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Original Article

Risk factors for venous thrombosis associated with peripherally inserted central venous catheters

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Abstract: To evaluate the risk factors associated with an increased risk of symptomatic peripherally inserted central venous catheter (PICC)-related venous thrombosis. Retrospective analyses identified 2313 patients who received PICCs from 1 January 2012 to 31 December 2013. All 11 patients with symptomatic PICC-related venous thrombosis (thrombosis group) and 148 who did not have thromboses (non-thrombosis group) were selected randomly. The medical information of 159 patients (age, body mass index (BMI), diagnosis, smoking history, nutritional risk score, platelet count, leucocyte count as well as levels of D-dimer, fibrinogen, and degradation products of fibrin) were collected. Logistic regression analysis was undertaken to determine the risk factors for thrombosis. Of 2313 patients, 11 (0.47%) were found to have symptomatic PICC-related venous thrombosis by color Doppler ultrasound. Being bedridden for a long time (odds ratio [(OR]), 17.774; P=0.0017), D-dimer >5 mg/L (36.651; 0.0025) and suffering from one comorbidity (8.39; 0.0265) or more comorbidities (13.705; 0.0083) were the major risk factors for PICC-catheter related venous thrombosis by stepwise logistic regression analysis. Among 159 patients, the prevalence of PICC-associated venous thrombosis in those with ≥1 risk factor was 10.34% (12/116), in those with ≥2 risk factors was 20.41% (10/49), and in those with >3 risk factors was 26.67% (4/15). Being bedridden >72 h, having increased levels of D-dimer (>5 mg/L) and suffering from comorbidities were independent risk factors of PICC-related venous thrombosis.

Keywords: Peripherally inserted central catheter, thrombosis, risk factors

Introduction

Peripherally inserted central venous catheters (PICCs) are used widely because they are associated with fewer complications with regard to insertion and because they require a shorter time for insertion than central venous catheters (CVCs). This is especially true for those who need long-term infusion therapy or chemotherapy [1, 2]. PICC-related venous thrombosis is the formation of blood clots in the vessel or adhesive wall of the catheter after catheter insertion due to damage to the vascular intima, patient-related factors or catheter-related factors [3], and is one of the most serious complications of PICCs [4-7]. PICC-related venous thrombosis can delay treatment, increase the risk of catheter-related bloodstream infection, and even lead to pulmonary embolism or other serious complications [8-12]. Hence, research on PICC-related thrombosis is very important.

Studies on PICC-related venous thrombosis in the upper extremities have focused on patients undergoing chemotherapy or intensive care [3]. Bonnie [13] summarized 28 risk factors of catheter-related thrombosis, including catheter-related factors, technical factors and patient status, but did not study the correlation between levels of D-dimer, fibrinogen, the degradation products of fibrinogen, and catheter-related thrombosis. D-dimer, fibrinogen, and the degradation products of fibrinogen are very important because they reflect blood coagulation and fibrinolytic activity.

We hypothesized that increased expression of the markers of thrombosis would increase the risk of developing PICC-related venous thrombosis. Hence, we investigated the patient-level risk factors of PICC-related venous thrombosis in Chongqing, China, by analyses of medical records to select patients at high risk of thrombosis.

Table 1. Demographic and clinical characteristics of patients with a peripherally inserted central catheter (PICC) stratified according to the presence or absence of symptomatic venous thrombosis

Project	Thrombus group, n=11 (%)	Non-thrombus group, n=148 (%)	P
Sex			NS
Male	10 (90.91)	87 (41.22)	
Female	1 (9.09)	61 (58.78)	
Age			NS
>65 years	4 (36.36)	80 (54.05)	
≤65 years	7 (63.64)	68 (45.95)	
BMI (mean, SD)	22.835±4.1681	22.98±3.2147	NS
Number of comorbidities			0.0029
0	3 (27.27)	104 (70.27)	
1	4 (36.36)	33 (22.3)	
≥2	4 (36.36)	11 (7.43)	
Bedridden >72 h			0.0006
Yes	8 (72.73)	31 (20.95)	
No	3 (27.27)	117 (79.05)	
Smoker			0.0013
Yes	4 (36.36)	40 (27.03)	
No	3 (27.27)	101 (68.24)	
Ceased >1 year	4 (36.36)	7 (4.73)	
Nutritional risk score			0.0054
<3	5 (45.45)	125 (84.46)	
≥3	6 (54.55)	23 (15.54)	
Catheter brand			NS
Bard	7 (63.64)	88 (59.46)	
Braun	4 (36.36)	60 (40.54)	
WBC count ($\times 10^9$/L)			NS
<3.5	2 (18.18)	20 (13.51)	
3.5-6	2 (18.18)	62 (41.89)	
6-10	4 (36.36)	57 (38.51)	
>10	3 (27.27)	9 (6.08)	
Platelet count ($\times 10^9$/L)			NS
≥300	1 (9.09)	11 (7.43)	
<300	10 (90.01)	137 (92.57)	
D-dimer (mg/L)			0.0237
<0.55	3 (27.27)	68 (45.95)	
0.55-5	5 (45.45)	74 (50)	
>5	3 (27.27)	6 (4.05)	
Fibrinogen (mean, SD)	4.266±1.184	3.714±1.376	NS
Degradation product of fibrinogen (mean, SD)	5.446±6.053	3.511±2.959	NS

All *P* values based on Fisher's exact test. NS, not statistically significant (P>0.05). SD, standard deviation; BMI, body mass index; WBC, white blood cell.

Materials and methods

Between 1 January 2012 to 31 December 2013 at the First Affiliated Hospital of Chongqing Medical University (Chongqing, China) we identified 11 symptomatic PICC-related thromboses in 2313 PICCs. All PICCs were inserted by a skilled PICC Nursing Team. Thrombosis was diagnosed by color Doppler ultrasound while patients suffered from pain, swelling of limbs, or other related symptoms. We defined 11 patients with PICC-related venous thrombosis as the "thrombus group". We randomly selected 148 patients with PICCs who did not suffer venous thrombosis over the same period as the "non-thrombosis group".

We acquired relevant data using the electronic medical record database in our hospital in addition to the archive of the PICC service. Patient data (sex, age, body mass index (BMI), medical diagnosis, smoking history, nutritional status (assessed by the Nutrition Screening Scale (NRS2002 [14]), platelet count, leukocyte count, as well as levels of D-dimer, fibrinogen and degradation products of fibrinogen) before PICC were collected to ascertain the factors associated with an increased risk of symptomatic PICC-related venous thrombosis. These actions were undertaken to help nursing staff identify high-risk patients before PICC, and to initiate preventive measures to reduce PICC-associated venous thrombosis. Patients with a history of venous thrombosis are not allowed to have PICCs at our center, so a history of venous thrombosis was not relevant

Statistical analyses

Data are given as numbers and percentages. Analyses were undertaken using by SAS v9.2 (SAS, Cary, NC, USA). Quantitative data are the mean ± standard deviation. Fisher's exact test was used to detect the potential factors of PICC-related venous thrombosis. We inputted the risk factors identified by Fisher's exact test ($P<0.05$) into multivariate regression analysis. Then, using stepwise regression analysis, we identified the independent risk factors for symptomatic PICC-related venous thrombosis. $P<0.05$ was considered significant.

Results

We assessed 159 medical records (97 males and 62 females; mean age, 59.79 ± 14.16 years (range, 18-88 years). The catheter brands used were B-Braun or Bard. Among 11 patients of the thrombus group, thrombosis occurred in the cephalic vein, basilic vein, subclavian vein, and axillary vein in a total of 10 patients; thrombosis occurred in the internal jugular vein in the remaining patient. Thrombosis occurred within: 1 week of insertion in 8 patients (72.73%); 2 weeks in 2 patients (18.18%); 4 months in 1 case (9.09%).

The demographic characteristics of the patient population stratified according to the presence or absence of symptomatic venous thrombosis are compared in **Table 1**. There were significant associations between factors of venous thrombosis and being bedridden for >72 h, smoking, nutritional risk score ≥3, D-dimer >0.55 mg/L, and comorbidities ($P<0.05$).

The results of logistic regression analysis are shown in **Table 2**. Being bedridden for >72 h, increased levels of D-dimer, and comorbidities were the main causes of PICC-related venous thrombosis. The prevalence of PICC-associated venous thrombosis in patients with ≥1 risk factor was 10.34% (12/116), and in those with ≥2 risk factors was 20.41% (10/49). With the increase in D-dimer level and the medical diagnosis, the risk of patients having PICC-related venous thrombosis increased. The prevalence of patients with a D-dimer level of 0.55-5 mg/L was 4.20% (5/119), and that of patients with a D-dimer level >5 mg/L was 33.33% (3/9). A total of 10.81% (4/37) of patients with one comorbidity suffered symptomatic PICC-related venous thrombosis, and the prevalence in patients with ≥2 types of comorbidities was 26.67% (4/15).

Discussion

The prevalence of symptomatic PICC-related venous thrombosis in the present study was 0.47%. This figure is in accordance with that of Evans [15] (0.6%). This prevalence is not high but can lead to increased medical costs, exacerbations, and even death. Special attention must be paid to thrombosis prevention to reduce the risk of symptomatic PICC-related venous thrombosis.

We confirmed being bedridden >72 h to be a major risk factor for PICC-related venous thrombosis, in accordance with the work of Seeley [16]. That is, the longer the duration of being bedridden, the greater the risk of PICC-related venous thrombosis. Spencer [17] found that 46.5% of patients with CVC-associated venous thrombosis remained in bed for >72 h after PICC. In long-term bedridden patients, the velocity of blood flow is decreased and leads to blood stasis, which can result in deep-vein thrombosis (DVT). Also, many long-term bedridden patients suffer from multiple chronic diseases, fractures, or tumors, which increase the risk of PICC-related venous thrombosis.

No study has identified the prevalence of PICC-associated venous thrombosis in critically ill patients. However, many studies have shown

Table 2. Logistic regression analysis of risk factors associated with thrombosis in patients with peripherally inserted central catheters (PICCs) (n=159)

Risk factor	Regression coefficient	Chi square test	P	SD	OR	95% CI
Long-term bedridden (>72 h)	1.4389	9.8994	0.0017	0.4573	17.774	2.96-106.738
D-dimer (0.55-5 mg/L)	0.4095	0.2203	0.6388	0.8724	1.506	0.272-8.326
D-dimer (>5 mg/L)	3.6014	9.1629	0.0025	1.1898	36.651	3.559-377.413
2 comorbidities	2.1271	4.9214	0.0265	0.9588	8.39	1.281-54.945
≥3 comorbidities	2.6178	6.9586	0.0083	0.9924	13.705	1.96-95.847

SD, standard deviation; 95% CI, 95% confidence interval.

that critically ill patients carry a higher risk of PICC-related venous thrombosis [18]. In the meta-analysis by Chopra [19], the prevalence of PICC-associated venous thrombosis in critically ill patients was 13-91%, higher than that in cancer patients (6-67%). The present study also showed that the number of medical diagnoses was related to the risk of PICC-related venous thrombosis. This relationship may be associated with poor physical status, the requirement for complicated drug regimens, and low activity. Hence, the advantages and disadvantages of PICC should be considered before insertion of PICCs to reduce the risk of complications.

The correlation between D-dimer level and PICC-associated venous thrombosis has not been shown clearly in previous studies. Our study confirmed that high D-dimer level before PICC can increase the risk of symptomatic PICC-related venous thrombosis, especially for patients with D dimer level >5 mg/L (odds ratio, 36.651; 95% CI, 3.559-377.413). Cushman [20] suggested that D-dimer level can be used as an independent risk factor for predicting the future venous thrombus embolism (VTE). A case-control study by Douketis [21] showed that, in 474 patients who suffered primary DVT, the D-dimer level was 70% higher than the normal control group <6 months after VTE was diagnosed, and the risk of thrombosis was 2.2-times greater than normal. Therefore, patients with elevated levels of D-dimer should be specifically evaluated before PICC. If necessary, prophylactic anticoagulation therapy should be initiated to prevent PICC-related venous thrombosis.

Joffe [22] stated that smoking is one of the main risk factors of catheter-related thrombosis. Moran [23] found that malnutrition was a risk factor for PICC-related thrombosis. However, logistic regression analysis in our study showed no significant correlation between thrombosis and smoking history or nutritional status. This finding is similar to the results of Shi in China [24]. Studies have shown that increases in age, sex, obesity, white blood cell count, and platelet count are risk factors of PICC-related venous thrombosis [25], but our study did not show these features.

The results of the present study showed that patients with ≥2 risk factors have a higher risk for PICC-related thrombosis than patients with one risk factor. This finding may suggest that thrombus formation is the result of multiple factors, and there may be a synergistic effect between different risk factors. In future studies, we will try to create a scoring system for different risk factors to quantify the risk of PICC-related thrombosis to enable preventive measures to be adopted before catheter insertion.

The most important limitation of our study was its retrospective nature. However, some variables not explored previously were examined, adding value to our study. Recent prospective trials have been limited in the variables examined or just focused specifically on cancer patients or critically ill patients. The results of our study could be used in wider patient populations. Another limitation was that we evaluated only symptomatic PICC-related venous thrombosis and did not consider asymptomatic PICC-related venous thrombosis, which has been reported to occur more frequently. Further prospective studies are needed to determine the prevalence of PICC-related venous thrombosis, evaluate risk factors for PICC-related venous thrombosis, and to find effective interventions.

In conclusion, we confirmed that being bedridden for a long time, increased levels of D-dimer,

and comorbidity were independent risk factors of PICC-related venous thrombosis for hospitalized patients. These findings will help to guide nursing staff. If patients with these risk factors need PICC, specific attention should be paid to preventive measures, observation of symptoms, and catheter function. If necessary, conventional vascular ultrasound and preventive anticoagulant therapy can be undertaken to reduce the prevalence of catheter-related venous thrombosis.

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Disclosure of conflict of interest

None.

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