICC line thrombosis.

In conclusion, despite being a risk factor for venous thromboembolism, our pilot study suggests that there is no association between ABO blood groups and PICC line–related thrombosis. Furthermore, it suggests a protective effect of using venous thromboprophylaxis to prevent PICC-related thrombosis; further research on a large scale may lead to a more prominent finding.

Declaration of Conflicting Interests

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