Comparison of the efficacy and safety of catheter-directed thrombolysis using different approaches in the treatment of deep venous thrombosis of the lower limbs

Yuankai Luo, MM[1,2,*], Yong Li, MD[2,3], Shaorui Zhang, BM[4], Weiguo Xu, MD[2], Jicai Ma MM[5], Qingsong Wu, MD[1,*]

[1] Hepatobiliary and Pancreatic Tumor Diagnosis and Treatment Center, Department of Hepatobiliary Surgery, Yuebei People's Hospital, Shaoguan, China

[2] Zhuhai Interventional Medical Centre, Zhuhai People's Hospital (Zhuhai Clinical Medical College of Jinan University), Zhuhai, China

[3] Zhuhai Institute of Translational Medicine, Guangdong Provincial Key Laboratory of Tumor Interventional Diagnosis and Treatment, Zhuhai People's Hospital (Zhuhai Clinical Medical College of Jinan University), Zhuhai, China

[4] Department of Ultrasound Medicine, Zhanjiang Central People's Hospital, Zhanjiang, China

[5] Department of Neurology, Yuebei People's Hospital, Shaoguan, China

[*] **Corresponding authors**:

Yuankai Luo, MM

Hepatobiliary and Pancreatic Tumor Diagnosis and Treatment Center, Department of Hepatobiliary Surgery, Yuebei People's Hospital, Shaoguan, China

Zhuhai Interventional Medical Centre, Zhuhai People's Hospital (Zhuhai Clinical Medical College of Jinan University), Zhuhai, China

Postal address: No. 133, Huimin South Road, Shaoguan 512026, China

Phone: +86-13058353630

Email: sgwylyk@163.com

Qingsong Wu, MD

Hepatobiliary and Pancreatic Tumor Diagnosis and Treatment Center, Department of Hepatobiliary Surgery, Yuebei People's Hospital, Shaoguan, China

Postal address: No. 133, Huimin South Road, Shaoguan 512026, China

Phone: +86-13826368658

Email: 13826368658@163.com

Electronic Supplementary Materials

Supplementary Methods

CDT procedures

The patients underwent procedures on an operating table with continuous electrocardiographic monitoring. Angiographic imaging via a contralateral femoral approach confirmed vena cava patency before placement of a vena cava filter to prevent thrombus migration. CDT was performed using antegrade and retrograde approaches [1].

In the antegrade approach, the catheter was placed in the direction of venous flow through the popliteal, peroneal, posterior tibial, anterior tibial, small saphenous, or great saphenous veins under ultrasound guidance. Based on thrombus involvement, the puncture point was chosen, usually in the prone position, and a 5F sheath was inserted. Segment-by-segment venography with a single-curved catheter delineated the thrombus extent, and a 30–50 cm thrombolytic catheter was positioned accordingly.

In the retrograde approach, the catheter was inserted into the vein of affected limbs with ultrasound-guided puncture of the contralateral femoral or internal jugular vein in the supine position. The subsequent steps mirrored those in the antegrade group.

Regardless of the approach, a continuous thrombolytic infusion was delivered via a micropump and an indwelling thrombolytic catheter. Balloon angioplasty or stent implantation was performed in patients with iliac vein compression.

Postoperative thrombolytic therapy involved urokinase intermittent infusion (250,000 IU every 8 h) via a micropump and an indwelling thrombolytic catheter. Anticoagulation included low-molecular-weight heparin (100 IU/kg every 12 h), with INR and fibrinogen levels monitored daily. Dosing was adjusted based on fibrinogen levels: halved if <1.5 g/L and stopped if <1.0 g/L. Low-molecular-weight heparin was discontinued when the INR was >2 [2]. Daily lower-limb venography was used to assess thrombus clearance until the end of thrombolytic therapy.

Efficacy evaluation

Multiple indicators were used to objectively compare the efficacy of different CDT approaches for lower-limb DVT. These indicators assess the impact of treatment on lower limb swelling, thrombolysis, and venous patency at the end of thrombolytic therapy, offering an in-depth understanding of treatment effectiveness.

Swelling rate of the thighs and calves

Swelling was measured by comparing the limb circumference 15 cm above and 10 cm below the mid-patella in both legs. Preoperative differences between the affected and unaffected limbs served as baseline swelling. Treatment effectiveness was assessed based on the change in circumference before and after CDT. The swelling rate (circumference reduction rate) was calculated as follows:

$$Swelling\ rate\ = \frac{(Pretreatment\ circumference\ -\ Posttreatment\ circumference)}{Pretreatment\ circumference} \times 100$$

Porter score and venous patency rate

Lower-extremity veins were categorized into seven segments: the popliteal, distal superficial femoral, proximal superficial femoral, common femoral, external iliac, common iliac, and inferior vena cava. Each segment was scored as follows: 0 for complete patency, 1 for partial patency with segmental, non-occlusive thrombus, and 2 for occlusive thrombus [3]. The total venous patency score was the sum of all segments, with pre- and post-treatment differences calculated for comparative analyses. This assessment comprehensively quantifies lower-extremity vein patency to compare CDT approaches.

The venous patency rate was calculated as follows:

$$Venous\ patency\ rate\ = \frac{Pretreatment\ venous\ patency\ score\ -\ Posttreatment\ venous\ patency\ score}{Pretreatment\ venous\ patency\ score} \times 100$$

This indicator objectively measures venous patency improvement, which is critical for evaluating CDT efficacy.

Patency grading

Different CDT approaches may affect thrombus clearance in different ways. Thrombus clearance was assessed using DSA and categorized into three grades based on contrast retention, symptom relief and signs in the affected limb, and thrombus clearance rate [4]:

Grade 3 indicated no significant contrast retention, complete symptom resolution, unblocked veins, and a clearance rate of >95%. Grade 2 was defined as minimal contrast retention, nearcomplete symptom relief, and a clearance rate of 50–95%. Grade 1 reflected significant contrast retention, minimal symptom relief, and a clearance rate of <50% or only side branch opening.

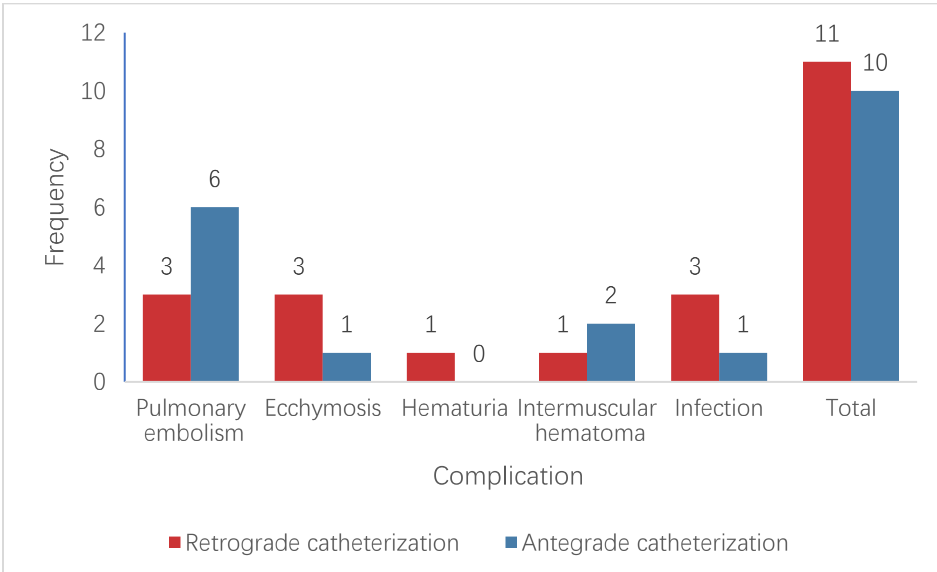
PSM

Propensity score matching (PSM) was applied to balance covariates between treatment groups, minimizing selection bias, and creating a setting similar to a randomized controlled trial (RCT). As a widely used statistical method in observational studies, PSM reduces confounding and improves treatment effect evaluation [5, 6]. The core principle is to match patients with similar baseline characteristics but different CDT approaches, thereby simulating random allocation effects.

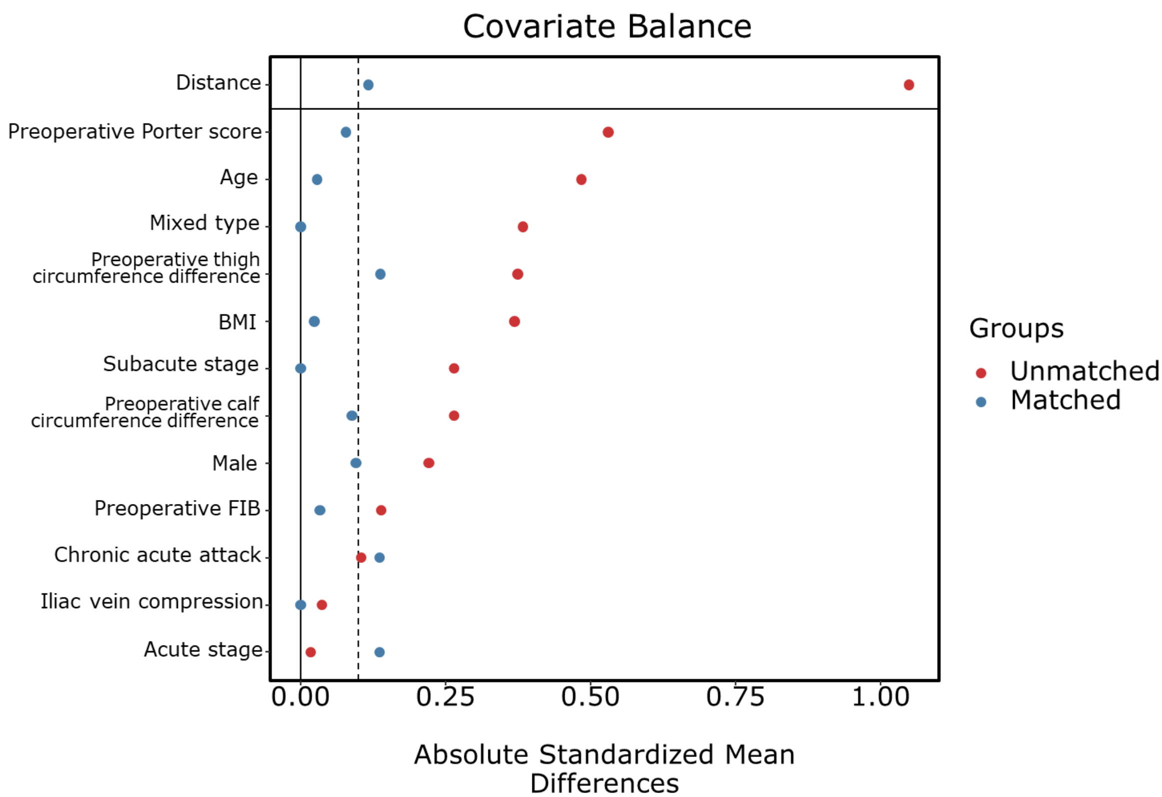
Potential confounders were chosen based on clinical relevance and PSM principles [7–9], including patient age, sex, BMI, disease stage, classification [10], affected limb (left or right), preoperative thigh and calf circumference differences, and preoperative FIB levels. Propensity scores were calculated for each patient to represent the probability of receiving a specific CDT approach.

A 1:1 matching ratio was used to pair patients with similar propensity scores from the different treatment groups, ensuring no significant baseline differences. This approach controlled for confounding variables, making comparisons between CDT approaches more reliable for evaluating efficacy and safety outcomes.

Supplementary Figures



ESM Fig. 1 Comparison of complication frequencies in patients who underwent retrograde and antegrade catheterization after PSM. Red bars represent retrograde catheterization, and blue bars represent antegrade catheterization



ESM Fig. 2 Comparison of covariate balance before and after propensity score matching in the popliteal and infrapopliteal vein approach subgroups. Absolute SMDs are presented for each covariate, with red dots representing unmatched samples and blue dots representing matched samples. The vertical dashed line serves as a reference for assessing covariate balance

ESM Table 1. Baseline covariates before and after matching in the popliteal vein and infrapopliteal vein approach subgroups

Variables		Before Matching			After Matching		
		Infrapopliteal vein approach	**Popliteal vein approach**	**SMD[a]**	**Infrapopliteal vein approach**	**Popliteal vein approach**	**SMD[a]**
n		**47**	**28**		**21**	**21**	
Age (years), Mean (SD)		56.45 (14.81)	61.29 (9.99)	0.484	60.90 (13.08)	60.62 (9.90)	-0.029
BMI (kg/m^2), Mean (SD)		24.03 (3.56)	25.48 (3.95)	0.369	25.36 (4.07)	25.27 (3.68)	-0.023
Sex (%)	Female	20 (42.6)	15 (53.6)	0.221	10 (47.6)	9 (42.9)	-0.095
	Male	27 (57.4)	13 (46.4)	-0.221	11 (52.4)	12 (57.1)	0.095
Stage (%)	Acute onset during the chronic stage	5 (10.6)	4 (14.3)	0.104	2 (9.5)	3 (14.3)	0.136
	Acute stage	40 (85.1)	24 (85.7)	0.017	19 (90.5)	18 (85.7)	-0.136
	Subacute stage	2 (4.3)	0 (0.0)	-0.266	0 (0.0)	0 (0.0)	0.000
Type (%)	Central	8 (17.0)	2 (7.1)	-0.384	2 (9.5)	2 (9.5)	0.000
	Mixed	39 (83.0)	26 (92.9)	0.384	19 (90.5)	19 (90.5)	0.000
Preoperative thigh circumference difference, Mean (SD)		3.21 (2.73)	4.11 (2.39)	0.374	3.73 (2.02)	4.06 (2.56)	0.137
Preoperative calf Circumference difference, Mean (SD)		2.67 (3.11)	3.17 (1.89)	0.264	2.75 (3.96)	2.92 (2.05)	0.088
Preoperative Porter score, Mean (SD)		6.17 (2.86)	7.79 (3.05)	0.530	6.95 (2.85)	7.19 (2.91)	0.078
Preoperative FIB, Mean (SD)		2.82 (1.05)	2.69 (0.97)	-0.139	2.78 (0.93)	2.81 (0.99)	0.033

[a]Standardized Mean Difference

FIB: Serum fibrinogen level

ESM Table 2. Comparison of post-procedure outcomes between the popliteal vein and infrapopliteal vein approaches after PSM

	Antegrade catheterization				
Characteristic	**Overall, N = 42[a]**	**Infrapopliteal vein approach, N = 21[a]**	**Popliteal vein approach, N = 21[a]**	**Statistic**	**p-value**
Hospitalization days	8.29 ± 2.63	8.57 ± 2.99	8.00 ± 2.24	0.70	0.488[b]
Thigh swelling rate, (%)	4.9 ± 3.5	4.9 ± 3.7	5.0 ± 3.5	-0.09	0.932[b]
Calf swelling rate, (%)	4.1 (2.7, 7.3)	5.8 (3.5, 7.5)	3.5 (1.3, 4.5)	308.50	0.028[c]
Postoperative Porter score	2.00 (0.25, 2.00)	1.00 (0.00, 2.00)	2.00 (1.00, 2.00)	185.00	0.360[c]
Score differences	5.45 ± 2.92	5.57 ± 3.16	5.33 ± 2.73	0.26	0.795[b]
Thrombolytic dose, kIU	205 (150, 258)	225 (180, 320)	200 (130, 240)	271.00	0.207[c]
Days of thrombolysis	3.50 (2.25, 4.00)	4.00 (2.00, 5.00)	3.00 (3.00, 4.00)	252.50	0.417[c]
Postoperative patency grading					0.037[d]
Grade 2	8 (25.00%)	1 (6.25%)	7 (43.75%)		
Grade 3	24 (75.00%)	15 (93.75%)	9 (56.25%)		
Complication					>0.999[d]
No	35 (83.33%)	18 (85.71%)	17 (80.95%)		
Yes	7 (16.67%)	3 (14.29%)	4 (19.05%)		

[a] Median (IQR); Mean ± SD; n (%)

[b] Welch Two-Sample t-test

[c] Wilcoxon rank sum test

[d] Fisher's exact test

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