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Original Article

Analysis of the risk factors of peripherally inserted central catheter-associated venous thrombosis after chemotherapy in patients with lung cancer

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Abstract: Objective: The goal of this study was to identify the risk factors of venous thrombosis after placement of peripherally inserted central catheter (PICC) in lung cancer patients undergoing chemotherapy. Methods: A total of 200 patients with lung cancer who underwent PICC placement after chemotherapy were enrolled. Forty patients who had venous thrombus 3 months after PICC placement were included as the venous thrombus group, and 160 patients who underwent PICC placement at the same period but had no venous thrombus were enrolled in the control group. Baseline data, disease and disease history, PICC information, and laboratory indicators were compared. One-way and multifactor logistic regression analyses were performed to identify the risk factors of PICC-associated venous thrombosis. Results: Patients with PICC-associated venous thrombus that developed within 2 weeks after PICC placement (T1) were more than any other time points ($p=0.002$). In the logistic regression analysis, sex, body mass index (BMI), fibrinogen level, PICC-inserted veins, frequent elbow bending after PICC, high-strength manual labor, administration of prophylactic doses and anticoagulant drugs, chemotherapy history, and history of PICC use/CVC were independent risk factors for development of PICC-associated venous thrombosis. Conclusion: Risk factors such as BMI, fibrinogen level, PICC-inserted veins, and PICC use/CVC history should be highlighted in the prevention of PICC-associated venous thrombosis after chemotherapy in patients with lung cancer.

Keywords: Lung cancer, chemotherapy, PICC, venous thrombosis, risk factor

Introduction

Lung cancer is the most frequent malignancy in the respiratory system, and its prevalence and mortality rate have been increasing owing to the influences of environmental factors and unhealthy lifestyle [1]. Recently, published data worldwide have shown that lung cancer, with its annual incidence and mortality rates being the highest, severely affects the health of human beings [2]. In an early stage, lung cancer shows no obvious clinical features, and this contributes to an acute increase in the incidence of moderate- or advanced-stage lung cancer, for which venous chemotherapy is used as the major treatment method. In current clinical practice, venous access should be established for chemotherapeutics infusion in venous chemotherapy for patients with lung cancer patients, and peripherally inserted central catheter (PICC) placement is regarded as a safe and effective intubation technique and is frequently applied in establishing venous access [3, 4].

PICC is a catheter made of silica gel or polyurethane-urea inserted from the peripheral veins in the elbow, close to the large vein that directly reaches the heart, thereby delivering and diluting chemotherapeutics rapidly while averting the recurrent puncture and direct contact between the erosive chemotherapeutics and the elbow venous blood. Hence, PICC can minimize damage of chemotherapeutics to the vessels, protect the upper veins, reduce the incidence of venous inflammation, and alleviate the pains in chemotherapy, which is conducive to the improvement of the comfort and life quality of patients [5, 6]. Currently, PICC is preferred by patients with cancer who are receiving chemotherapy and has been frequently applied in

Table 1. Comparison of basic data between patients with venous thrombosis and those without venous thrombosis

	Venous embolization group (n=40)	No venous thrombosis group (n=160)	X^2	P
Sex				
Male	12	83	6.14	0.013*
Female	28	77	6.14	
Age (years)				
< 50	18	79	0.245	0.621
≥ 0.6	22	81	0.245	
Obesity				
Yes	26	87	1.47	0.225
No	14	73	1.47	

Note: *indicates P < 0.05.

the treatment of cancer [5]. However, PICC, as an interventional operation, has given rise to complications such as venous thrombosis [7, 8]. Cancer patients who have received a PICC have an incidence rate of venous thrombosis of as high as 58.09%. Thus, PICC placement can hardly mitigate the physiological or psychological burden of patients, but affects the anticipated efficacy of normal chemotherapy [9, 10]. Hence, this study aimed to investigate the risk factors of venous thrombosis after PICC placement in lung cancer patients undergoing chemotherapy.

Materials and methods

General data

As study subjects, 200 patients with lung cancer who underwent PICC placement after chemotherapy in our hospital were enrolled. Three months after PICC placement, 40 patients had a venous thrombus and was included as the venous thrombus group, including 20 men and 20 women, aged between 36 and 80 years (mean, 50.34 ± 8.42 years). Simultaneously, 3 months after PICC placement, 160 patients who had no venous thrombus were enrolled in the control group, including 86 men and 74 women, aged between 35 and 80 years (mean, 50.62 ± 8.12 years).

The inclusion criteria were as follows: (1) Patients with pathological diagnosis of lung cancer conforming to the international diagnostic criteria for lung cancer; patients with normal coagulation function; patients with no history of infection diseases, infection, administration of anticoagulant drugs or mental disorders; patients with no cognitive dysfunction or disturbance of consciousness; and patients with no tumors other than lung cancer, allergy to the PICC, or intolerance to the chemotherapeutics for lung cancer. (2) The exclusion criteria were patients who failed to cooperate with the treatment or quit the study, and patients who were unresponsive to the follow-up. This study was approved by the institutional ethics committee, and the patients and their families signed the written informed consent form.

Major apparatus and methods

Major apparatus: PICC (4F7617405, Bard, USA).

PICC intubation: Prior to surgery, patients underwent routine blood test, blood biochemical test, echocardiography, coagulation function test, and lateral radiographic examination to rule out the contraindication of surgeries. Intubation was performed by medical professionals who received professional training for PICC intubation or possessed the corresponding certificate. The Groshong PICC was used in the intubation, which was performed from the basilic, median cubital, or cephalic vein, using. During surgery, the patients were required to remain in the supine position. Before puncture, local anesthesia was performed using 1% lidocaine, with the catheter head placed in the superior vena cava. A 3 M transparent dressing was used to cover the puncture site and external part of the catheter. Immediately after the PICC insertion, the position was identified accurately in a radiographic examination. The radiographic image showed that the tip of the catheter was located in the superior vena cava, which suggested successful intubation of the PICC. After intubation, the patients underwent chemotherapy in strict accordance with the physician's advice. To prevent blockage of the catheter, 20 mL of 0.9% NaCl was used to rinse the PICC after chemotherapy.

Diagnosis of venous thrombosis: During retention of the PICC, the medical staff observed and recorded the condition of the limbs with the PICC every day, and the arm circumference to determine the swelling of the arms. In addition, pain in the PICC-inserted arms was also

Table 2. Comparison of information between the two groups of diseases and medical history

	Venous embolization group (n=40)	No venous thrombosis group (n=160)	X^2	P
Tumor				
Yes	35	98	9.898	0.002*
No	5	62	9.898	
Hypertension				
Yes	26	92	0.744	0.388
No	14	68	0.744	
Coronary heart disease				
Yes	20	101	2.307	0.129
No	20	59	2.307	
PICC/CVC management history				
Yes	16	27	10.14	0.002*
No	24	133	10.14	
History of chemotherapy				
Yes	17	33	8.167	0.004*
No	23	127	8.167	

Note: *indicates P < 0.05.

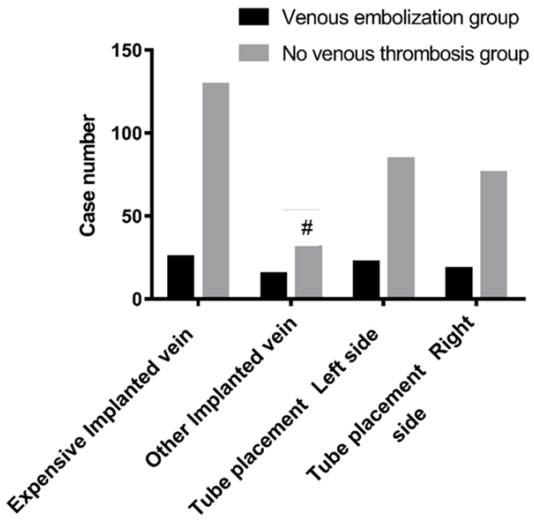

Figure 1. Comparison of the two groups of selected indwelling vein information #P < 0.05.

recorded. Any patients with suspicious venous thrombosis were immediately subjected to color Doppler ultrasonic examination for venous thrombosis.

Statistical methods

The SPSS 22.0 software (IBM, New York, USA) was used for data analysis. Enumeration data expressed as number (%) were compared between the groups by using the Chi-square test. Measurement data are expressed as Mean ± SD, and t-test was used for comparison between two groups. PICC-associated risk factors of venous thrombosis were analyzed using the one-way and multifactor logistic regression analyses. A *p* value of < 0.05 suggests that the difference was of statistical significance.

Results

Comparison of baseline data

Differences in sex, instead of age or obesity ($p > 0.05$), between the venous thrombosis and control groups showed statistical significance (*p*-0.013; **Table 1**).

Comparison of disease history between the venous thrombosis and control groups

Comparison of the history of hypertension or coronary heart disease between the two groups showed no statistically significant differences ($p > 0.05$), while the differences in tumor (*p=0.002*), PICC/CVC intubation history (*p=0.002*), and chemotherapy history (*p=0.004*) showed statistical significance ($p < 0.05$; **Table 2**).

Comparison of the data regarding to the intubation veins

Comparison of the intubation site between the two groups showed no statistically significant difference ($p > 0.05$), while the differences in the veins where the PICC was inserted had statistical significance (*p*=0.002; **Figure 1**).

Comparison of laboratory indicators between the two groups

Differences in platelet count and prothrombin levels between the two groups showed no statistical significance ($p > 0.05$), while the difference in fibrinogen level between the two groups showed statistical significance (*p*=0.001; **Table 3**).

Table 3. Comparison of laboratory indicators between the two groups

	Venous embolization group (n=40)	No venous thrombosis group (n=160)	X^2	*P*
Platelet count				
< 300×10^9/L	30	123	0.063	0.803
≥ 300×10^9/L	10	37	0.063	
Fibrinogen				
< 4 g/L	14	102	10.86	0.001*
≥ 4 g/L	26	58	10.86	
Prothrombin				
< 10 g/L	23	87	0.126	0.722
≥ 10 g/L	17	73	0.126	

Note: *indicates P < 0.05.

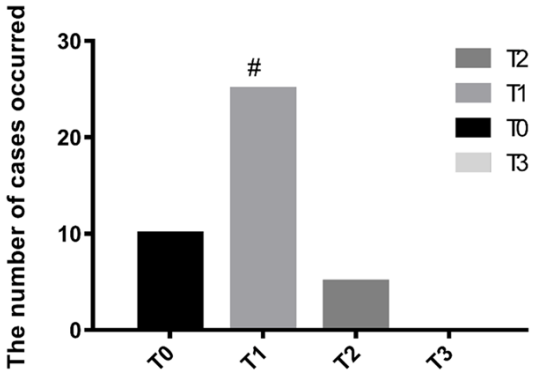

Figure 2. Onset time of PICC-related venous embolism. The recorded onset times of PICC-related venous thrombosis are shown. The number sign indicates that the number of PICC-related venous thrombosis at T1 was significantly higher than those at the other time points, with statistically significant differences ($p < 0.05$). #P < 0.05.

Onset time of PICC-associated venous thrombosis

Onset time: Fourteen patients had venous thrombosis within 1 week after intubation (T0); 21, within 2 weeks (T1); 5, within 3 weeks (T2); and 0, within 4 weeks (T4). The number of patients with venous thrombosis at T1 was significantly higher than those at any other time points, and the differences had statistical significance (*p=0.002*; **Figure 2**).

One-way analysis of the risk factors of PICC-associated venous thrombosis after chemotherapy in the patients with lung cancer

In the one-way logistic regression analysis of the risk factors of PICC-associated venous thrombosis after chemotherapy in the patients with lung cancer, sex, BMI, fibrinogen level, intubated veins, frequent elbow bending after intubation, high-strength labor, administration of prophylaxis dose and anticoagulant drugs, tumor, chemotherapy history, and PICC/CVC intubation history correlated with PICC-associated venous thrombosis and were the risk factors that affected the onset of PICC-associated venous thrombosis (**Table 4**).

Multifactor analysis of the risk factors of PICC-associated venous thrombosis after chemotherapy in the patients with lung cancer

Risk factors related to the onset of PICC-associated venous thrombosis were also tested using a multifactor logistic regression analysis. The results showed that sex, BMI, fibrinogen level, intubated veins, frequent elbow bending after intubation, high-strength labor, administration of prophylaxis dose and anticoagulant drugs, manual labor, tumor, chemotherapy history, and PICC/CVC intubation history were the independent risk factors of PICC-associated venous thrombosis (**Table 5**).

Discussion

Chemotherapy is an important treatment method for lung cancer, and most chemotherapeutics are administered via venous infusion. However, chemotherapeutics erodes the vessels, resulting in exosmosis and vasculitis or skin and soft tissue ulcer, or even infection [11-13]. Thus, it is quite important to establish a high-quality venous access. Otherwise, long-term administration is required for some specific chemotherapeutics. For example, administration of some chemotherapeutics persists for 2 days or even longer, which needs long-term retention of infusion access, instead of general infusion [14, 15]. However, PICC averts the above-mentioned problems while reducing patients' pain caused by recurrent venous puncture [16]. PICC is a catheter inserted from the peripheral vein to the central veins through puncture, thereby delivering the catheter tip to the superior vena cava, close to the heart [17]. For PICC placement, the basilic vein is preferred, followed by the median cubital vein and then the cephalic vein. PICC also has its own indications and the possibility of complications

Table 4. Univariate analysis of risk factors for PICC-associated venous thrombosis after chemotherapy in patients with lung cancer

Factor	Venous embolization group (n=40)	No venous thrombosis group (n=160)	X^2	P
Sex				
Male	12	83	6.14	0.013*
Female	28	77	6.14	
Age (years)				
< 50	18	79	0.245	0.621
≥ 0.6	22	81	0.245	
Body mass index (kg/m^2)				
< 19.50	3	34	4.013	0.045*
19.50~25.00	15	88	3.924	0.048*
≥ 0.048*	22	38	14.88	< 0.001*
Platelet count				
< 300 elet c	30	123	0.063	0.803
≥ 0.803 let c	10	37	0.063	
Fibrinogen				
< 4 g/L	14	102	10.86	0.001*
≥ 0.001	26	58	10.86	
Prothrombin				
< 10 g/L	23	87	0.126	0.722
≥ 0.722 L	17	73	0.126	
Implanted vein				
Expensive vein	25	129	5.936	0.015*
Other	15	31	5.936	
Tube placement				
Left side	22	84	0.08	0.777
Right side	18	76	0.08	
Always bend elbows				
Yes	25	37	23.19	< 0.001*
No	15	123	23.19	
Manual labor				
High-strength	21	48	7.169	0.007*
Low-strength	19	112	7.169	
Prophylaxis dose and anticoagulant drugs				
Yes	11	48	0.096	0.757
No	29	112	0.096	
Tumor				
Yes	35	98	9.898	0.002*
No	5	62	9.898	
History of chemotherapy				
Yes	17	33	8.167	0.004*
No	23	127	8.167	
PICC/CVC history				
Yes	16	27	10.14	0.002*
No	24	133	10.14	

Note: *indicates P < 0.05.

such as errhysis, hematoma, infection, increased risk of venous thrombosis, and accidents with the catheter, including rupture or blockage [18, 19]. Aster chemotherapy, patients with

Table 5. Multivariate analysis of PICC-associated venous thrombosis after chemotherapy in patients with lung cancer

Influencing factor	*β*	*SE*	*Wald*	*P*	*Exp (β)*	*95% CI*
Sex	0.875	0.256	8.243	0.034	4.065	1.231~4.803
Body mass index	0.899	0.286	8.623	0.026	2.905	1.244~3.723
Fibrinogen	0.736	0.280	7.021	0.012	2.642	1.474~3.768
Implanted vein	0.900	0.299	9.698	0.016	3.994	1.452~4.505
Frequent elbow bending	-0.196	0.101	15.990	0.034	2.003	1.012~2.034
Physical strength	-2.009	0.212	10.556	0.019	0.201	0.072~0.215
Tumor	0.886	0.186	8.583	0.206	2.493	1.394~3.584
History of chemotherapy	0.803	0.270	7.903	0.022	1.975	1.474~3.768
PICC/CVC history	0.790	0.249	9.385	0.026	3.005	1.553~4.639

lung cancer have a quite complicated pathogenesis of PICC-associated venous thrombosis. In this study, the goal was to identify the risk factors associated with PICC-related venous thrombosis after chemotherapy in patients with lung cancer [4].

In this study, 200 patients with lung cancer who were admitted to our hospital for treatment and underwent PICC placement after chemotherapy were retrospectively evaluated. Among these patients, 40 who developed a venous thrombus within 3 months after PICC placement were enrolled in the venous thrombosis group, while 160 had no venous thrombosis 3 months after PICC placement were enrolled in the control group. All the patients were diagnosed as having lung cancer through pathological examination, in accordance with to the international diagnostic criteria for lung cancer.

Previous studies confirmed that sex, BMI, fibrinogen level, intubated veins, frequent elbow bending after intubation, labor strength, administration of prophylaxis dose and anticoagulant drugs, tumor, chemotherapy history, and PICC/CVC intubation history are correlated with PICC-associated venous thrombosis [20, 21]. The risk of venous thrombus during chemotherapy for lung cancer is highest in the first 2 weeks after PICC intubation [22]. On the basis of the above-mentioned results, one-way and multifactor logistic regression analyses were performed to identify the risk factors. The results of the one-way logistic regression analysis of the risk factors of PICC-associated venous thrombosis after chemotherapy in the patients with lung cancer showed that sex, BMI, fibrinogen level, intubated veins, frequent elbow bending after intubation, labor strength, administration of prophylaxis dose and anticoagulant drugs, tumor, chemotherapy history, and PICC/CVC intubation history were the risk factors that affected the onset of PICC-associated venous thrombosis. The risk factors related to the onset of PICC-associated venous thrombosis were also tested using a multifactor logistic regression analysis. The results showed that sex, BMI, fibrinogen level, intubated veins, frequent elbow bending after intubation, labor strength, administration of prophylaxis dose and anticoagulant drugs, tumor, chemotherapy history, and PICC/CVC intubation history were the independent risk factors of PICC-associated venous thrombosis. Accumulating evidence regarding the correlation between PICC intubation and venous thrombosis supports the conclusion of this study [3, 4].

In this study, owing to the insufficient number of samples, a big data analysis could not be performed, which may have contributed to the contingency of the results. Patients are also affected by different geographical environments and the overall level of local medical care. In future studies, the sample size will be expended and standard treatment and care will be offered to further perfect the study.

In conclusion, sex, BMI, fibrinogen level, intubation veins, frequent elbow bending after intubation, labor strength, administration of prophylaxis dose and anticoagulant drugs, chemotherapy history, and PICC/CVC intubation history were identified as the risk factors of PICC-associated venous thrombosis. Before and after PICC intubation, these factors should be monitored closely. This is significant for the prophylaxis of PICC-associated venous thrombosis after chemotherapy for patients with lung cancer patients.

Disclosure of conflict of interest

None.

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