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Exploring the efficacy of recombinant human pro-urokinase in catheter-directed thrombolysis for acute lower extremity deep venous thrombosis patients

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Abstract

Background Effective and innovative treatment for patients with acute lower-extremity deep venous thrombosis (DVT) is lacking. This study explored the use of recombinant human pro-urokinase (rhPro-UK) in catheter-directed thrombolysis for acute DVT patients.

Methods A retrospective analysis included 85 acute DVT patients undergoing CDT from January 2021 to December 2023. Patients were divided into an observation group ($n=43$, rhPro-UK) and a control group ($n=42$, UK). Outcomes assessed included total effective rate, venous patency score, limb circumference differences, coagulation parameters (PT, APTT, Fg), adverse events (BARC criteria), and post-thrombotic syndrome (PTS) incidence at 6 months (Villalta scale).

Results The observation group treated with rhPro-UK demonstrated superior clinical outcomes compared to the control group receiving urokinase. The total effective rate was significantly higher in the rhPro-UK group ($P=0.011$), with improved venous patency reflected by a lower post-treatment patency score ($P=0.009$) and higher patency rate (80.86% vs. 72.86%, $P=0.045$). Limb swelling reduction was more pronounced in the rhPro-UK group, evidenced by smaller thigh ($P=0.002$) and calf circumference differences ($P=0.001$). Coagulation function improved significantly, with prolonged PT ($P=0.002$) and APTT ($P=0.001$), alongside reduced fibrinogen levels ($P<0.001$). Safety outcomes favored rhPro-UK, with fewer total bleeding events (14.29% vs. 4.65%, $P=0.039$) and no major bleeding (BARC Type 3) observed. At 6-month follow-up, the rhPro-UK group exhibited a markedly lower incidence of post-thrombotic syndrome (9.3% vs. 26.2%, $P=0.034$) and sustained venous patency, confirming its long-term efficacy.

Conclusion CDT with rhPro-UK significantly improves venous patency, reduces limb swelling, optimizes coagulation function, and minimizes complications compared to UK. Its fibrin-targeted mechanism enhances clinical efficacy and safety, supporting its adoption as a superior thrombolytic for acute DVT.

Trial registration Not applicable.

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Keywords Acute lower extremity deep venous thrombosis, Catheter-directed thrombolysis, Recombinant human pro-urokinase, Venous patency of affected limb, Limb circumference difference

Introduction

Deep venous thrombosis (DVT) of the lower extremities is a common vascular and cardiovascular disease in clinical practice, often caused by factors such as trauma, surgery, tumors, or prolonged bed rest [1]. Studies have shown roughly 20–30% of calf DVTs will extent proximally to the thigh if left untreated, of which approximately 40% will result in pulmonary embolism [2]. Clinical manifestations in patients include leg pain, swelling, and leg ulcers, posing a serious threat to their life. Catheter-directed thrombolytic therapy is one of the main methods for treating these issues [3, 4] This procedure involves placing a catheter in the patient's blood vessel through intravenous manipulation, and administering medication to the thrombotic site, allowing the drug to merge with the thrombus location to achieve the thrombolysis effects [5].

Historically, urokinase (UK) has been used in the clinical treatment of thrombotic diseases, effectively aiding in thrombus dissolution in patients but leading to adverse reactions such as bleeding and allergies [6]. Liu et al. conducted a prospective study with 534 acute cerebral infarction patients [7]. According to their clinical data, the incidence of symptomatic intracranial hemorrhage was 4.1%. The occurrence of adverse reactions increases the difficulty of treatment, prolongs treatment duration, and may result in unsatisfactory therapeutic effects. Therefore, it is of great significance to select a scientifically effective treatment method that enhances the safety of clinical treatment for patients and ensures their efficacy. With further clinical research, some scholars have proposed recombinant human pro-urokinase (rhPro-UK) as a protein suitable for the treatment of thrombotic diseases in patients, representing a new generation of thrombolytic drugs [8, 9]. rhPro-UK is a specific plasminogen activator with the ability to effectively target sites of thrombosis within the body, demonstrating high local fibrinolytic specificity, a high rate of reperfusion, and minimal adverse reactions [10, 11]. Data indicates that the clinical use of rhPro-UK effectively promotes the clinical recovery of patients while minimizing the occurrence of adverse reactions, demonstrating high clinical safety and efficacy [12].

However, there is limited clinical reporting on the effect of using rhPro-UK treatment in catheter-directed thrombolysis on the venous patency of affected limbs and the limb circumference difference in patients with acute DVT. This study aims to thoroughly investigate this aspect, seeking to gain deeper insights into the advantages and limitations of using rhPro-UK treatment in catheter-directed thrombolysis for improving venous patency and limb circumference difference in patients with acute DVT. The objective is to provide clinicians with more comprehensive and accurate information, enabling improved treatment planning and decision-making in order to advance further research in the medical field regarding the treatment of patients with acute DVT.

Materials and methods

General information

This was a retrospective, non-randomized study. Patients were allocated to the observation or control group based on the thrombolytic agent used during their treatment period. The choice of rhPro-UK or UK was determined by institutional protocol shifts over time, with rhPro-UK introduced as a newer agent in 2021. Group assignment was not influenced by patient characteristics. A total of 85 acute DVT patients who underwent catheter-directed thrombolysis from January 2021 to December 2023 were selected. The patients were divided into the observation group ($n = 43$, treated with rhPro-UK) and the control group ($n = 42$, treated with urokinase (UK) thrombolysis).

Inclusion criteria were as follows: (1) Patients with acute proximal lower extremity DVT (involving femoral, common femoral, or iliac veins) confirmed by venography and color Doppler ultrasound, deemed appropriate for catheter-directed thrombolysis (CDT) based on the following: symptom duration ≤ 14 days, thrombus burden requiring localized thrombolysis, and absence of irreversible limb ischemia. Preference for CDT was determined by multidisciplinary consensus involving vascular surgeons and interventional radiologists; (2) Diagnosed with DVT by lower limb venography and color Doppler ultrasound examination (including proximal deep-vein thrombosis involving the femoral, common femoral, or iliac vein); (3) First-time treatment; (4) No contraindications for thrombolysis; (5) Complete clinical data; (6) Informed consent signed by the patients and their family members.

Exclusion criteria were as follows: (1) Absolute contraindications to thrombolysis: active bleeding, recent major surgery (< 10 days), intracranial hemorrhage history, or coagulopathy (INR > 1.5, platelets < 100×10^9/L); relative contraindications included uncontrolled hypertension (systolic > 180 mmHg), recent minor surgery (< 3 days), or pregnancy; (2) Severe liver (Child-Pugh C) or kidney disease (eGFR < 30 mL/min/1.73 m^2), or end-stage organ failure; (3) Neurological disorders: stroke with residual disability (modified Rankin Scale ≥ 3), dementia

(Mini-Mental State Examination < 20); (4) Cardiovascular diseases: unstable angina, myocardial infarction within 3 months, NYHA Class III/IV heart failure, or severe arrhythmias requiring intervention; (5) Pulmonary diseases: severe COPD (FEV1 < 50% predicted), pulmonary hypertension (mean PAP ≥ 25 mmHg), or active tuberculosis; (6) Immune system disorders requiring immunosuppressive therapy (e.g., systemic lupus erythematosus, rheumatoid arthritis); (7) Contrast allergy refractory to premedication (e.g., corticosteroids, antihistamines).

This study was approved by the Ethics Committee of Hospital. Informed consent was waived for this retrospective study due to the exclusive use of de-identified patient data, which posed no potential harm or impact on patient care. This study did not use artificial intelligence (AI)– assisted technologies (such as Large Language Models [LLMs], chatbots, or image creators) in the production of submitted work.

Operation methods

Low-molecular-weight heparin, 200 IU/kg of dalteparin (Pfizer, New York, NY, USA), or 1.0 mg/kg of enoxaparin (Sanofi, Paris, France) was administered to all patients on the day of diagnosis.

Initially, all patients underwent venography to determine the range of the blood clot, lower limb venous reflux status, and collateral circulation compensation. A temporary inferior vena cava filter (Manufacturer: Bard Peripheral Vascular, Germany; Model: DL950F) was placed via the healthy femoral vein. The procedures included: (1) Balloon predilation: A venous needle was placed in the dorsal foot vein of the affected limb, and if the iliac vein was obstructed and the deep vein could not reflux, a balloon (8–10 mm) was used for predilation under real-time fluoroscopy and guidance. Subsequently, a thrombolytic catheter (Manufacturer: Shandong Dongchen Medical Equipment Co., Ltd., Dezhou; Model: FIS4-135-20SQ) was inserted after intracavitary manipulation; (2) Anticoagulant therapy: Both groups received standard anticoagulant therapy with subcutaneous injection of low molecular weight heparin sodium at a dose of 100 U/kg every 12 h; (3) Thrombolytic therapy: The control group received UK (Manufacturer: Guangdong Timpson Biopharmaceutical Co., Ltd.; Specification: 50,000 units, Batch number: National Drug Approval Number H44024033) added to 500 mL of saline, administered continuously at a rate of 25 mL/h using an infusion pump. The observation group received rhPro-UK (Manufacturer: Shenzhen Techpool Bio-Pharma Co., Ltd.; Specification: 5 mg (500,000 IU)/vial, Batch number: National Drug Approval Number S20110003) added to 100 mL of saline, infused at a rate of 50 mL/h using a microinfusion pump. Both groups received continuous infusion of heparin sodium injection through the sheath to prevent thrombosis [Manufacturer: Changzhou Qianhong Biochemical Pharmaceutical Co., Ltd.; Specification: 2 mL: 12,500 units, Batch number: National Drug Approval Number H32022088] at a dose of 3000–5000 U; (4) Monitoring indicators: APTT was rechecked every 6 h during thrombolysis, and coagulation function indicators were assessed daily. By adjusting the dose of heparin, the activated partial thromboplastin time (APTT) was maintained at 60–80 s. Venography was performed on the third day of thrombolysis, and if the thrombus was completely dissolved, the catheter was removed. For the remaining patients, venography was repeated on the fifth day of thrombolysis, the catheter was removed, and lower limb pressure therapy and ankle pump exercises were continued to promote venous return.

In cases of iliac vein obstruction or impaired deep venous reflux, balloon predilation was performed under fluoroscopic guidance. The balloon diameter was selected based on the target venous segment: Iliac vein: 10–12 mm diameter balloons (Boston Scientific, Marlborough, MA, USA; Model: Mustang™); Common femoral vein: 8–10 mm diameter balloons (Medtronic, Dublin, Ireland; Model: Admiral™ Xtreme); Superficial femoral vein: 6–8 mm diameter balloons (Bard Peripheral Vascular, Tempe, AZ, USA; Model: Armada™ 35); Predilation was performed using a stepwise inflation protocol: initial inflation at 8 atm for 30 s, followed by incremental increases to 12 atm for 60 s if resistance was encountered. Post-dilation venography confirmed luminal patency before thrombolytic catheter placement. Stents (Venovo™, Bard Peripheral Vascular) were deployed only in cases of residual stenosis > 50% after predilation or elastic recoil. Stent diameters matched the predilation balloon size (e.g., 10 mm stent for a 10 mm balloon).

Observation indicators

Patient demographic and clinical data, including age, gender, body mass index, symptom onset time, and affected limb location (left/right), were retrospectively collected from electronic medical records. Postoperative anticoagulation duration (days) was calculated from the date of thrombolysis completion to discontinuation of anticoagulants. IVC filter removal time (days) was recorded as the interval between thrombolysis initiation and filter retrieval. Complete documentation of baseline variables and follow-up assessments was required for inclusion. Treatment efficacy was evaluated at 1 week post-intervention according to the European Society for Vascular Surgery (ESVS) 2021 Clinical Practice Guidelines on the Management of Venous Thrombosis [13]. Patients were classified as having a significant effect if the affected limb exhibited ≤ 10% residual swelling, mild pain (Visual Analog Scale [VAS] ≤ 3) during prolonged activity, and imaging-confirmed smooth venous walls, patent

valves, and ≤ 20% residual thrombus. Effective outcomes were defined as 10–30% residual swelling, moderate pain (VAS 4–6) relieved by rest, and partial recanalization (21–50% residual thrombus) on imaging. Ineffective outcomes included > 30% residual swelling, persistent pain (VAS ≥ 7), or imaging evidence of deep venous stenosis/occlusion or > 50% residual thrombus. The total effective rate was calculated as the proportion of patients classified as having significant or effective outcomes.

Venous patency was assessed by two blinded vascular radiologists using pre- and post-treatment imaging, with inter-rater reliability confirmed (κ = 0.85). A venous patency score (0–10) was assigned, where higher scores indicated poorer patency. One point was deducted for each venous segment (postcava, common femoral vein, proximal superficial femoral vein, distal superficial femoral vein, common iliac vein, external iliac vein, and popliteal vein) demonstrating ≥ 50% stenosis. The venous patency rate was calculated as the percentage reduction in patency score post-treatment relative to baseline. Limb circumference differences were measured 15 cm above and 10 cm below the patella using a standardized tape measure by trained nurses at baseline and 1 week post-treatment.

Coagulation function indicators—prothrombin time (PT), activated partial thromboplastin time (APTT), and fibrinogen (Fg)—were analyzed in blood samples collected in 3.2% sodium citrate anticoagulant tubes (9:1 blood-to-anticoagulant ratio) after withholding low molecular weight heparin (LMWH) for 12 h. Plasma was separated by centrifugation (3,000 rpm, 15 min) and analyzed using optical coagulation methods (PT/APTT) and immunoturbidimetry (Fg).

Bleeding events were categorized per the Bleeding Academic Research Consortium (BARC) criteria [14]: Type 3 (major) included clinically overt bleeding with hemoglobin drop ≥ 3 g/dL, transfusion requirement, or hemodynamic compromise; Type 2 (minor) involved non-major clinically overt bleeding (e.g., subcutaneous hematoma, puncture site oozing); Type 1 (minimal) referred to non-actionable bleeding (e.g., ecchymosis). All bleeding events were recorded within 1 week post-treatment.

Post-thrombotic syndrome (PTS) was assessed at 6-month follow-up via clinic visits or telephone interviews using the Villalta scale [15], which evaluates symptoms (pain, cramps, heaviness) and signs (edema, skin induration, hyperpigmentation). A score ≥ 5 indicated PTS. Venous patency was confirmed by duplex ultrasound.

Statistical processing

SPSS 25.0 software was used for data analysis. Categorical data is presented as percentages and analyzed using the χ^2 test or Fisher's exact test as appropriate; normally distributed quantitative data is presented as mean ± standard deviation (SD) and analyzed using the t-test, while non-normally distributed data is presented medians and interquartile ranges (IQR) and compared using the Mann-Whitney U test, with $P < 0.05$ indicating statistical significance.

Results

Comparison of basic information between the two groups

Our study evaluated the efficacy of rhPro-UK in improving venous patency, coagulation function, and clinical recovery in patients with acute lower extremity DVT. Baseline characteristics, including age, gender, body mass index, onset time, and location of the affected limb, were comparable between the observation group and the control group, balloon diameters and inflation protocols were standardized across both groups. No significant differences were observed in predilation parameters between the observation and control groups (all $P > 0.05$) (Table 1).

Postoperative management and outcomes

Postoperative management protocols, including anticoagulation duration and IVC filter retrieval, were

Table 1 Comparison of basic information between the two groups

Parameter	Observation Group (*n* = 43)	Control Group (*n* = 43)	χ^2/Z/t	*P* value
Age (years)	54.74 ± 5.77	54.85 ± 5.84	0.085	0.932
Gender (male)	20 (46.51%)	22 (52.38%)	0.105	0.746
Body Mass Index (kg/m2)	22.37 ± 1.08	21.92 ± 1.03	1.966	0.053
Onset Time (days)	4.39 ± 0.66	4.53 ± 0.14	1.406	0.166
Affected Limb (left lower limb/right lower limb)	30 (69.77%) / 13 (30.23%)	28 (66.67%) / 14 (33.33%)	0.005	0.941
Balloon Diameter (mm)				
- Iliac vein	10.8 ± 1.2	10.5 ± 1.1	1.20	0.342
- Common femoral vein	8.6 ± 0.9	8.4 ± 0.8	1.08	0.415
- Superficial femoral vein	6.9 ± 0.7	7.1 ± 0.6	-1.11	0.278
Stent Placement Rate	4 (9.3%)	5 (11.9%)	0.16	0.682

Table 2 Postoperative management and IVC filter outcomes

Parameter	Observation Group (*n* = 43)	Control Group (*n* = 43)	χ^2/Z/t	*P* value
Post-op Anticoagulation (days)	90.2 ± 12.5	88.7 ± 11.3	0.63	0.532
IVC Filter Removal Time (days)	14.5 ± 3.2	15.1 ± 4.0	0.82	0.412
IVC Filter Retrieval Rate	41 (95.3%)	38 (90.5%)	0.901	0.342

Table 3 Comparison of therapy outcome between two group

Group	Observation Group (*n* = 43)	Control Group (*n* = 42)	χ^2/Z/t	*P* value
clinical effective rate				
Markedly Effective	28(65.12%)	20(47.62%)		
Effective	13(30.23%)	12(28.57%)		
Ineffective	2(4.65%)	10(23.81%)		
Total Effective Rate	41(95.35%)	32(76.19%)	6.432	0.011
Treatment time (minute)	70.65 ± 15.44	82.67 ± 18.45	3.255	0.002
Hospitalization time(day)	8.99 ± 1.85	10.66 ± 2.57	3.437	0.001
Number of residual stenosis lesions	5.53 ± 2.77	7.56 ± 3.06	3.212	0.002
Venous Patency Rate (%)	80.86 ± 7.92	72.86 ± 11.87	3.648	<0.001

Table 4 Bleeding events classified by BARC criteria

BARC Type	Observation Group (*n* = 43)	Control Group (*n* = 42)	χ^2	*P*-value
Type 3	0	2 (4.76%)	Fisher's exact	0.121
Type 2	1 (2.33%)	4 (9.52%)	1.872	0.154
Type 1	1 (2.33%)	2 (4.76%)	Fisher's exact	0.498
Total	2 (4.65%)	6 (14.29%)	4.242	0.039

consistent between groups. No significant differences were observed in anticoagulation duration ($P = 0.532$), IVC filter removal timing ($P = 0.412$), or retrieval rates ($P = 0.342$) (Table 2). This uniformity ensured that outcome differences could be attributed to the thrombolytic agents rather than postoperative care variability.

Comparison of therapy outcome between two group

The total effective rate, treatment time, hospitalization time, number of residual stenosis lesions, and incidence of adverse reactions were used to evaluate the efficacy, recovery, and safety of rhPro-UK treatment in patients, as showed in Table 3. The observation group showed a higher clinical overall effective rate (95.35% vs. 76.19%, x^2=6.432, $P = 0.011$), shorter treatment time and hospitalization time (70.65 ± 15.44 vs. 82.67 ± 18.45, 8.99 ± 1.85 vs. 10.66 ± 2.57, t = 3.255, 3.437, $P = 0.002$, 0.001), lower number of residual stenosis lesions (5.53 ± 2.77 vs. 7.56 ± 3.06, t = 3.212, $P = 0.002$), a higher venous patency rate than the control group (80.86 ± 7.92 vs. 72.86 ± 11.87, t = 3.648, $P<0.001$) compared to the control group. The total incidence of bleeding complications was significantly lower in the observation group (rhPro-UK) compared to the control group (UK). Using BARC criteria: Major bleeding (BARC Type 3): 0 cases (0%) in the observation group vs. 2 cases (4.76%) in the control group ($P = 0.121$). Minor/minimal bleeding (BARC Type 1–2): 2 cases (4.65%) in the observation group vs. 6 cases (14.29%) in the control group ($P = 0.039$). No intracranial hemorrhages occurred. Puncture site bleeding (BARC Type 2) was the most common minor event (Table 4). These results indicate that rhPro-UK treatment in the observation group exhibited superior efficacy, recovery effect, and safety profile.

Comparison of coagulation function between two group before and after treatment

There are significant differences in venous patency, blood flow obstruction, and coagulation function between the observation and control groups following treatment, as showed in Fig. 1. Initially, the venous patency scores, circumference differences between affected and healthy limbs, and coagulation function indicators (PT, APTT, and Fg) were comparable between the two groups. However, after treatment, the observation group exhibited lower venous patency scores (1.69 ± 0.85 vs. 2.33 ± 1.28, t = 2.685, $P = 0.009$), a significantly smaller difference in circumference between the affected and healthy limbs in both the thigh (0.64 ± 0.21 vs. 0.86 ± 0.38, t = 3.233, $P = 0.002$) and calf (0.71 ± 0.25 vs. 0.95 ± 0.41, t = 3.346, $P = 0.001$), higher PT and APTT indicators (14.25 ± 2.28 vs. 12.63 ± 2.45, 43.27 ± 4.54 vs. 40.12 ± 4.11, t = 3.164, 3.349, $P = 0.002$, 0.001), and a lower Fg indicator (2.11 ± 0.81 vs. 2.81 ± 0.79, t = 4.045, $P<0.001$) compared to the control group.

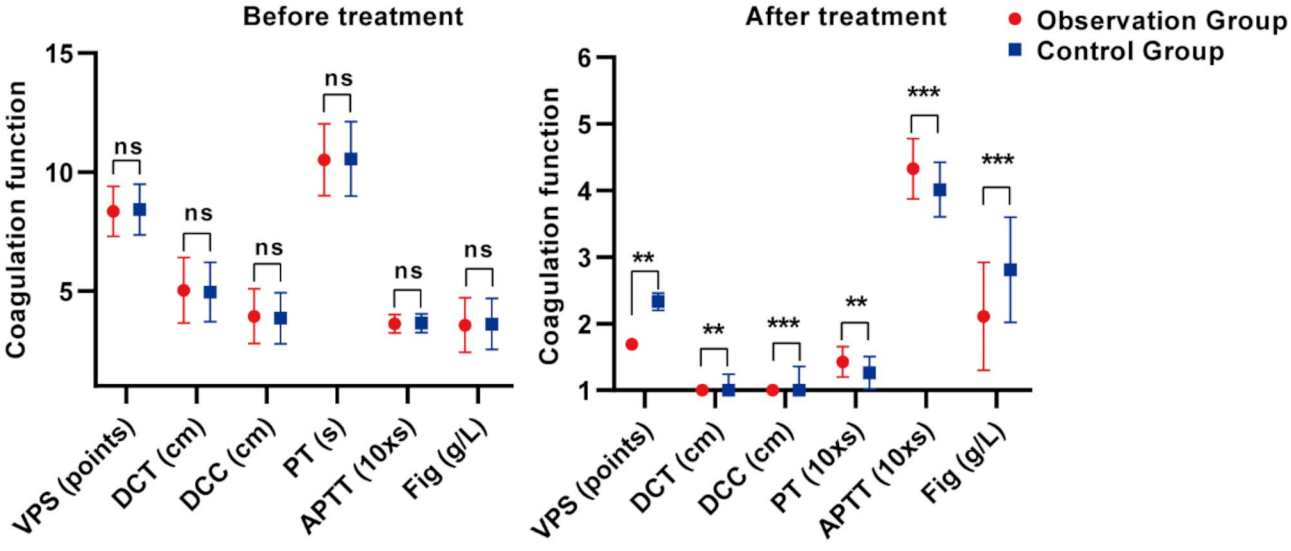

Fig. 1 Comparison of Coagulation Function between two group before and after treatment

Table 5 Coagulation function and anticoagulant use

Parameter	Observation Group ($n=43$)	Control Group ($n=42$)	χ^2/Z	*P*-value
PT (s)	14.25 ± 2.28	12.63 ± 2.45	3.164	0.002
APTT (s)	43.27 ± 4.54	40.12 ± 4.11	3.349	0.001
Fg (g/L)	2.11 ± 0.81	2.81 ± 0.79	4.045	< 0.001
LMWH Duration (days)	7.2 ± 1.5	8.1 ± 1.8	-2.271	0.023

Table 6 PTS incidence and venous patency at 6-Month Follow-Up

Outcome	Observation Group ($n=43$)	Control Group ($n=42$)	χ^2	*P*-value
PTS Incidence	4 (9.3%)	11 (26.2%)	$\chi^2 = 4.512$	0.034
Severe PTS	0 (0%)	3 (7.1%)	Fisher's exact	0.048
Venous Patency	38 (88.4%)	30 (71.4%)	$\chi^2 = 4.021$	0.045

Both groups received LMWH (100 U/kg every 12 h) during thrombolysis. Post-treatment measurements were performed 12 h after the last LMWH dose. The observation group exhibited significantly prolonged PT and APTT ($P < 0.05$), reflecting enhanced anticoagulation efficacy with rhPro-UK. Fg levels decreased more markedly in the observation group ($P < 0.001$) (Table 5).

Post-Thrombotic syndrome and Long-Term venous patency

The observation group demonstrated a significantly lower incidence of PTS compared to the control group. PTS Incidence (Villalta ≥ 5): 9.3% (4/43) in the observation group vs. 26.2% (11/42) in the control group ($\chi^2 = 4.512$, $P = 0.034$). Severe PTS (Villalta ≥ 10): 0% (0/43) vs. 7.1% (3/42) ($P = 0.048$). Duplex ultrasound confirmed sustained venous patency in 88.4% (38/43) of the observation group versus 71.4% (30/42) of the control group ($\chi^2 = 4.021$, $P = 0.045$) (Table 6).

Discussion

This study demonstrates that CDT with rhPro-UK) significantly improves clinical outcomes in patients with acute lower extremity DVT. Compared to traditional UK, rhPro-UK achieved a higher total effective rate, superior venous patency, and reduced limb circumference differences. These results align with rhPro-UK's fibrin-targeted mechanism, which minimizes systemic fibrinolytic activation while maximizing clot dissolution [16, 17, 18]. The lower incidence of PTS in the rhPro-UK group further underscores its potential to mitigate long-term complications.

The 9.3% PTS incidence in the rhPro-UK group is notably lower than the 26.2% in the UK group, reinforcing the long-term benefits of targeted thrombolysis. This is consistent with the CAVENT trial [19], which reported a 28% relative risk reduction in PTS with CDT versus anticoagulation alone. The higher sustained venous patency rate in the rhPro-UK group correlates with reduced residual thrombus burden, a known predictor of PTS [20]. By minimizing endothelial damage and inflammation

through localized fibrinolysis, rhPro-UK may mitigate the pathological remodeling underlying PTS.

Wang et al. [21] conducted a clinical study using rhPro-UK for the clinical treatment of patients and found that it effectively dissolved selective clots in patients. In this study, rhPro-UK was used in the clinical treatment of the observational group, and the results showed that the venous patency scores were lower but the venous patency rates were higher after treatment in the observation group compared to the control group. Furthermore, the circumference difference between the affected and healthy limbs in the observational group was lower after treatment. Venous patency scores, patency rates, and the circumference difference between the affected and healthy limbs are all important indicators for evaluating the function of the affected limbs in patients. Previous studies have found that DVT can lead to blockage in the body's blood flow to the heart, resulting in hindrance to the patient's blood circulation, causing inflammation in the surrounding tissues, leading to limb swelling and pain, and obstructing venous return, resulting in impaired limb function, swelling, and pain [22, 23]. On the other hand, the amino acid sequence of rhPro-UK is the same as that of natural urokinase. It is not active upon entering the bloodstream but can be adsorbed on the surface of the thrombus. After being activated by plasminogen, it can be converted into urokinase, thereby exerting its thrombolytic effect and improving limb patency in patients [24, 25]. In comparison, while UK can dissolve blood clots in patients, the injection of rhPro-UK significantly increases the concentration of thrombolytic drugs around the clot, significantly increases the contact area between the thrombolytic drug and the clot compared to peripheral venous thrombolysis, promotes the drug's effects, and leads to a higher improvement in limb function for patients.

The data from this study indicate that the observation group exhibited lower treatment time, hospitalization time, and the number of residual stenosis lesions; After treatment, the observation group showed higher PT and APTT indicators but lower Fg indicator, indicating that rhPro-UK can to some extent improve coagulation function and promote patient recovery. Mechanistically, rhPro-UK acts in balance with tissue plasminogen activator, thrombin, and coagulation factors to regulate coagulation and bleeding in the body. It exerts a selective thrombolytic effect, mainly due to its ability to activate partial plasminogen, which dissolves partial blood clots bonded to the Y/E fragment of blood fibrin. As a result, the levels of this Y/E fragment in the blood clot significantly increase. Induced by this, rhPro-UK dissolves the clot more effectively, ultimately improving coagulation function in patients and promoting their recovery [26]. By effectively improving the patient's coagulation function and limb condition, it promotes blood circulation, ultimately leading to the improvement of symptoms such as limb pain, swelling, and shortened treatment and hospitalization time, effective dissolution of blood clots, and reduction of residual stenosis lesions in patients.

Previous studies have shown that rhPro-UK thrombolytic treatment exhibits high reperfusion rates and fewer adverse bleeding reactions, emphasizing its advantages in selective fibrinolysis, earning it the title of a second-generation plasminogen activator [27]. In this study, the clinical total effective rate of patients in the observation group was higher compared to the control group; the observation group also had a lower total rate of adverse reactions, and efficacy minimizes bleeding risks, with major bleeding (BARC Type 3) absent in the rhPro-UK group versus 4.76% in controls, indicating that rhPro-UK treatment is associated with high safety and effectiveness. It is worth noting that UK is a first-generation thrombolytic drug that catalyzes the dissolution of endogenous fibrinolytic systems to achieve thrombolysis. Although it remains one of the main thrombolytic drugs in clinical practice due to its low cost and convenience in quickly dissolving fresh blood clots, it has several drawbacks, including lack of targeting, poor selectivity, and multiple adverse reactions. On the other hand, rhPro-UK, as a urokinase precursor and a second-generation thrombolytic drug, exhibits high selectivity in promoting the dissolution of thrombus fibrin due to its ability to preferentially activate external fibrinogen plasminogen, thereby showing a stronger safety profile compared to UK [28].

Compared to UK, tissue plasminogen activator (tPA) is the predominant thrombolytic agent in the United States, while UK remains widely used in China and parts of Europe due to cost-effectiveness and historical clinical familiarity [29]. A 2021 nationwide prospective Chinese registry study comparing UK and tPA for acute ischemic stroke (AIS) found that UK may be as effective and carry a similar safety profile as recombinant tPA (rt-PA) in treating mild to moderate AIS within Chinese guidelines [30]. However, further validation is needed for acute lower extremity DVT. Regional preferences reflect variations in drug availability and guideline recommendations; for instance, the European Society for Vascular Surgery (ESVS) 2023 guidelines endorse tPA as first-line therapy but acknowledge UK as an alternative in resource-limited settings [13]. Additional head-to-head trials are warranted to optimize thrombolytic agent selection.

In addition, mechanical thrombectomy (MT) has emerged as a complementary strategy to pharmacologic thrombolysis, particularly for large thrombus burdens. Studies demonstrate that MT showed good results in reducing the risk of PTS [31]. At the same time, it can significantly shorten the thrombolysis time [32]. However, MT requires specialized devices (e.g., AngioJet,

Penumbra) and operator expertise, which may limit its adoption in resource-constrained centers [33]. Future investigations could explore hybrid approaches combining rhPro-UK with MT to optimize efficiency.

It is important to acknowledge the limitations of this study. The research selected acute DVT patients who underwent endovascular catheter-directed thrombus suction reduction and catheter-directed thrombolysis within a specific time frame in our hospital, which may not fully exclude potential confounding factors and information bias. Additionally, this study was based on a small sample size and conducted in a single center, which may limit the generalizability of the findings to other medical institutions with different backgrounds. Future research can address these limitations through a more refined and comprehensive design, such as a large-sample, multi-center study. Despite these limitations, this study provides substantial support for patients undergoing rhPro-UK treatment and offers theoretical support for clinical practice.

Conclusion

In summary, for acute DVT patients undergoing endovascular catheter-directed thrombus suction reduction and catheter-directed thrombolysis, the use of rhPro-UK significantly improves venous patency, coagulation function, and reduces the circumference difference between healthy and affected limbs, promoting clinical recovery with fewer adverse reactions and a higher overall effectiveness.

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Author contributions
Tao Ma: study design, data analysis, drafting and revision of the manuscript. Cangtuo Li, Guang Song, Shaoxin Yao: data collection and analysis, drafting the manuscript, investigation. All authors read and approved the final version of the manuscript.

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Data availability
All data generated or analyzed in this study are included in the present manuscript.

Declarations

Ethics approval and consent to participate
This study was approved by the Ethics Committee of Tangshan Gongren Hospital on 4th May, 2024 ([2024] No. (069)) and conducted in compliance with the Helsinki Declaration. Informed consent was waived for this retrospective study due to the exclusive use of de-identified patient data, which posed no potential harm or impact on patient care.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Clinical trial number
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