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Application of different approaches in interventional thrombolysis of deep vein thrombosis of lower extremities

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Abstract: Objective To investigate the application effects of the popliteal vein approach versus the infrapatellar vein approach in interventional thrombolysis for the treatment of deep vein thrombosis (DVT) in the lower extremities, and its impact on thromboelastography (TEG) parameters, coagulation function, and cell adhesion factor levels. **Methods** A total of 78 DVT patients from the Affiliated Hospital of Hebei University of Engineering, between August 2022 and August 2023, were selected and randomly divided into two groups, with 39 patients in each group. Interventional thrombolysis was conducted via the popliteal vein approach in observation group, and via infrapatellar vein approach in control group. Perioperative indicators and thrombus clearance effects were observed in both groups. The swelling of the affected limb, TEG parameters [reaction time (R value), kinetic time (K value)], coagulation indexes [fibrinogen (Fib), D-dimer (D-D)], and levels of cell adhesion factors [vascular cell adhesion molecule-1 (VCAM-1), platelet endothelial cell adhesion molecule-1 (PECAM-1), P-selectin] were analyzed and compared before and after surgery, as well as the incidence of complications. Patients were followed up for one year after discharge, and the Villalta score was used to assess prognosis. **Results** The observation group had shorter surgical times, reduced X-ray exposure times, and lower contrast agent doses compared to the control group (P<0.05). There was no statistically significant difference in thrombus clearance effects between the two groups (Z=0.187, P=0.951). One week after surgery, the circumferences of the calf and thigh in both groups showed a significant reduction compared to preoperative measurements (P<0.05). One-week post-surgery, R and K values increased significantly in both groups, while Fib, D-D, VCAM-1, PECAM-1, and P-selectin levels decreased significantly compared to preoperative values (P<0.05). There was no statistically significant difference in the incidence of complications during hospitalization between the two groups (2.56% *vs* 15.38%, χ^2=2.511, P=0.113). At one-year follow-up, there was no statistically significant difference in the distribution of Villalta scores (Z=0.027, P=0.978). **Conclusion** Both the popliteal vein approach and the infrapatellar vein approach for interventional thrombolysis effectively clear thrombus, improve coagulation function, and reduce limb swelling in DVT patients, with good long-term effects and safety. Although the former approach has distinct advantages in terms of surgical time, X-ray exposure time, and contrast agent usage, the actual choice of approach should be determined based on the individual patient's condition.

Keywords: Lower extremity deep vein thrombosis; Interventional hemolytic surgery; Popliteal vein approach; Subpatellar venous approach; Swelling; Thromboelastography; Cell adhesion factor

Deep venous thrombosis (DVT) is a common disease with multiple etiologies, and is highly prone to triggering thrombotic syndrome and pulmonary embolism, which is one of the leading causes of mortality in patients [1]. With the increasing aging population in recent years, the incidence of DVT has shown a gradual rising trend, becoming one of the major clinical concerns for the elderly [2]. The treatment principle for DVT is to remove the thrombus, restore venous patency, protect valve function, and prevent complications [3]. Anticoagulation therapy is the basic treatment for DVT. However, studies have shown that the incidence of post-thrombotic syndrome can reach up to 50% within five years of anticoagulation therapy alone, and it can even lead to the loss of the patient's work capacity [4]. Relevant literature reports that interventional thrombolysis has shown good prospects in DVT treatment, as it can effectively remove thrombus and improve lower limb blood flow [5-6]. With the continuous development of interventional thrombolysis in clinical practice, the approach for interventional thrombolysis has gained clinical attention, and designing a personalized approach can effectively improve the success rate of the procedure. This study selected DVT patients from our hospital for cohort analysis, exploring the application value of popliteal vein approach versus below-knee vein approach in interventional thrombolysis, aiming to provide reference for surgical approach selection in patients.

1 Data and Methods

1.1 Study Subjects

This study was conducted in accordance with the relevant requirements of the *Declaration of Helsinki* [7] and was approved by the Ethics Committee of Affiliated

Hospital of Hebei University of Engineering (Ethical approval number: 2024[K]004). A total of 78 DVT patients from the Affiliated Hospital of Hebei University of Engineering, between August 2022 and August 2023, were selected for the study, all of whom signed an informed consent form.

Inclusion criteria:

(1) Met the diagnostic criteria of the *Practice Guidelines for the Diagnosis and Treatment of Lower Limb Deep Venous Thrombosis* and confirmed by ultrasound;
(2) Clinical symptoms included lower limb swelling, pain, and discomfort;
(3) Had unilateral limb involvement;
(4) No contraindications for surgery or medication.

Exclusion criteria:

(1) With malignant tumors, coagulation disorders, or lower limb venous occlusion;
(2) With severe heart, liver, or kidney dysfunction;
(3) With mental illness or cognitive impairment.

A total of 78 eligible patients were included and randomly divided into an observation group and a control group, with 39 patients in each group. The differences in general data between the two groups were not statistically significant (P>0.05). See **Table 1**.

Tab.1 Comparison of general information between two groups (n=39)

Group	Age(years, $\bar{x}\pm s$)	Gender (cases)		BMI (kg/m^2, $\bar{x}\pm s$)	Affected side (cases)		DVT classification (cases)			Cause (cases)	
		Male	Female		Left	Right	Surrounding	Central	Mixed	Yes	No
Observation group	58.94±4.77	19	20	22.84±1.63	18	21	17	16	6	9	30
Control group	60.11±4.58	22	17	23.22±1.71	16	23	15	19	5	11	28
***t*/χ^2 value**	1.105	0.463		1.005	0.209		0.473			0.269	
***P* value**	0.273	0.496		0.318	0.648		0.789			0.604	

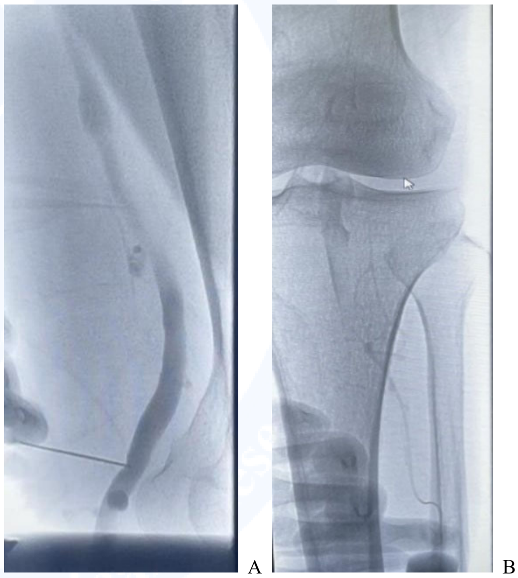
1.2 Methods

Upon admission, all patients underwent relevant tests including blood routine, coagulation function, and imaging. Heparin was administered for anticoagulation therapy. A caval filter was placed via the healthy side [Kossel Medtech (Suzhou), Model: KVF34].

In the observation group, an interventional thrombolysis was performed via the popliteal vein approach. The patient was positioned prone, with the puncture site disinfected and sterile surgical drapes applied, followed by local anesthesia. Under fluoroscopy, a contrast agent was injected through a needle retained in the foot. Using the Seldinger technique, a puncture was made through the affected side popliteal vein, and a catheter sheath and guidewire were inserted. A thrombolysis catheter was retained at the thrombus segment, with the thrombolysis length completely covering the thrombus length. For patients with concomitant iliac vein stenosis, balloon dilation was performed before thrombolysis.

In the control group, an interventional thrombolysis was performed via the below-knee venous approach. The patient was in a supine position, with anesthesia applied in the same manner as the observation group. Using the Seldinger technique, puncture was made through the sub-knee vein on the affected side, and a thrombolysis catheter was retained at the thrombus segment. Other procedures were the same as in the observation group.

Thrombolysis: a micro-pump was used to continuously administer heparin and urokinase through the sheath. See **Figure 1**.



Note: A was popliteal vein approach; B was below-knee venous approach.
Fig.1 X-ray imaging of interventional thrombolysis through different venous approaches

1.3 Observational Indicators

(1) Perioperative Indicators: Surgery time, X-ray exposure time, dosage of urokinase, dosage of contrast agent, thrombolysis time, postoperative hospital-stay.

(2) Thrombus Clearance Effect: Digital subtraction angiography via the dorsalis pedis artery was performed, and venous patency was evaluated based on the degree of venous flow: Level 1 represents significant contrast agent retention with venous patency less than 50%; Level 2 represents minimal contrast agent retention with venous patency between 50% and 90%; Level 3 represents no significant contrast agent retention with venous patency greater than 90%.

(3) Swelling of the Affected Limb: The circumference of the affected and unaffected lower limbs at 15 cm above and below the knee joint was measured preoperatively and one week postoperatively using a tape measure. The differences in thigh and calf circumference and the

preoperative *vs*. postoperative difference were calculated.
(4) Thromboelastography (TEG) Parameters: The reaction time (R value) and clotting time (K value) were measured using a TEG (Haemonetics Corporation, Model: 5000); fibrinogen (Fib) and D-dimer (D-D) levels were measured using a coagulometer (Accriva Diagnostics, Inc., Model: Hemochron Signature Elite).
(5) Cell Adhesion Molecules: 5 mL of peripheral venous blood was collected preoperatively and postoperatively, allowed to coagulate at room temperature, centrifuged at 3,500 r/min for 10 minutes at 4°C, and the upper serum was stored at -70°C. The levels of vascular cellular adhesion molecule-1 (VCAM-1) and platelet-endothelial cell adhesion molecule 1 (PECAM-1) were detected by enzyme-linked immunosorbent assay (ELISA), using kits purchased from BIOHIT OYJ.
(6) Complications: Incision infection, puncture point bleeding, skin bruising, and hematochezia during hospitalization were recorded.
(7) Prognosis: Follow-up was conducted for one-year post-discharge to observe patient prognosis. The Villalta score was used to assess the prognosis, with scoring based on the severity of symptoms: 0 points for none symptoms, 5–9 points for mild, 10–14 points for moderate, and ≥15 points for severe.

1.4 Statistical Methods

Data were analyzed using SPSS 25.0 software. Count data were described using n(%), and the chi-square test was used for comparisons. Rank data were analyzed using rank-sum test. Measurement data were distributed with homogeneous variances, expressed as $\bar{x} \pm s$, and comparisons between groups were performed using independent-sample t-tests, while paired t-tests were used for intra-group comparisons. All tests were two-tailed, with a significance level of α=0.05.

2 Results

2.1 Comparison of Perioperative Indicators

The surgery time, X-ray exposure time, and contrast agent dose in the observation group were shorter and lower than those in the control group (P<0.05). While there was no significant difference in the dosage of urokinase, thrombolysis time, postoperative hospital-stay between two groups (P>0.05). See **Table 2**.

2.2 Comparison of Thrombus Clearance Effect

In the observation group, the thrombus clearance effect was Grade 1 in 4 cases, Grade 2 in 4 cases, and Grade 3 in 31 cases. In the control group, the thrombus clearance effect was Grade 1 in 3 cases, Grade 2 in 6 cases, and Grade 3 in 30 cases. There was no statistically significant difference between the two groups regarding thrombus clearance effect (Z=0.559, P>0.05).

2.3 Comparison of Swelling of the Affected Limb

There was no significant difference between the two groups regarding the circumference difference and swelling improvement rate of the calf and thigh at 1-week post-surgery compared to pre-surgery (P>0.05). However, the circumference difference of the calf and thigh was significantly reduced in both groups at 1-week post-surgery compared to pre-surgery (P<0.05). See **Table 3**.

2.4 Comparison of TEG Parameters

There was no statistically significant difference between the two groups in terms of R value, K value, Fib, D-D, and their differences preoperatively and at 1-week post-surgery (P>0.05). At 1-week post-surgery, both groups showed a significant increase in R and K values and a significant decrease in Fib and D-D compared to pre-surgery (P<0.05). See **Table 4** and **Table 5**.

2.5 Comparison of Cell Adhesion Molecules

There was no statistically significant difference between the two groups in terms of adhesion molecule levels and their differences preoperatively and at 1-week post-surgery (P>0.05). At 1-week post-surgery, both groups showed a significant reduction in VCAM-1, PECAM-1, and P-selectin levels compared to pre-surgery (P<0.05). See **Table 6**.

Tab.2 Comparison of perioperative indicators between two groups (n=39, $\bar{x} \pm s$)

Group	Operation time (min)	X-ray exposure time (min)	Urokinase (×10^4 u)	Dosage of contrast agent (mL)	Time of thrombolysis (d)	Postoperative hospital-stay (d)
Observation group	55.39±15.83	15.61±4.72	300.59±75.48	50.98±12.39	6.95±1.86	9.32±1.35
Control group	62.28±11.47	20.39±8.43	318.43±77.63	72.76±15.77	7.08±1.93	9.08±1.28
t value	2.201	3.090	1.029	6.782	0.303	0.806
P value	0.031	0.003	0.307	<0.001	0.763	0.423

Tab.3 Comparison of swelling before and after surgery between two groups (n=39, $\bar{x} \pm s$)

Group	Difference in circumference of limb calf			Difference in circumference of thigh		
	Pre-operative (cm)	1 week after operation (cm)	Swelling improvement rate (%)	Pre-operative (cm)	1 week after operation (cm)	Swelling improvement rate (%)
Observation group	4.87±1.02	1.31±0.31[a]	73.10±5.96	6.99±1.35	1.41±0.58[a]	79.83±6.84
Control group	4.95±1.03	1.29±0.29[a]	73.93±6.48	7.14±1.48	1.43±0.62[a]	79.97±6.65
t value	0.345	0.294	0.589	0.468	0.147	0.092
P value	0.731	0.769	0.578	0.641	0.883	0.927

Note: Compared with pre-operative, [a]P<0.05.

Tab.4 Comparison of TEG indexes before and after surgery between two groups (n=39, $\bar{x}\pm s$)

Group	R value(min)			K value(min)		
	Pre-operative	1 week after operation	Difference	Pre-operative	1 week after operation	Difference
Observation group	2.89±0.53	5.39±1.05[a]	2.50±0.72	0.83±0.29	1.51±0.44[a]	0.68±0.31
Control group	3.08±0.47	5.41±1.12[a]	2.33±0.83	0.79±0.31	1.58±0.42[a]	0.79±0.35
***t* value**	1.675	0.081	0.966	0.589	0.719	1.469
***P* value**	0.098	0.935	0.337	0.558	0.475	0.146

Note: Compared with pre-operative, [a]P<0.05.

Tab.5 Comparison of coagulation indexes before and after surgery between two groups (n=39, $\bar{x}\pm s$)

Group	Fib(g/L)			D-D(mg/L)		
	Pre-operative	1 week after operation	Difference	Pre-operative	1 week after operation	Difference
Observation group	6.85±1.22	5.42±0.69[a]	1.43±0.84	1.18±0.35	0.45±0.20[a]	0.73±0.25
Control group	7.01±1.34	5.39±0.73[a]	1.62±0.82	1.20±0.37	0.51±0.19[a]	0.69±0.27
***t* value**	0.551	0.187	1.011	0.245	1.358	0.679
***P* value**	0.583	0.853	0.315	0.807	0.178	0.499

Note: Compared with pre-operative, [a]P<0.05.

Tab.6 Comparison of coagulation indexes before and after surgery between two groups (n=39, $\bar{x}\pm s$)

Group	VCAM-1(μg/L)			PECAM-1(μg/L)			P- selectin (ng/mL)		
	Pre-operative	1 week after operation	Difference	Pre-operative	1 week after operation	Difference	Pre-operative	1 week after operation	Difference
Observation group	139.36±11.48	83.85±8.48[a]	56.01±8.53	108.54±15.77	69.53±8.58[a]	39.01±5.76	50.84±5.81	23.48±4.98[a]	27.36±4.55
Control group	141.47±12.79	85.72±8.76[a]	55.75±8.72	111.49±16.23	70.21±8.73[a]	41.28±5.53	49.93±5.62	24.03±5.23[a]	25.90±4.91
***t* value**	0.767	0.958	0.133	0.814	0.347	1.775	0.703	0.476	1.362
***P* value**	0.446	0.341	0.895	0.418	0.730	0.080	0.484	0.636	0.177

Note: Compared with pre-operative, [a]P<0.05.

2.6 Comparison of Complication Rates During Hospitalization

During hospitalization, one case of puncture point bleeding occurred in the observation group, while the control group had 3 cases of incision infection, 1 case of puncture point bleeding, 1 case of skin bruising, and 1 case of hematochezia. There was no statistically significant difference between the two groups in terms of complication rates during hospitalization (2.56% *vs* 15.38%, χ^2=2.511, P=0.113).

2.7 Comparison of Prognosis

In the one-year follow-up, 4 patients in the observation group and 3 in the control group were lost to follow-up. There was no statistically significant difference in Villalta score distribution between the two groups (P>0.05). See **Table 7**.

Tab.7 Comparison of Villalta scores between two groups during 1-year follow-up [case(%)]

Group	Cases	No	Mild	moderate	severe
Observation group	35	23	8	3	1
Control group	36	23	10	3	0
***Z* value**				1.208	
***P* value**				0.751	

3 Discussion

Interventional thrombolysis is one of the main treatment options for deep vein thrombosis (DVT). By catheterizing and directly infusing thrombolytic drugs to the thrombus site, it can accelerate thrombus dissolution and regression, promote venous patency, reduce damage to venous valve function, and improve the long-term prognosis of DVT [11-12]. Currently, there are various approaches for interventional thrombolysis, including the popliteal vein approach, the healthy-side vein approach, the jugular vein approach, and the below-knee vein approach. Among these, the popliteal vein approach is an antegrade catheterization, which conforms to anatomical structures and is less challenging to perform. However, it requires higher surgical expertise, involves positional changes during the procedure, and necessitates postoperative immobilization, which may reduce patient cooperation. Moreover, there is a higher risk of puncture failure in cases where the thrombus involves occlusion of the popliteal vein [13]. In contrast, the healthy-side vein approach and the jugular vein approach are retrograde routes that are farther from the thrombus location, which may damage venous valve function and result in poor thrombolysis effects [14-15]. The below-knee vein approach typically uses the small saphenous vein, which is deeper in position, has sufficient effective length, and is connected to deep veins by communicating branches. However, it carries the risk of anatomical variations [16]. This study conducts a prospective cohort analysis to explore safe and reliable approaches for interventional thrombolysis to improve patient outcomes.

Zhao *et al.* [9] found that the cost of thrombolysis treatment through the popliteal vein approach is lower than that through the below-knee vein approach, thus making the popliteal vein the preferred access route for BVT. In this study, the observation group had shorter surgery time, less X-ray exposure time, and lower contrast agent dose compared to the control group, further supporting this conclusion. The analysis suggests that the popliteal vein is positioned more superficially, requiring no skin dissection for puncture. Its larger diameter makes catheter insertion simpler, more stable, and less restricted in movement. The study showed no statistically significant differences between the two groups in terms of thrombus removal effect, calf and thigh circumferences, and swelling improvement rate at one-week post-operation, indicating that the popliteal vein approach and the below-knee vein approach yield similar results in thrombus removal and lower limb swelling improvement. This is primarily because both popliteal and below-knee veins puncture into the deep veins, and while the below-knee vein is more challenging to operate on, digital imaging can still help administer thrombolytic drugs to the thrombus site, achieving therapeutic effects. Related studies have shown that coagulation dysfunction is closely related to the occurrence and progression of DVT. Therefore, detecting coagulation function is not only important for diagnosing DVT but also for assessing treatment effectiveness [17]. TEG is a physical and chemical combined detection method for coagulation status. Its parameters reflect the dynamic process of coagulation function and can effectively assess the coagulation mechanism from initial thrombus formation to complete thrombolysis in DVT patients [18]. This study found that the R-value and K-value were higher at one-week post-operation compared to pre-operation, while Fib and D-D values were lower, though the differences between the groups were not statistically significant. This suggests that both surgical approaches effectively remove the thrombus and improve the patient's blood circulation.

Post-thrombotic syndrome (PTS) refers to a series of symptoms caused by impaired venous blood flow in the lower limbs, blood reflux, and increased venous pressure, with an incidence rate of over 20%. Among them, 5%–23% of patients have more severe symptoms, which is an important factor affecting the prognosis of DVT patients [19]. Some studies suggest that platelet adhesion to the inner walls of deep veins forms the basis for new thrombus formation, and cell adhesion molecules can mediate cell-cell and cell-matrix signaling to promote the formation of new thrombi [20-21]. VCAM-1 and PECAM-1 are both cell adhesion molecules. The former, a member of the immunoglobulin family, participates in the adhesion of monocytes and macrophages to the vascular wall, while the latter inhibits blood cell aggregation and regulates leukocyte migration and signaling, playing an important role in arterial and venous thrombosis and vascular diseases. Literature indicates that in DVT patients, those without recanalization have significantly higher serum levels of cell adhesion molecules compared to those with recanalization, and these levels correlate with the risk of post-thrombotic syndrome [22]. Therefore, decreasing VCAM-1 and PECAM-1 levels is important for preventing and treating DVT. P-selectin, mainly found on the membranes of platelets and endothelial cells, can bind to leukocytes and participate in thrombus formation [23]. This study showed that postoperative levels of VCAM-1, PECAM-1, and P-selectin were significantly lower than preoperative levels. However, the differences between the groups and the Villalta scores at one-year post-operation were not statistically significant, indicating that both the popliteal vein and below-knee vein approaches for interventional thrombolysis can remove thrombi, improve blood circulation, and suppress the expression of cell adhesion molecules, with good long-term effects.Surgical safety is a major concern in clinical practice, as it affects the patient's prognosis. Zhang *et al.* [24] found that reducing tissue damage during DVT thrombolysis can effectively reduce the incidence of complications. In this study, the observation group had a lower complication rate during hospitalization than the control group. This is primarily due to the deeper and smaller diameter of the below-knee vein, which requires skin incision during puncture, increasing the risk of venous damage or even rupture during catheter sheath insertion. Additionally, removing the filter via the below-knee vein after thrombolysis is more challenging, increasing the risk of complications. However, the difference between the two groups was not statistically significant, which may be attributed to the relatively small sample size in this study.

In conclusion, interventional thrombolysis through both the popliteal vein and below-knee vein access routes is safe and reliable in DVT treatment. It can suppress cell adhesion molecule expression, improve coagulation function, and provide good long-term effects. However, both access routes have limitations in practice, and the choice of route should be based on the patient's specific condition. Furthermore, the small sample size in this study may introduce bias, and further large-scale studies are needed for validation.

Conflict of Interest None

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· 论　著 ·

不同入路方式在下肢深静脉血栓形成介入性溶栓中的应用

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摘要：目的　探讨腘静脉入路与膝下静脉入路行介入性溶栓术在下肢深静脉血栓形成（DVT）治疗中的应用效果，及其对血栓弹力图（TEG）参数、凝血功能、细胞黏附因子水平的影响。**方法**　选取 2022 年 8 月至 2023 年 8 月河北工程大学附属医院 78 例 DVT 患者，按随机数字表法分为两组，各 39 例。观察组行腘静脉入路介入性溶栓术，对照组行膝下静脉入路介入性溶栓术。观察两组围手术期指标、血栓清除效果，比较手术前后患肢肿胀情况、TEG 参数［反应时间（R 值）、凝固时间（K 值）］、凝血功能［纤维蛋白原（Fib）、D-二聚体（D-D）］、细胞黏附因子［血管细胞黏附分子-1（VCAM-1）、血小板内皮细胞黏附分子-1（PECAM-1）、P-选择素］水平及并发症发生率。出院后随访 1 年，采用 Villalta 评分法评估患者预后。**结果**　观察组手术时间、X 线曝光时间、造影剂剂量均低于对照组（$P<0.05$）；两组血栓清除效果比较差异无统计学意义（$Z=0.187$，$P=0.951$）；术后 1 周两组患肢小腿、大腿周径差较术前明显减小（$P<0.05$）；术后 1 周两组 R 值、K 值较术前明显升高，Fib、D-D、VCAM-1、PECAM-1、P-选择素水平较术前明显降低（$P<0.05$）；住院期间两组并发症发生率差异无统计学意义（2.56% *vs* 15.38%，$\chi^2=2.511$，$P=0.113$）。随访 1 年 Villalta 评分比较差异无统计学意义（$Z=0.027$，$P=0.978$）。**结论**　经腘静脉入路与膝下静脉入路介入性溶栓术治疗 DVT 患者，均能有效清除血栓，改善患者凝血功能，减轻下肢肿胀程度，具有较好的远期效果及安全性，尽管前者在手术时间、X 线曝光时间及造影剂使用量方面具有明显优势，但仍需根据患者实际情况选择入路。

关键词：下肢深静脉血栓形成；介入性溶栓术；腘静脉入路；膝下静脉入路；血栓弹力图；细胞黏附因子
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Application of different approaches in interventional thrombolysis of deep vein thrombosis of lower extremities

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Abstract: Objective　To investigate the application effects of the popliteal vein approach versus the infrapatellar vein approach in interventional thrombolysis for the treatment of deep vein thrombosis (DVT) in the lower extremities, and its impact on thromboelastography (TEG) parameters, coagulation function, and cell adhesion factor levels. **Methods**　A total of 78 DVT patients from the Affiliated Hospital of Hebei University of Engineering, between August 2022 and August 2023, were selected and randomly divided into two groups, with 39 patients in each group. Interventional thrombolysis was conducted via the popliteal vein approach in observation group, and via infrapatellar vein approach in control group. Perioperative indicators and thrombus clearance effects were observed in both groups. The swelling of the affected limb, TEG parameters [reaction time (R value), kinetic time (K value)], coagulation indexes [fibrinogen (Fib), D-dimer (D-D)], and levels of cell adhesion factors [vascular cell adhesion molecule-1 (VCAM-1), platelet endothelial cell adhesion molecule-1 (PECAM-1), P-selectin] were analyzed and compared before and after surgery, as well as the incidence of complications. Patients were followed up for one year after discharge, and the Villalta score was

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used to assess prognosis. **Results** The observation group had shorter surgical times, reduced X-ray exposure times, and lower contrast agent doses compared to the control group ($P<0.05$). There was no statistically significant difference in thrombus clearance effects between the two groups ($Z=0.187$, $P=0.951$). One week after surgery, the circumferences of the calf and thigh in both groups showed a significant reduction compared to preoperative measurements ($P<0.05$). One-week post-surgery, R and K values increased significantly in both groups, while Fib, D-D, VCAM-1, PECAM-1, and P-selectin levels decreased significantly compared to preoperative values ($P<0.05$). There was no statistically significant difference in the incidence of complications during hospitalization between the two groups (2.56% *vs* 15.38%, $\chi^2=2.511$, $P=0.113$). At one-year follow-up, there was no statistically significant difference in the distribution of Villalta scores ($Z=0.027$, $P=0.978$). **Conclusion** Both the popliteal vein approach and the infrapatellar vein approach for interventional thrombolysis effectively clear thrombus, improve coagulation function, and reduce limb swelling in DVT patients, with good long-term effects and safety. Although the former approach has distinct advantages in terms of surgical time, X-ray exposure time, and contrast agent usage, the actual choice of approach should be determined based on the individual patient's condition.

Keywords: Lower extremity deep vein thrombosis; Interventional hemolytic surgery; Popliteal vein approach; Subpatellar venous approach; Thromboelastography; Cell adhesion factor

下肢深静脉血栓(deep vein thrombosis, DVT)是一种多因素疾病,极易诱发血栓形成综合征、肺动脉栓塞,是造成患者死亡的重要原因之一[1]。近年随着老龄化加剧,DVT 发生率呈逐渐升高趋势,成为临床关注的老年问题之一[2]。DVT 治疗原则是清除血栓、恢复静脉通畅、保护瓣膜功能、预防并发症发生[3]。抗凝治疗是 DVT 基础疗法,但有研究显示,单独抗凝治疗 5 年内血栓后综合征发生率高达 50%,甚至造成患者劳动能力丧失[4]。相关文献报道,介入性溶栓术在 DVT 治疗中展现了良好的应用前景,可有效清除血栓,改善下肢血流[5-6]。随着介入性溶栓术在临床不断开展,介入性溶栓术的入路得到了临床重视,设计个性化入路可有效提高手术的成功率。本研究选取 DVT 患者分组开展队列分析,探讨腘静脉入路与膝下静脉入路行介入性溶栓术的应用价值,旨在为患者手术入路选择提供参考。报告如下。

1　资料与方法

1.1　*研究对象*　本研究遵循《赫尔辛基宣言》[7]中相关要求开展研究,并通过医院伦理委员会审批通过(伦理批号:2024[K]004)。选取 2022 年 8 月至 2023 年 8 月河北工程大学附属医院收治的 DVT 患者,患者签署知情同意书。纳入标准:符合《下肢深静脉血栓形成的诊断和治疗实践指南》[8]中诊断标准,并经超声诊断确诊;临床症状为下肢肿胀、疼痛不适;均为单侧肢体患病;无手术或药物禁忌证。排除标准:合并恶性肿瘤、凝血功能障碍者;下肢静脉闭塞者;合并心、肝、肾功能严重不全者;精神疾病或认知功能障碍者。共纳入符合标准患者78 例,采用随机数字表法分为观察组和对照组,各 39 例。两组一般资料比较差异无统计学意义($P>0.05$)。见表 1。

表 1　两组 DVT 患者一般资料比较　($n=39$)

Tab. 1　Comparison of general information between two groups　($n=39$)

组别	年龄(岁, $\bar{x}\pm s$)	性别(例)		BMI (kg/m², $\bar{x}\pm s$)	患侧(例)		DVT 分型(例)			病因(例)	
		男	女		左侧	右侧	周围型	中央型	混合型	有诱因	无诱因
观察组	58.94±4.77	19	20	22.84±1.63	18	21	17	16	6	9	30
对照组	60.11±4.58	22	17	23.22±1.71	16	23	15	19	5	11	28
t/χ^2 值	1.105	0.463		1.005	0.209		0.473			0.269	
P 值	0.273	0.496		0.318	0.648		0.789			0.604	

1.2　*方法*　术前:入院后患者均行血常规、凝血功能、影像等相关检测;给予肝素进行抗凝治疗;经健侧置入腔静脉滤器[厂家:科塞尔医疗科技(苏州),型号:KVF34]。观察组采用腘静脉入路介入性溶栓术,患者取俯卧位,穿刺部位消毒铺无菌手术巾,予以局部麻醉。透视下经足部留置针推注造影剂,采用 Seldinger 技术经患侧腘静脉穿刺,置入导管鞘及导丝,血栓段留置溶栓导管,溶栓长度完全覆盖血栓长度,合并髂静脉狭窄患者,先采用扩张球囊扩张后再行溶栓治疗。对照组行膝下静脉入路行介入性溶栓术,患者仰卧位,麻醉方式同观察组,Seldinger 技术经患侧膝下静脉穿刺,血栓段留置溶栓导管。其余操作同观察组。溶栓治疗:鞘

管采用微泵持续泵入肝素和尿激酶。见图 1。

1.3　观察指标　(1) 围手术期指标:手术时间、X 线曝光时间、尿激酶剂量、造影剂剂量、溶栓时间、术后住院时间。(2) 血栓清除效果:经足背动脉进行数字减影血管造影,根据静脉通畅程度进行评估,1 级为造影剂明显残留,静脉通畅程度低于 50%;2 级为少量造影剂残留,静脉通畅程度 50%~90%;3 级为造影剂无明显残留,静脉通畅程度>90%[9]。(3) 患肢肿胀情况:术前、术后 1 周采用卷尺测量患侧与健侧膝关节上下 15 cm 位置下肢周径,计算大腿、小腿周径差及手术前后差值。(4) 血栓弹力图(thromboelastography, TEG)参数:采用血栓弹力图仪(Haemonetics Corporation,型号:5000)检测反应时间(reaction time, R 值)、凝固时间(kinetic time, K 值);以血凝分析仪(Accriva Diagnostics, Inc.,型号:Hemochron Signature Elite)检测纤维蛋白原(fibrinogen, Fib)、D-二聚体(D-dimer, D-D)水平。(5) 细胞黏附因子:采集患者术前及术后外周静脉血 5 mL,室温凝固,4 ℃环境以 3 500 r/min 离心半径 10 cm 离心 10 min,分离上层血清-70 ℃低温储藏。采用酶联免疫吸附试验检测血清血管细胞黏附分子-1(vascular cellular adhesion molecule-1, VCAM-1)、血小板内皮细胞黏附分子-1(platelet-endothelial cell adhesion molecule 1, PECAM-1)、水平,试剂盒购自 BIOHIT OYJ。(6) 并发症:记录患者住院期间切口感染、穿刺点渗血、皮肤瘀斑、便血等情况。(7) 预后情况:出院后随访 1 年,采用 Villalta 评分法[10]评估患者预后,根据患者症状程度进行评分,无为 0 分,轻度为 5~9 分,中度为 10~14 分,重度为≥15 分。

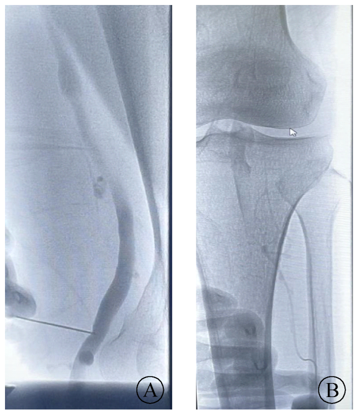
1.4　统计学方法　采用 SPSS 25.0 软件分析收集数据,计数资料以例(%)描述,比较采用 χ^2 检验;等级资料采用秩和检验。计量资料均服从正态分布且具备方差齐性,以 $\bar{x}\pm s$ 表示,组间比较采用独立样本 t 检验,组内比较采用配对 t 检验。检测均为双侧检验,检验水准 $\alpha=0.05$。

2　结　果

2.1　围手术期指标比较　观察组手术时间、X 线曝光时间短于对照组,造影剂剂量少于对照组($P<0.05$);两组尿激酶剂量、溶栓时间、术后住院时间比较差异无统计学意义($P>0.05$)。见表 2。

2.2　血栓清除效果比较　两组血栓清除效果比较差异无统计学意义($P>0.05$)。见表 3。

2.3　两组患肢肿胀情况　两组术前、术后 1 周患肢小腿、大腿周径差及肿胀改善率比较差异无统计学意义($P>0.05$);术后 1 周两组患肢小腿、大腿周径差较术前明显减小($P<0.05$)。见表 4。



注:A 为腘静脉入路;B 为膝下静脉入路。

图 1　不同静脉入路行介入性溶栓术 X 线片

Fig. 1　X-ray imaging of interventional thrombolysis through different venous approaches

表 2　两组患者围手术期指标比较　($n=39$, $\bar{x}\pm s$)

Tab. 2　Comparison of perioperative indicators between two groups　($n=39$, $\bar{x}\pm s$)

组别	手术时间(min)	X 线曝光时间(min)	尿激酶(万单位)	造影剂剂量(mL)	溶栓时间(d)	术后住院时间(d)
观察组	55.39±15.83	15.61±4.72	300.59±75.48	50.98±12.39	6.95±1.86	9.32±1.35
对照组	62.28±11.47	20.39±8.43	318.43±77.63	72.76±15.77	7.08±1.93	9.08±1.28
t 值	2.201	3.090	1.029	6.782	0.303	0.806
P 值	0.031	0.003	0.307	<0.001	0.763	0.423

表 3　两组患者血栓清除效果比较　(例)

Tab. 3　Comparison of thrombus clearance effects between two groups　(case)

组别	例数	1 级	2 级	3 级
观察组	39	4	4	31
对照组	39	3	6	30
Z 值			0.187	
P 值			0.951	

2.4　两组 TEG 参数、凝血指标比较　术前、术后 1 周两组 R 值、K 值、Fib、D-D 值及差值比较,差异无统计学意义($P>0.05$);术后 1 周两组 R 值、K 值较术前明显升高,Fib、D-D 较术前明显降低($P<0.05$)。见表 5、表 6。

2.5　两组细胞黏附因子比较　术前、术后 1 周两组黏附因子水平及差值比较差异无统计学意义($P>$

0.05)；术后 1 周两组 VCAM-1、PECAM-1、P-选择素水平较术前均明显降低($P<0.05$)。见表 7。

2.6　两组住院期间并发症发生率比较　住院期间，观察组发生穿刺点渗血 1 例；对照组发生切口感染 3 例，穿刺点渗血、皮肤瘀斑和便血各 1 例。住院期间观察组和对照组并发症发生率比较差异无统计学意义[2.56%(1/39) *vs* 15.38%(6/39)，$\chi^2=2.511$，$P=0.113$]。

2.7　两组预后比较　随访 1 年，观察组失访 4 例，对照组失访 3 例。两组 Villalta 评分分布比较，差异无统计学意义($P>0.05$)。见表 8。

表 4　两组患者手术前后肿胀情况比较　($n=39$，$\bar{x}\pm s$)

Tab. 4　Comparison of swelling before and after surgery between two groups　($n=39$，$\bar{x}\pm s$)

组别	患肢小腿			患肢大腿		
	术前小腿周径差(cm)	术后 1 周小腿周径差(cm)	肿胀改善率(%)	术前大腿周径差(cm)	术后 1 周大腿周径差(cm)	肿胀改善率(%)
观察组	4.87±1.02	1.31±0.31[a]	73.10±5.96	6.99±1.35	1.41±0.58[a]	79.83±6.84
对照组	4.95±1.03	1.29±0.29[a]	73.93±6.48	7.14±1.48	1.43±0.62[a]	79.97±6.65
t 值	0.345	0.294	0.589	0.468	0.147	0.092
P 值	0.731	0.769	0.578	0.641	0.883	0.927

注：与本组术前比较，[a]$P<0.05$。

表 5　两组患者手术前后 TEG 参数比较　($n=39$，$\bar{x}\pm s$)

Tab. 5　Comparison of TEG indexes before and after surgery between two groups　($n=39$，$\bar{x}\pm s$)

组别	R 值(min)			K 值(min)		
	术前	术后 1 周	差值	术前	术后 1 周	差值
观察组	2.89±0.53	5.39±1.05[a]	2.50±0.72	0.83±0.29	1.51±0.44[a]	0.68±0.31
对照组	3.08±0.47	5.41±1.12[a]	2.33±0.83	0.79±0.31	1.58±0.42[a]	0.79±0.35
t 值	1.675	0.081	0.966	0.589	0.719	1.469
P 值	0.098	0.935	0.337	0.558	0.475	0.146

注：与本组术前比较，[a]$P<0.05$。

表 6　两组患者手术前后凝血指标比较　($n=39$，$\bar{x}\pm s$)

Tab. 6　Comparison of coagulation indexes before and after surgery between two groups　($n=39$，$\bar{x}\pm s$)

组别	Fib(g/L)			D-D(mg/L)		
	术前	术后 1 周	差值	术前	术后 1 周	差值
观察组	6.85±1.22	5.42±0.69[a]	1.43±0.84	1.18±0.35	0.45±0.20[a]	0.73±0.25
对照组	7.01±1.34	5.39±0.73[a]	1.62±0.82	1.20±0.37	0.51±0.19[a]	0.69±0.27
t 值	0.551	0.187	1.011	0.245	1.358	0.679
P 值	0.583	0.853	0.315	0.807	0.178	0.499

注：与本组术前比较，[a]$P<0.05$。

表 7　两组患者细胞黏附因子比较　($n=39$，$\bar{x}\pm s$)

Tab. 7　Comparison of coagulation indexes before and after surgery between two groups　($n=39$，$\bar{x}\pm s$)

组别	VCAM-1(μg/L)			PECAM-1(μg/L)			P-选择素(ng/mL)		
	术前	术后 1 周	差值	术前	术后 1 周	差值	术前	术后 1 周	差值
观察组	139.36±11.48	83.85±8.48[a]	56.01±8.53	108.54±15.77	69.53±8.58[a]	39.01±5.76	50.84±5.81	23.48±4.98[a]	27.36±4.55
对照组	141.47±12.79	85.72±8.76[a]	55.75±8.72	111.49±16.23	70.21±8.73[a]	41.28±5.53	49.93±5.62	24.03±5.23[a]	25.90±4.91
t 值	0.767	0.958	0.133	0.814	0.347	1.775	0.703	0.476	1.362
P 值	0.446	0.341	0.895	0.418	0.730	0.080	0.484	0.636	0.177

注：与本组术前比较，[a]$P<0.05$。

表 8　两组患者随访 1 年 Villalta 评分比较　(例)

Tab. 8　Comparison of Villalta scores between two groups during 1-year follow-up　(case)

组别	例数	无	轻度	中度	重度
观察组	35	23	8	3	1
对照组	36	23	10	3	0
Z 值			0.027		
P 值			0.978		

3　讨　论

介入性溶栓术是治疗 DVT 的主要方案之一，经导管将溶栓药物直接灌注血栓部位，可加快血栓溶解、消退，促进静脉通畅，减轻静脉瓣膜功能损伤，提高 DVT 长期预后[11-12]。目前介入性溶栓术入路方式较多，包括腘静脉入路、健侧静脉入路、颈静脉入

路、膝下静脉入路等,其中腘静脉入路顺行插管,符合解剖结构,操作难度较低,但手术要求较高,术中需变换体位,术后要求制动,不利于患者配合,且血栓累及腘静脉闭塞患者穿刺失败风险较高[13]。而健侧静脉入路、颈静脉入路均为逆行入路,且距血栓位置较远,会破坏静脉瓣膜功能,且溶栓效果不佳[14-15]。膝下静脉入路多采用小隐静脉入路,位置较深,有效长度充足,有与深静脉连接的交通支,但存在解剖变异的风险[16]。本研究开展前瞻性队列分析,旨在探讨介入性溶栓术安全、可靠的入路方案,以改善患者预后。

赵得银等[9]研究显示,经腘静脉入路行置管溶栓治疗成本低于膝下静脉入路,因此,可作为 DVT 首选入路方案。而本研究中,观察组手术时间、X 线曝光时间、造影剂剂量均较对照组少,进一步证实这一结论。分析认为腘静脉位置较浅,无需分离皮肤即可进行穿刺,且直径较大,导管穿刺简单,且有较好的稳定性,活动不受限制。本研究显示,两组血栓清除效果、术后 1 周患肢小腿、患肢大腿周径差及肿胀改善率间均差异无统计学意义,提示经腘静脉入路与膝下静脉入路行介入溶栓治疗在血栓清除和下肢肿胀改善方面效果相当。这主要是腘静脉与膝下静脉穿刺进入深静脉的本质一样,尽管膝下静脉操作难度较大,但借助数字造影同样可将溶栓药物灌注血栓位置,以达到治疗效果。相关研究显示,凝血功能异常与 DVT 发生及进展密切相关。因此,检测凝血功能不仅能作为 DVT 诊断的重要依据,还能评估治疗效果[17]。TEG 是凝血状态物理及化学联合检测方法,其参数能反映凝血全功能的动态过程曲线图,可有效评估 DVT 患者初始血栓形成至溶解完整的凝血机制[18]。本研究显示,术后 1 周两组 R 值、K 值高于术前,Fib、D-D 低于术前,但组间差异无统计学意义,这主要与两种手术方案均能有效清除血栓,改善患者血液循环有关。

DVT 形成后综合征是指因下肢静脉血液回流障碍、血液逆流及静脉压升高而引起的一系列症状,发生率超过 20%,其中 5%~23%患者病情较为严重,是影响 DVT 患者预后的重要因素[19]。有研究显示,血小板黏附深静脉内壁是新血栓形成基础,细胞黏附因子可通过介导细胞与细胞间、细胞与细胞基质间信号转导促进新生血栓形成[20-21]。VCAM-1、PECAM-1 均为细胞黏附因子,前者属于免疫球蛋白家族,可参与单核细胞、巨噬细胞在血管壁的黏附作用,而后者可抑制血细胞聚集、调节白细胞迁徙、信号转导,在动静脉血栓、血管性疾病中发挥重要作用。且有文献表明,在 DVT 患者中,未开通患者血清细胞黏附因子浓度明显高于开通患者,且浓度与 DVT 形成后综合征风险呈相关性[22]。因此,降低 VCAM-1、PECAM-1 水平对防治 DVT 具有积极意义。P-选择素主要分布于血小板和内皮细胞的质膜上,可与白细胞结合参与血栓的形成[23]。本研究显示,术后 VCAM-1、PECAM-1、P-选择素水平较术前明显降低,但组间及随访 1 年 Villalta 评分分布差异无统计学意义,提示腘静脉入路与经膝下静脉行介入性溶栓术可清除血栓,改善血液循环,抑制细胞黏附因子表达,具有较好的远期疗效。手术安全性是临床关注的焦点,会影响患者预后结局。张炎锋等[24]研究显示,DVT 溶栓过程中减轻组织损伤,可有效减少并发症发生。本研究中,观察组住院期间并发症发生率少于对照组,这主要是膝下静脉位置深且较细,穿刺时需切开皮肤,在导管鞘置管过程中极易损伤静脉,甚至破裂,同时在溶栓结束后滤器经膝下静脉取出难度较大,因此,并发症风险较高。但两组间比较差异无统计学意义,可能与本研究样本量较小有关。

综上所述,在 DVT 治疗中,经腘静脉入路与膝下静脉入路行介入性溶栓术安全可靠,可抑制细胞黏附因子表达,改善凝血功能,有较好的远期疗效。但在实际应用中,两种入路方式均存在局限性,应根据患者实际情况选择入路。另外,本研究选取样本量较小,会造成研究结果出现偏倚,有待后续开展大样本进行进一步分析验证。

利益冲突　无

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