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Comparative Study of Catheter Structure Types on Venous Thrombosis in Cancer Patients with Peripherally Inserted Central Catheters

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Abstract

Background: Cancer patients with peripherally inserted central catheters (PICCs) are prone to venous thrombosis, occlusion, and other complications due to the disease itself, chemotherapy, age, and other factors.
Objectives: The present study aimed to assess the effect of different catheter materials on thrombosis in cancer patients with PICCs.
Methods: The clinical data of 110 cancer patients with PICCs implanted in an outpatient clinic of our hospital from January 2018 to June 2019 were collected. The valveless group comprised patients with catheter cancers without valvular structures and high-pressure resistant polyurethane material (n=58), and the valved group comprised patients with catheter cancers with valvular structures and high-pressure resistant polyurethane material (n=52).
Results: In the valveless group, 25 (43.1%) patients had total venous thrombosis, which was significantly higher than that of the valved group (n=11 patients; 21.15%) (P=0.028). In 7 out of 11 (78.85%) patients with thrombosis in the valved group, the thrombosis initiation vein was the axillary vein/subclavian vein, while the basilica/brachial vein was the thrombosis initiation vein in 18 out of 25 patients (43.10%) in the valveless group (P=0.043). There was no statistical difference between the two groups in terms of underlying diseases, thrombosis time, and extension in patients with thrombosis(P>0.05).
Conclusion: As evidenced by the obtained results, the catheter-inverted cone structure may be a factor of venous thrombosis. Therefore, the structure of catheters before catheterization should be considered and evaluated.

Keywords: Cancer, Peripherally inserted central catheter catheterization, Venous thrombosis, catheter structure

1. Background

Peripherally inserted central catheters (PICCs) have been widely used in intravenous therapy, especially for chemotherapy and nutritional support in cancer patients, since they cause less trauma and are safer than other methods (1,2). Nonetheless, they also increase the probability of venous thrombosis in upper limb vessels, leading to further complications, such as thrombophlebitis and pulmonary embolism, and affecting cancer patients' treatment and quality of life (3). A venous catheter is a foreign item to the body, and long-term placement in the blood vessels can damage endothelial cells, induce platelet coagulation, and greatly increase the probability of thrombosis in cancer patients (4). At present, there are two kinds of catheters commonly used in clinics. One is made from medical silica gel; the other is made with medical polyurethane (5). The medical polyurethane high-pressure catheter is divided into valveless catheters with front openings and valved catheters (6). Recently, Tennankore et al. (7) reported a proof of concept for the application of a hydrogel catheter based on polyacrylamide and poly (ethylene glycol) diacrylate in medical care. Although the materials of venous catheters are continuously optimized, there are differences in the quality, structure, and histocompatibility of venous catheters. There is a dearth of studies on the effects of different materials and structures of catheters on blood vessels.

2. Objectives

This study retrospectively analyses the probability of puncture venous thrombosis of two different structures of catheters in our hospital after PICC to provide a theoretical basis for clinical research on catheter-related venous thrombosis and optimize the placement process to reduce the complications of PICCs and play their due value.

3. Methods

3.1 Study design and participants

This retrospective study was conducted on cancer patients who were treated with PICCs in our hospital from January 2018 to June 2019. A certain percentage of patients treated with different catheter materials was selected according to the odd and even numbers at the end of hospitalization. The inclusion criteria were as follows: 1) age > 18 years, 2) diagnosis of malignancy and eligibility for PICC placement, 3) placement of high-pressure resistant polyurethane catheters with or without valves, and 4) the catheter tip positioned in the middle and lower part of the superior vena cava. On the other hand, the exclusion criteria entailed 1) non-malignant tumors and 2) silicone material placement.

A total of 165 patients were screened, among whom 28 cases with non-malignant tumors and 17 patients with silicone implants were excluded. Finally, 110 patients who met the criteria of this study were assigned to two groups: the valveless group consisted of 58 cases of high-pressure resistant polyurethane non-valved catheters. The valved group consisted of 52 subjects of high-pressure resistant polyurethane valve catheters. The difference between the two groups was analyzed in terms of venous thrombosis.

3.2. Data collection

Data collection was based on patients' general information, including age, gender, diagnosis, placement limb, catheter material, placement site, placement vein, catheter tip position, and placement date. Each record sheet of the use and maintenance of catheters and complications included the patient's name, age, diagnosis, catheter maintenance time, various complications, time of thrombosis, vein of thrombosis, and time of extubation.

3.3. Peripherally inserted central catheter procedure

The PICC cases of cancer patients selected in this study were operated by two full-time nurses, including one chief nurse and one charge nurse. They obtained qualification certificates from the PICC Specialist Technical Training Course of the Chinese Nursing Association, and each had 10 years of PICC placement experience with an annual placement volume of more than 500 tubes. The patient's vascular conditions, treatment plan, and past history were evaluated for catheter placement. The catheter material and type were selected according to the treatment plan, vascular diameter, and the patient's wishes. All catheter placements were performed using the modified Seldinger technique under ultrasound guidance. The placement process was strictly aseptic with the implementation of the maximum aseptic area, and the placement sites were all 10cm above the cubital crease. The first choice for vein selection was the basilic vein, while the second choice was the brachial vein. The success rates of the first needle puncture and first delivery were about 90% and 70%, respectively. The chest film was taken for positioning after placement, and the catheter tip was located in the lower middle of the superior vena cava in all selected patients.

3.4. Outcome measurement and follow-up

The information about the number of cases of venous thrombosis after catheter placement in the two groups of cancer patients and the basis of thrombosis was collected during the period of the PICC placement. The patients were observed daily during hospitalization for the puncture site, and records were made for arm circumference, changes to limb skin color, and patients' complaints. The out-of-hospital patients were observed by telephone follow-up during catheter maintenance. The thrombosis tracking times were 7±3 days, 15±3 days, and one month±3 day after catheterization.

If symptoms, such as blood and ooze from the puncture site, limb discomfort, shoulder heaviness, pressure and redness at the puncture site, and limb swelling, were present, venous thrombosis was suspected, and a color Doppler ultrasonography was performed as prescribed by the doctor to confirm the diagnosis. The diagnostic criteria included: 1) the official lumen of the vessel not being able to completely close under the pressure of the ultrasound probe, 2) poor entrant sounds in the lumen and a medium to low cloudy echogenicity detectable in the vessel appendage, and 3) a filling defect of the blood flow signal, out-of-phase change of the blood flow spectrum, and disappearance or weakening of the blood flow signal enhancement in the distal part of the squeezed limb (8). The ultrasonography report results demonstrated venous thrombosis, and the number of thrombosis cases, thrombosis veins, and its extension were recorded according to the report results.

3.5. Statistical analysis

The data were analyzed in SPSS software (version 17.0) using Chi-square and t-tests. A p-value less than 0.05 was considered statistically significant.

4. Results

4.1. General patients' information

The general patient information is illustrated in Table 1. The mean age of patients in the valve group was 66.15±16.15 years, and 63.46% of cases were male in this group. The mean age of patients in the valveless group was 62.53±12.07 years, and 56.90% of subjects were male in the valveless group. There was no statistical difference between the two groups in terms of gender, age, disease classification, placement limb, placement vein, and catheter indwelling days ($P > 0.05$). There were statistical differences between the valveless group and the valved group in the number/type of catheter lumens ($P=0.016$), whether they would undergo chemotherapy ($P<0.001$), whether there was tumor metastasis ($P< 0.001$) and whether there was an underlying disease ($P= 0.015$).

4.2. Thrombosis occurrence

In the valveless group, 25 (43.1%) patients had total venous thrombosis, which was significantly higher than the valved group (n=11; 21.15%) ($P= 0.028$). Out of 11 patients, 6 (54%) cases with thrombosis in the valved group had underlying

Table 1. Comparison of general information of patients in two groups (n=110)

	Item	Valved group (n =52)	Valveless group (n =58)	P value*
Gender	Male	33 (63.46%)	33 (56.90%)	0.483
	Female	19 (36.54%)	25 (43.10%)	
	Age, year	66.15±16.15	62.53±12.07	0.091
Placement limb	Left upper limb	19 (36.54%)	13 (22.41%)	0.103
	Right upper limb	33 (63.46%)	45 (77.59%)	
Placement vein	Basilic vein	39 (75.00%)	42 (72.41%)	0.759
	Brachial vein	13 (25.00%)	16 (27.59%)	
Number of catheter lumen/type	Single lumen 4Fr	26 (50.00%)	42 (72.41%)	0.016
	Double lumen 5Fr	26 (50.00%)	16 (27.59%)	
Disease classification	Lung cancer	11 (21.15%)	9 (15.52%)	0.659
	Digestive tract malignancies	28 (53.85%)	31 (53.45%)	
	Other malignant tumors	13 (25.00%)	18 (31.03%)	
Whether undergo chemotherapy	Yes	26 (50.00%)	50 (86.21%)	<0.001
	No	26 (50.00%)	8 (13.79%)	
With underlying disease**	Yes	28（53.84)	18（31.04)	0.015
	No	24（46.16)	40（68.96)	
Tumor metastasis	Yes	36 (69.23%)	46 (79.31%)	<0.001
	No	16 (30.77%)	12 (20.69%)	
	Catheter indwelling days	148.90±54.11	91.19±73.67	0.075

*Chi Square Test, ** Including hypertension, diabetes, obesity, asthma, heart disease, kidney disease, liver disease, cancer, etc

diseases. In the valveless group, out of 25 patients, 6 (24%) cases with thrombosis had underlying diseases. There was no statistical difference between the two groups in terms of underlying diseases in patients with thrombosis (P=0.238, Table 2); therefore, we considered that underlying diseases are not the main influencing factor of thrombosis.

4.3. Thrombosis time

In the valveless group with thrombosis, the earliest thrombosis occurred on day two, and the latest occurred on day 266 after catheter placement. In the valved group with thrombosis, the earliest thrombosis occurred on day two, and the latest occurred on day 135 after catheter placement. There was no significant difference in the indwelling time between the two groups (P>0.05) (Figure 1). Among the 25 cases of thrombosis in the valveless group, 12 (48%) cases occurred >12 weeks after catheterization, and 7 (20%) cases occurred within two weeks after catheterization. Among the 11 cases of thrombosis in the valved group, thrombosis was more concentrated in eight cases in the two weeks after catheterization, accounting for 72% of cases. The two groups had no statistical difference (P=0.051) (Table 3, Figure 1). Therefore, we concluded that the time factor was not relevant to thrombosis.

Table 2. Comparison of the underlying diseases of patients with thrombosis in the two groups

Group (number of cases)	None	1 underlying disease	2 underlying diseases	P-value*
Valved group (11)	5 (45.5%)	5 (45.5%)	1 (9%)	0.155
Valveless group (25)	19 (76%)	4 (16%)	2 (8%)	

* Chi Square Test

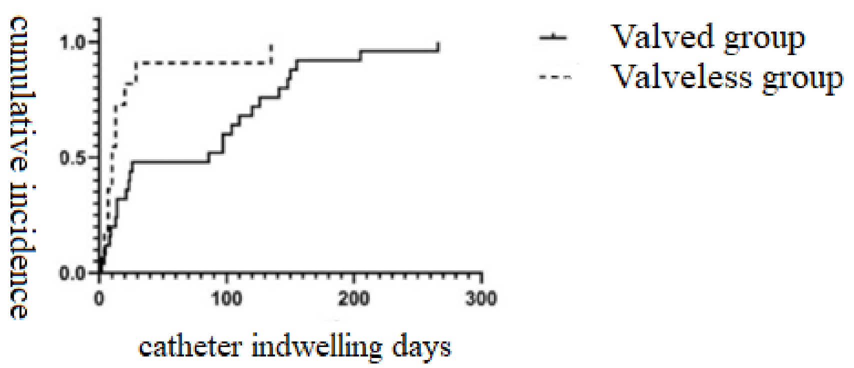

Figure 1. Curves of cumulative incidence of thrombosis versus days after catheterization

Table 3. Comparison of time of thrombosis in the two groups (n=36, weeks)

Group	Cases (n)	Time of thrombosis (weeks)				P value*
		<2	2-4	4-12	>12	
Valved group	11	8	1	1	1	0.051
Valveless group	25	7	5	1	12	
Total	36	15	6	2	13	

* Chi Square Test

4.4. Thrombosis place

For 18 cases in the valveless group and four cases in the valved group, the thrombosis initiation vein was basilic or brachial, while for seven cases in the valveless group and seven cases in the valved group, the thrombosis initiation vein was axillary or subclavian. There was a significant difference between the two groups in the thrombosis initiation vein (P=0.043) (Table 4).

4.5. Thrombosis extension

Comparing the extension of thrombus from the puncture vein upwards in the two groups, there were 11 (61.10%) cases of extension of 18 cases with thrombosis in the valveless group. In the valved group, out of four cases with thrombosis, three (75%) cases of the extension were observed, and there was no significant difference between the two groups in the extension of thrombus from the punctured vein upwards (P=0.601) (Table 5).

Table 4. Comparison of thrombosis initiation veins between the two groups (n=36)

Item	Valved group (n=11)	Valveless group (n=25)	P value*
Basilic vein / Brachial vein	4 (21.15%)	18 (43.10%)	0.043
Axillary vein / Subclavian vein	7 (78.85%)	7 (56.90%)	

* Chi Square Test

Table 5. Comparison of thrombus extension from the puncture vein to the axillary and subclavian veins in the two groups (n=36)

	Item	Valved group (n=4)	Valveless group (n=18)	P value*
Thrombus extension from the puncture vein	Yes	3 (75.00%)	11 (61.10%)	0.601
	No	1 (25.00%)	7 (38.90%)	

* Chi Square Test

5. Discussion

The results of this study pointed to a significant difference in venous thrombosis between the valveless group and the valved group using high-pressure polyurethane catheters, as well as a significant difference in the initial vein of thrombosis. In addition, the number/type of catheter lumens, whether the patient undergoes chemotherapy, tumor metastasis, and any associated potential diseases can affect venous thrombosis.

After the PICC is placed in the body, regardless of the material of the catheter, it is a foreign item in the human body. Long-term retention inevitably causes damage to the intima, and the catheter itself is one of the main factors leading to PICC-related venous thrombosis (8). There are three special designs of valve devices at the end of high-pressure resistant catheters. In addition to preventing blood from flowing back into the catheter and reducing the formation of the thrombus in the catheter, it is made of heat-sensitive polyurethane, which softens when it enters the body (due to the body's increased temperature) and may float in the blood vessel with relatively little impact on the vessel wall and better histocompatibility. There was a significant difference in the total thrombosis between the two types of catheters. A catheter with different structures of the same material was selected for the study. The results showed a significant difference in the total thrombosis rate between the two groups, which can be ascribed to the fact that the material of the polyurethane catheter was harder and more likely to cause damage to the intima. By observing the shape of the withdrawn catheter, it was found that the non-valved high-pressure resistant catheter would form a certain curved shape due to the direction of the blood vessel *in vivo*, indirectly indicating that the catheter might not be in a floating state in the blood vessel and is more likely to stick to the vessel wall, exerting a greater impact on the intima of the blood vessel and increasing the risk of venous thrombosis after long-term retention.

In addition to the effect of the catheter material on blood vessels, the special inverted conical design of the catheter end might also be a factor affecting venous thrombosis. Both catheters collected in this study were polyurethane catheters with an inverted tapered design, and the rate of venous thrombosis was statistically 21.15%-43.1%. The higher rate of thrombosis in this study may be related to ultrasound screening for asymptomatic venous thrombosis prior to extubation, the inverted tapered design of the catheter, and the presence of a polyurethane catheter.

According to 52.B.3 of the *Infusion Therapy Standard of Practice* (INS 2016),(9) the inverted tapered design at the end of the catheter allows the largest outer diameter portion of the catheter to be placed in the smallest diameter peripheral vein and is considered a risk factor for venous thrombosis. The PICC catheters with an inverted taper design begin to thicken at around 5cm from the end, and the diameter of the thickened portion of the catheter is larger than the diameter of the micro insertion sheath. The diameter of the sheath is larger than the outside diameter of the catheter due to the skin closure and micro insertion sheath, which often results in a relatively large puncture wound after placement and movement of the catheter with limb movement, leading to less healing for the puncture wound and the potential for skin bacteria to migrate inwards along the wound. The original intent of the inverted conical design of the catheter was to close the puncture opening with a thickened portion of the catheter, reducing infection and leakage of blood and fluid from the puncture site. Nevertheless, the PICC placement puncture vein is a distal superficial vein with a relatively fine diameter, and the diameters of veins in the human body in its natural state are generally about 4mm. The diameter of veins is also easily affected by the patient's emotions, temperature, diet, and other factors, and the diameter of the vessels may change somewhat during and after placement.

The *Chinese Expert Consensus on Infusion Catheter-related Venous Thrombosis* and the *Infusion Therapy Standard of Practice* (INS 2016) (9) recommend that the appropriate catheter model be selected according to the conditions of the proposed placement vessel, with a recommended ratio of ≤45% for the catheter outer diameter to the inner diameter of the placement vein. The clinical adult placement of PICC catheters should usually be performed with a 4Fr-5Fr model, which has an outer diameter of 1.4–1.7mm, and the outer diameter of its inverted cone structure part is comparable to that of 6Fr-7Fr catheters; therefore, it increases its catheter occupancy effect. This affects the intravascular blood flow velocity and the chance of contact with the inner wall of the vessel and increases the risk of thrombosis. The literature reports that the diameter of the catheter has a close relationship with deep vein thrombosis, and the ratio of the diameter of the placement vein to the catheter is a key factor affecting PICC-related venous thrombosis (10,11).

In this study, there was a significant difference in the initial vein of thrombosis between the two groups; however, there was no significant difference in the thrombosis of the two groups from the initial vein up, which might be related to the clinical finding of thrombosis with active anticoagulation intervention. Thrombosis occurs mostly at the early stage of catheter placement, which might be attributed to such factors as changing the blood flow of the vessel, the catheter occupancy effect, and damage to the intima of the vessel by catheter placement. The occurrence of thrombosis in the late stage of catheter placement might be related to the stiffness of the catheter material and mechanical irritation of the intima for long-term placement. Nonetheless, in general, there seemed to be no significant difference in the time period of thrombosis between the two groups.

Among the notable limitations of the study, we can refer to small sample size. Moreover, this study only discussed the effect of central venous catheters with different structures of the same material on venous thrombosis for the time being, and the effect of catheter materials needs further study. In addition, this study discussed the possible impact of chemotherapy on venous thrombosis; however, different types of chemotherapy may have different effects on venous thrombosis. Finally, the patients in this study may have had potential diseases, and this uncertainty may lead to a certain deviation in the results of the study.

6. Conclusion

As evidenced by the results of this study, catheter materials and the inverted conical structure of catheters might be a factor of venous thrombosis. Catheter placement operators must pay attention to the catheter material and structure before placement and evaluate the effect of the special structure of catheters on the placement vein. This will help in optimizing operation procedures, such as trimming the appropriate length of the PICC with an inverted conical structure, choosing larger diameter veins for ultrasound-guided placement to reduce the influence of the catheter-to-vein ratio, and considering the duration of retention according to the catheter material. This study provides a theoretical basis for the clinical study of catheter-related venous thrombosis in anticipation of reducing the complications of PICCs and making full use of their advantages.

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Footnotes

Conflicts of Interest: The authors declare that they have no conflict of interest regarding the publication of the present article.

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