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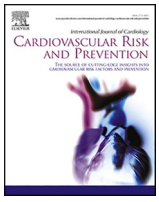

Analysis of risk factors for post-thrombotic syndrome after thrombolysis therapy for acute deep venous thrombosis of lower extremities

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ABSTRACT

Objective: The purpose of the research is to explore post-thrombotic syndrome (PTS) after catheter-directed thrombolysis (CDT) treatment for acute lower extremity deep vein thrombosis (DVT) risk factors.
Methods: We retrospectively selected 171 patients with acute lower extremity DVT undergoing CDT treatment, collected clinical data of the patients, grouped them according to the follow-up results of 1 year after treatment, and included patients with PTS into the concurrent group and patients who did not develop PTS assigned to the unconcurrent group. Univariate analysis and Logistic regression were applied to analyze the risk factors of PTS after catheterization and thrombolytic therapy for acute lower extremity DVT. We applied R4.2.3 software to build three hybrid machine-learning models, including a nomogram, decision tree, and random forest with independent influencing factors as predictive variables.
Results: The incidence of PTS after CDT in acute lower extremity DVT was 36.84 %. BMI >24.33 kg/m^2, disease time >7 d, mixed DVT, varicose vein history, stress treatment time>6.5 months, and filter category were independent risk factors for PTS after CDT treatment for acute lower extremity DVT. The AUC value predicted by the random forest model was higher than that of the nomogram model (Z = -2.337, P = 0.019) and the decision tree model (Z = -2.995, P = 0.003).
Conclusion: The occurrence of PTS after CDT treatment of acute lower extremity DVT is closely related to many factors, and the established random forest model had the best effect in predicting PTS complicated with PTS.

1. Introduction

Lower extremity deep vein thrombosis (DVT) is a disease of venous return disorders [1]. If treatment is delayed or fails, the thrombus will fall off, potentially triggering a pulmonary embolism, which can be fatal [2].

Thrombolysis is effective in the acute stage of lower extremity DVT, which can clear the thrombus early, maintain valve function, and reduce the occurrence of post-thrombotic syndrome (PTS) [3]. The ninth edition of the American College of Chest Physicians (ACCP) Guidelines [4] recommends catheter-directed thrombolysis (CDT) as the preferred option for acute central or mixed deep vein thrombosis. CDT has the advantage of complete thrombus removal. However, clinical practice has found that PTS still occurs in some patients with acute lower extremity DVT despite thrombolysis and anticoagulation therapy [5]. The main clinical manifestations of PTS are varicose veins, oedema, and sebum sclerosis of the lower extremities, which can form ulcers in severe cases, seriously affecting patients' quality of life and disease outcome, and cannot be ignored [6]. PTS usually has segment vascular disease, and local stenosis and occlusion are very serious. Studies have pointed out that several surgical treatment results are good, but there are problems with high long-term blockage rates and poor long-term treatment effects. Once DVT develops into PTS, its treatment is relatively limited. Therefore, the most effective response is to reduce the incidence of PTS at the root [7]. At present, the mechanism of occurrence of PTS is unknown. Identifying the risk factors of this complication and high-risk groups accordingly and implementing intervention are the keys to reducing the occurrence of PTS.

The factors influencing the occurrence and development of PTS are multi-faceted and still in the exploration stage. Previous studies have failed to determine the factors affecting acute lower extremity DVT complicated with PTS, and most of the studies focused on lower extremity DVT, ignoring the possible role of acute stage and multi-factor status of CDT treatment on the formation of PTS. Based on this, this

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study determined the risk factors of PTS through statistical analysis of the baseline data of patients with acute lower extremity DVT undergoing CDT treatment and compared the prediction efficiency of different algorithm models (nomogram model, decision tree model, and random forest model) based on the influencing factors, to provide references for reducing the incidence of PTS and promoting the prevention and management of PTS.

2. Materials and methods

2.1. Subjects

The research team adopted a retrospective analysis method to select 171 patients with acute lower extremity DVT who underwent CDT treatment in Beiliu People's Hospital and Guigang People's Hospital from January 2022 to December 2023. These patients should meet the following conditions: (1) Patients with varying degrees of pain and swelling in their lower extremities meet the diagnostic criteria for acute lower extremity DVT in the Guidelines for Diagnosis and Treatment of Deep Vein Thrombosis [8] and the diagnosis was confirmed by vascular ultrasound (96 cases) or CT examination (75 cases); (2) Duration of onset $\leq$14 days; (3) All patients had indications for thrombolytic therapy and were treated with CDT; (4) Over 18 years of age. We excluded the patients with the following conditions. (1) life expectancy <3 months or death during treatment; (2) bilateral acute lower extremity DVT; (3) The presence of blood system diseases such as iron deficiency anaemia and acute myeloid leukaemia; (4) Lack of clinical data.

2.2. Clinical data collection

Collect patient clinical data through hospital Electronic Medical Records, including (1) baseline data: Gender, age, Body Mass Index (BMI), disease time, diabetes mellitus, hypertension, malignancy, smoking history, recent surgical history, DVT history, DVT classification, affected limb, iliac vein thrombosis, calf intermuscular thrombosis, varicose vein history; (2) Blood and coagulation indexes before CDT treatment: Platelets, high-sensitivity C-reactive protein (hs-CRP), activated partial thromboplastin time (APTT), and prothrombin (PT) time), FDP (fibrinogen degradation product), plasma viscosity; (3) CDT treatment indexes: thrombolytic time, operation time, urokinase dosage, stress treatment time, anticoagulation program, catheterization approach, filter category, and thrombus clearance grade.

2.3. Definition and evaluation criteria of relevant indicators

BMI measures how fat or thin a person is and how healthy they are. Its calculation formula is BMI=Weight (kg) ÷ Height^2 (m^2) [9]. Smoking history refers to whether a person has an experience or habit of smoking. The DVT classification includes mixed type and central type. Lower extremity vein color ultrasound and deep venography showed that the iliofemoral vein thrombosis was the central type, and the whole deep vein thrombosis was the mixed type.

After collecting 3 mL of fasting venous blood from the patient in the morning, the laboratory doctor took the supernatant after centrifugation. They determined the contents of APTT, PT, and FDP and platelet count by an automatic coagulation instrument (H1204, Hongen Medical Equipment Co., LTD.). They detected plasma viscosity by an automatic blood viscosity instrument.

Pressure treatment time refers to the time of pressure treatment with elastic bandages or elastic socks after CDT treatment. The doctor evaluated the thrombus clearance grade by lower limb colour Doppler ultrasound. Grade I: The patients still had symptoms, such as pain and swelling of the affected limb, and the thrombi clearance rate was less than 50 %. Grade II: The symptoms of the affected limb disappeared basically, and the thrombi clearance rate was 50%–95 %. Grade III: The symptoms of the affected limb disappeared, and the thrombus clearance rate was greater than 95 %.

2.4. CDT treatment

After completing the coagulation routine and lower extremity venous ultrasonography, the doctor gave the patient inferior vena cava filter implantation and deep venous catheterization thrombolysis under local infiltration anesthesia. (1) They guided the patient to lie supine on the operating table. After successful local anesthesia, they punctured the common femoral vein on the healthy side and inserted a guide wire and catheter. Under the guidance of digital subtraction angiography (DSA), the doctor located the lower renal vein, transported the head end of the inferior vena cava filter to the level of the lower renal vein, and released it. (2) According to the scope of lesions evaluated by preoperative colour ultrasound, they determined the path of thrombolysis. The doctor guided the patients with popliteal vein thrombosis to be in the supine position and gave them catheterizing through the common femoral channel. At the same time, those without thrombus in the popliteal vein were placed in the prone position and then catheterized through the popliteal channel. For patients with thrombus intrusion into the distal popliteal vein, the thrombolysis catheter was turned over to the opposite limb through the healthy common femoral vein to bury the head end in the thrombus. For patients whose thrombus did not invade the popliteal vein, the operative punctured the popliteal vein under the guidance of colour ultrasound in a prone position, placed the vascular sheath, and placed the thrombolysis catheter anteriorly into the deep vein of the lower limb so that they can bury the head end in the thrombus. (3) The doctor fixed the vascular sheath and thrombolysis catheter. (4) They continuously pumped urokinase through a thrombolytic catheter, and the patient was given a subcutaneous injection of low molecular weight heparin for anticoagulation. (5) They detected the coagulation index of patients during treatment and performed regular venography to determine the thrombolytic effect. When achieving the ideal condition of thrombolysis, the doctor withdrew the thrombolysis catheter and vascular sheath and applied a sterile dressing to compress and bandage the puncture site. The thrombolysis ideal condition means that venography showed that the thrombus completely dissolved without residual thrombus. (6) After discharge, patients were treated with rivaroxaban or warfarin sodium tablets for anticoagulation for at least three months and were treated with elastic bandages or elastic stockings under pressure.

2.5. PTS criteria, follow-up results, and grouping

PTS was evaluated according to the Villalta score scale [10]. A score of 0–4 was considered PTS-free, and a score of 5–33 is confirmed as PTS occurring (5–14 were mild, and 15 to 33 were severe or accompanied by ulcers). According to the results of follow-up one year after treatment, patients with PTS were included in the concurrent group and patients without PTS in the unconcurrent group.

2.6. Statistical methods

We applied SPSS 23.0 software for statistical analysis. We expressed the statistical data rate (%) by the χ^2 test and the measurement data conforming to a normal distribution by Mean and standard deviation (Mean $\pm$ SD) and performed a *t*-test. We applied multivariate Logistic regression analysis to identify the risk factors of PTS after CDT treatment for acute lower extremity DVT. We analyzed correlations by Pearson (normal data) or Spearman (non-normal or rank data) correlation. $|r| >$ 0.8 indicates high correlation among variables; $0.5 < |r| \leq 0.8$ indicates moderate correlation among variables; $0.3 < |r| \leq 0.5$ indicates low correlation among variables; $|r| \leq 0.3$ indicates no linear correlation among variables. The standard of statistical difference was $P < 0.05$.

With independent influencing factors as predictors, we use the "gbm", "randomForest", "e1071", "neural net", and "rpart" packages of R4.2.3 software and its "gbm", "randomForest", "svm", "neural net",

"rpart", and other functions to construct the nomogram, decision tree, and random forest Machine learning model. We calculated each model's accuracy, sensitivity, specificity, precision, recall rate, and F1 value of each model. The higher the value, the more accurate the model prediction was. We drew the ROC curve to analyze the predictive ability of the model for the risk of concurrent PTS in acute lower extremity DVT patients. The difference of the predicted area under the curve (AUC) values between the models was tested by Z. The significant criterion was $P < 0.05$.

3. Results

3.1. Univariate analysis of PTS after CDT treatment for acute lower extremity DVT

There were 63 patients (concurrent group) with PTS and 108 patients (non-concurrent group) with PTS after CDT treatment, and the incidence of PTS was 36.84 %. Compared with the non-concurrent group, the concurrent group had higher BMI and shorter stress treatment time. In the concurrent group, the incidence time >7 days, mixed DVT, history of varicose veins, permanent filter, and thrombus clearance grade I/II were higher ($P < 0.05$) (Table 1).

3.2. Multivariate logistic regression analysis of PTS after CDT treatment for acute lower extremity DVT

We took acute lower extremity DVT after CDT treatment complicated PTS as the dependent variable (1 = complicated, 0 = no complicated), and the index with P < 0.05 in the results in Table 1 as the independent variable. (the assignment of each index in the model as shown in Table 2), incorporated into the multivariate Logistic regression model for analysis. The results showed as follows: BMI, disease time, DVT classification, varicose vein history, stress treatment time, and filter category were independent influencing factors for PTS after CDT treatment for acute lower extremity DVT (all $P < 0.05$) (Table 3). The Nagelkerke R2 of the goodness of fit test of the model is 0.770, indicating that the model has a powerful explanatory ability for dependent variables. ROC curve analysis suggested that the above independent influencing factors had a good predictive ability for patients with PTS, and the best cutoff values for BMI and Stress treatment time were 24.33 kg/m^2 and 6.5 months, respectively (Fig. 1, Table 4).

3.3. Correlation between influencing factors and Villalta score

BMI and filter category had a low positive correlation with Villalta score (r = 0.338, 0.312, $P < 0.05$), while stress treatment time had a moderate negative correlation with Villalta score (r = −0.516, $P < 0.05$), as shown in Fig. 2.

3.4. Construction of prediction model

We used independent influence indicators (BMI, onset time, DVT classification, varicose vein history, stress treatment time, and filter type) as predictors. Then, we randomly divided the sample data into training set and validation set, with a ratio of 7:3. We applied the training set data to construct three hybrid machine learning models, namely, the nomogram (Fig. 3), decision tree (Fig. 4) and random forest (Fig. 5), and used the verification set data to test the prediction effect of the model (Fig. 6).

In the training set, the AUC value predicted by the random forest model was higher than that of the nomogram model (Z = -2.337, $P = 0.019$) and the decision tree model (Z = -2.995, $P = 0.003$), and the accuracy, sensitivity, recall rate and F1 value predicted by the random forest model were the highest (Fig. 7A). In the validation set, the random forest model predicted the highest value of AUC (0.928). It was no statistical difference compared with the nomogram model (Z = 0.190, $P =$

Table 1
Univariate analysis.

Data	Concurrent group (n = 63)	Unconcurrent group (n = 108)	χ^2/t	P
(1) Basic data				
Gender [n(%)]			0.004	0.947
male	30(47.62)	52(48.15)		
female	33(52.38)	56(51.85)		
Age (Mean ± SD, year)	59.65 ± 3.36	60.23 ± 3.12	1.140	0.256
BMI (Mean ± SD, kg/m^2)	24.35 ± 3.42	21.56 ± 3.51	5.061	<0.001
Disease time [n(%)]			14.608	<0.001
>7 d	43(68.25)	41(37.96)		
≤7 d	20(31.75)	67(62.04)		
Diabetes mellitus [n (%)]			0.019	0.889
yes	6(9.52)	11(10.19)		
no	57(90.48)	97(89.81)		
Hypertension [n(%)]			0.033	0.857
yes	19(30.16)	34(31.48)		
no	44(69.84)	74(68.52)		
Malignancy [n(%)]			0.087	0.768
yes	5(7.94)	10(9.26)		
no	58(92.06)	98(90.74)		
Smoking history [n (%)]			0.145	0.703
yes	13(20.63)	25(23.15)		
no	50(79.37)	83(76.85)		
Recent surgical history [n(%)]			0.193	0.661
yes	10(15.87)	20(18.52)		
no	53(84.13)	88(.)81.48		
DVT history [n(%)]			0.145	0.703
yes	13(20.63)	25(23.15)		
no	50(79.37)	83(76.85)		
DVT classification [n (%)]			19.950	<0.001
mixed type	49(77.78)	46(42.59)		
central type	14(22.22)	62(57.41)		
Affected limb [n(%)]			0.116	0.733
Left side	39(61.90)	64(59.26)		
Right side	24(38.10)	44(40.74)		
Iliac vein thrombosis [n(%)]			0.309	0.578
yes	51(80.95)	91(84.26)		
no	12(19.05)	17(15.74)		
Calf intermuscular thrombosis			0.508	0.476
yes	28(44.44)	42(38.89)		
no	35(55.56)	66(61.11)		
Varicose vein history [n(%)]			11.340	0.001
yes	48(76.19)	54(50.00)		
no	15(23.81)	54(50.00)		
(2) Blood and coagulation indexes before CDT treatment				
Platelets (Mean ± SD, × 10^9/L)	215.20 ± 52.16	208.65 ± 54.33	0.772	0.441
hs-CRP (Mean ± SD, mg/L)	26.57 ± 6.58	26.39 ± 6.32	0.177	0.860
APTT (Mean ± SD, s)	31.22 ± 4.86	31.06 ± 5.13	0.201	0.841
PT (Mean ± SD, s)	10.65 ± 1.34	10.24 ± 1.55	1.752	0.082
FDP (Mean ± SD, μg/mL)	15.43 ± 4.25	15.96 ± 4.08	0.807	0.421
Plasma viscosity (Mean ± SD, mPa·s)	2.28 ± 0.22	2.31 ± 0.19	0.939	0.349
(3) CDT treatment indexes				
Thrombolytic time (Mean ± SD, h)	46.28 ± 9.36	47.03 ± 9.15	0.513	0.609
Operation time (Mean ± SD, h)	3.31 ± 1.02	3.12 ± 0.96	1.220	0.224
urokinase dosage (Mean ± SD, million units)	186.53 ± 39.56	194.26 ± 35.52	1.316	0.190
Stress treatment time (Mean ± SD, month)	4.39 ± 1.16	7.08 ± 2.24	8.857	<0.001

(continued on next page)

Table 1 (*continued*)

Data	Concurrent group (n = 63)	Unconcurrent group (n = 108)	χ^2/t	*P*
Anticoagulation program [n(%)]			0.148	0.701
warfarin	29(46.03)	53(49.07)		
Rivaroxaban	34(53.97)	55(50.93)		
Catheterization approach [n(%)]			0.191	0.662
affected popliteal vein	34(53.97)	62(57.41)		
normal femoral vein	29(46.03)	46(42.59)		
Filter category [n(%)]			18.867	<0.001
permanent	42(66.67)	35(32.41)		
temporarily	21(33.33)	73(67.59)		
Thrombus clearance grade [n(%)]			24.671	<0.001
I/II	28(44.44)	12(11.11)		
III	35(55.56)	96(88.89)		

Note: DVT: deep vein thrombosis; CDT: catheter-directed thrombolysis; BMI: Body Mass Index; hs-CRP: high-sensitivity C-reactive protein; APTT: activated partial thromboplastin time; PT: prothrombin time; FDP: fibrinogen degradation product.

Table 2
Assignment.

Independent variable	Assignment
BMI	measured value
Disease time	1 = >7 d, 0 = ≤7 d
DVT classification	1 = mixed type, 0 = central type
Varicose vein history	1 = yes, 0 = no
Stress treatment time	measured value
Filter category	1 = permanent, 0 = temporarily
Thrombus clearance grade	1 = I/II, 0 = III

Note: BMI: Body Mass Index; DVT: deep vein thrombosis.

0.849) and the decision tree model (Z = -0.791, *P* = 0.429), as shown in Table 5 and Fig. 7B.

4. Discussion

According to relevant statistics, 20%–50 % of patients with proximal DVT develop PTS of different degrees, and 5%–10 % of them are accompanied by a chronic venous ulcer, which is more serious [11]. The pathogenesis of PTS is unknown, its treatment is limited, and the optimization of DVT treatment is still a problem to solve urgently. To reduce the occurrence of PTS after CDT treatment for acute lower extremity DVT, the prevention of PTS is the key. According to the statistics of this study, the incidence of PTS after CDT treatment for acute lower extremity DVT was 36.84 %, which was higher than the 16 % reported by Nakamura et al. [12], which may be related to the different periods of DVT studied, suggesting that DVT in the acute stage may lead to more PTS, but more research evidence is needed to prove it.

We explored the risk factors of PTS after CDT treatment for acute lower limb DVT from patients' three perspectives: baseline data, acute stage factors, and DVT treatment indexes. The results showed that BMI>24.33 kg/m^2, time of onset >7 days, mixed DVT, history of varicose veins, time of pressure treatment >6.5 months, and permanent filter were independent risk factors for CDT complicated with PTS in acute lower extremity DVT. Siddiqui et al. [13] showed that BMI greater than 35 kg/m2 was closely related to PTS and was a significant risk factor for PTS development in patients with primary DVT. Our statistical analysis showed that the BMI cutoff value was low (24.33 kg/m^2), suggesting that PTS may be more common in acute lower extremity DVT than in non-acute DVT when BMI is abnormal. Abdominal circumference is generally larger in obese patients, and abdominal circumference is one of the objective indicators reflecting abdominal pressure [14]. The higher the abdominal pressure, the greater the pressure on the inferior vena cava, and the easier it is to obstruct the lower limb blood return [15]. Warming et al. [16] show that high intra-abdominal pressure is closely related to non-fatal pulmonary embolism. In addition, obese patients often lack exercise, and their lower leg muscle pump function is used less frequently, increasing the chance of the formation and development of PTS. The greater the BMI value, the less smooth the lower limb blood return, and the greater the risk of PTS after surgery. Clinically, patients with high BMI should be vigilant, and weight loss intervention (such as controlling diet and strengthening exercise, etc.) should be given according to the patient's situation. Compared with the subacute stage, PTS is more likely to be complicated with DVT in the acute stage [17]. The process of thrombosis formation is dynamic and complex. The longer the course of thrombosis, the more severe thrombus mechanization. At the same time, many wall-attached thrombi combine with vascular walls, which will damage blood vessels and restrict the activities of venous valves, thus aggravating valvular insufficiency and venous vascular malformation, resulting in an increased risk of PTS [18]. In mixed DVT, the higher the position of the thrombus, the greater the obstruction to lower limb blood return. Deep vein CDT can directly

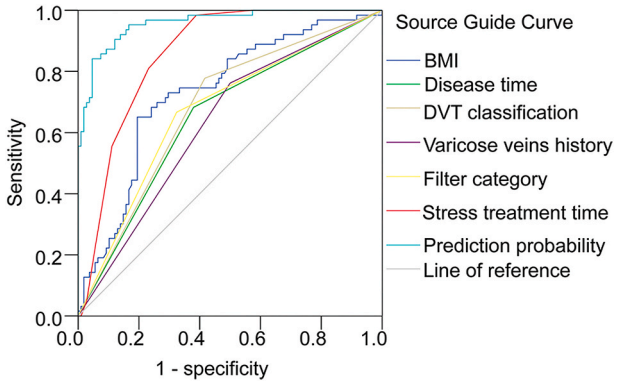

Fig. 1. The ROC curve of risk factors predicted PTS after CDT treatment for acute lower extremity DVT.
Note: BMI: Body Mass Index; DVT: deep vein thrombosis.

Table 3
Multivariate Logistic regression analysis of PTS after CDT treatment for acute lower extremity DVT.

Independent variable	B	S.E	Wals	*P*	OR	95 % CI
BMI	0.349	0.097	13.028	0.000	1.418	1.173–1.715
Disease time	1.537	0.595	6.679	0.010	4.649	1.450–14.911
DVT classification	2.373	0.645	13.515	0.000	10.730	3.028–38.021
Varicose veins history	1.614	0.626	6.645	0.010	5.022	1.472–17.132
Stress treatment time	−0.990	0.204	23.535	0.000	0.371	0.249–0.554
Filter category	1.268	0.569	4.960	0.026	3.554	1.164–10.846
Thrombus clearance grade	1.057	0.661	2.558	0.110	2.877	0.788–10.507
Constant	−7.313	2.398	9.296	0.002	0.001	–

Note: BMI: Body Mass Index; DVT: deep vein thrombosis.

Table 4
The prediction effect and AUC of risk factors of PTS after CDT treatment for acute lower extremity DVT.

Test result variable	AUC	Standard error	*P*	95 % CI	Sensitivity	Specificity	Optimum cutoff value
BMI	0.733	0.040	0.000	0.655–0.811	0.65	0.81	24.33
Disease time	0.651	0.044	0.001	0.566–0.737	0.68	0.62	–
DVT classification	0.681	0.042	0.000	0.598–0.763	0.78	0.58	–
Varicose veins history	0.631	0.043	0.004	0.546–0.716	0.76	0.50	–
Stress treatment time	0.859	0.028	0.000	0.804–0.914	0.98	0.61	6.5
Filter category	0.671	0.043	0.000	0.587–0.756	0.67	0.68	–
Prediction probability	0.959	0.014	0.000	0.931–0.987	–	–	–

Note: BMI: Body Mass Index; DVT: deep vein thrombosis.

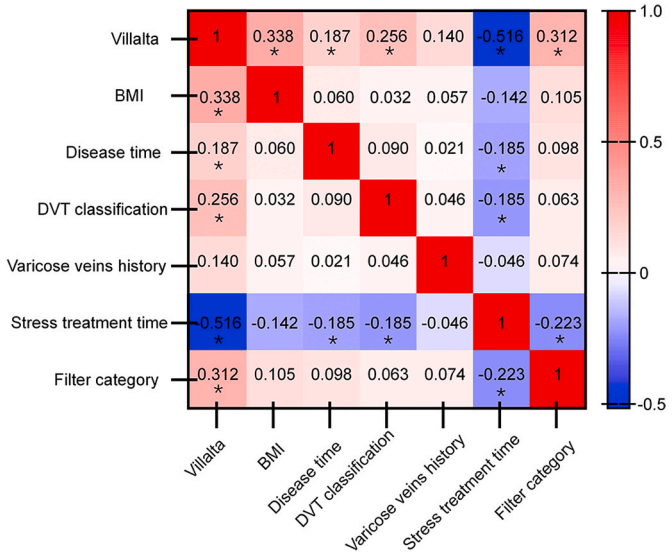

Fig. 2. Heat map of correlation between influencing factors and Villalta scores.
Note: BMI: Body Mass Index; DVT: deep vein thrombosis.

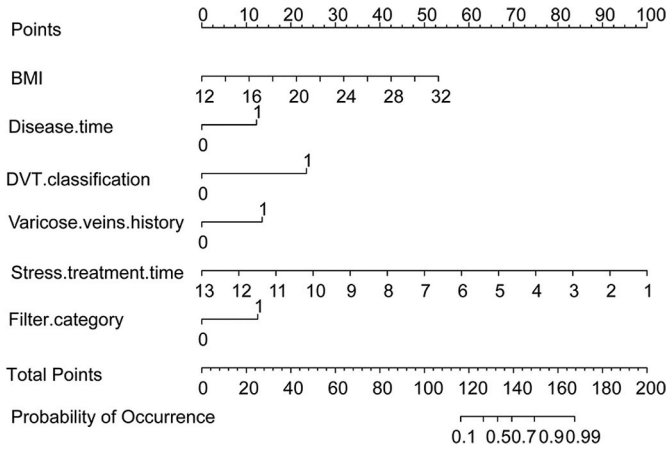

Fig. 3. Nomogram of PTS predicted by independent influencing factors.
Note: BMI: Body Mass Index; DVT: deep vein thrombosis.

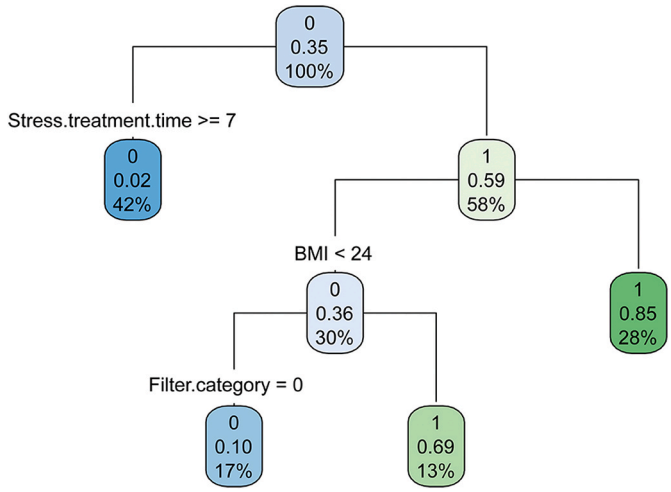

Fig. 4. Decision tree of PTS predicted by independent influencing factors.
Note: BMI: Body Mass Index.

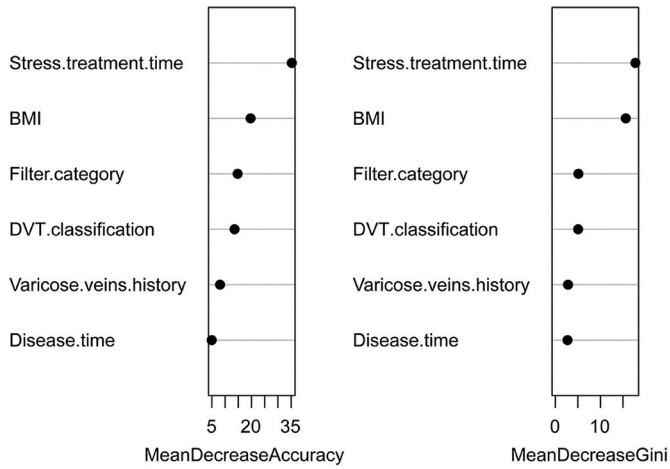

Fig. 5. Random forest plots of PTS predicted by independent influencing factors.
Note: BMI: Body Mass Index; DVT: deep vein thrombosis.

pump high-concentration thrombolytic drugs into the venous thrombus so that the thrombus can dissolve in a short time and relieve the venous lumen obstruction. The femoral vein approach on the healthy side or the popliteal vein approach on the affected side can effectively dissolve the venous thrombosis above the popliteal vein. However, the direct effect is weak for the thrombus far from the popliteal vein. The risk of PTS in mixed DVT is higher than that in central DVT, suggesting that vascular surgeons should pay attention to the treatment of thrombus far from the popliteal vein when performing CDT treatment in mixed DVT. Besides the popliteal vein approach, the tibial vein, small saphenous vein, and other routes can be considered [19]. The state of venous blood regurgitation induced by varicose veins of lower limbs may weaken the squeezing function of the muscle pump, affect the blood regurgitation of lower limbs, increase the venous pressure of limbs, aggravate the symptoms of limb oedema and skin pigmentation, and increase the risk of PTS. Mean et al. [20] found that previous varicose vein surgery was a predictor of PTS within 24 months after DVT, similar to the results of this study. Previous studies have shown that combined pressure therapy after hemolysis can promote postoperative recovery of patients and

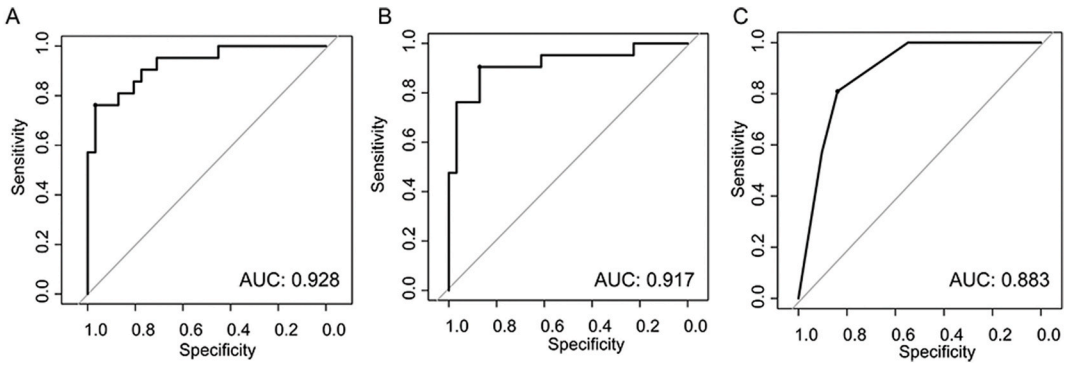

Fig. 6. ROC curve of three models predicting PTS (validation set).
Note: (A) Random forest model (AUC: 0.928); (B) Nomogram model (AUC: 0.917); (C) Decision tree model (AUC: 0.883).

Fig. 7. Comparison of three models. A:training set; B: validation set.

Table 5
Model prediction efficiency and internal validation.

Model	AUC (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	Precision (%)	Recall rate(%)	F1 score (%)
(1) Training set							
Random Forest	98.3#	93.2	93.6	90.1	92.0	94.1	93.3
Nomogram	96.8	90.8	92.2	90.5	93.4	92.2	92.8
Decision Tree	92.5	89.1	87.0	92.9	95.7	87.0	91.2
(2) Validation set							
Random Forest	92.8	86.5	93.5	76.2	93.5	85.3	89.2
Nomogram	91.7	84.2	89.6	76.2	87.1	84.4	85.7
Decision Tree	88.3	82.7	87.1	59	91.4	85	88.1

Note: # indicates that the AUC value of the model is compared with that of the nomogram model or the decision tree model, $P < 0.05$.

reduce oedema [21]. Long-term pressure treatment promotes the patient's body to drain blood veins, promote the blood circulation of the limb, and improve microcirculation. Early hemodynamic recovery helps improve prognosis [22]. Therefore, it suggested that patients should be encouraged to carry out pressure therapy after CDT treatment. Our study also confirmed that permanent filters increase the risk of PTS. The longer the placement time of the filter, the higher the probability of long-term complications such as prefilter thrombosis and inferior vena cava obstruction [23]. Chow et al. [24] showed that permanent filters led to a significant incidence of PTS, which was consistent with the results of this study. Therefore, we recommend that vascular surgeons prefer temporary retrievable filters for inferior vena cava filters placed before CDT

therapy to reduce the incidence of PTS. In this study, we analyzed the prediction efficiency of each influence index for PTS. We found that the combined prediction efficiency of each influence index for PTS (AUC: 0.962) was higher than that of a single index. These results indicate that these indexes can predict CDT complicated with PTS in acute lower extremity DVT and guide clinical intervention to a certain extent. After that, we further analyzed the correlation between influencing factors and the Villalta score. The final data showed that BMI and filter category were positively correlated with the Villalta score, while the time of stress treatment was negatively correlated with the Villalta score. From this, we know that the changes in BMI, filter type, and stress treatment time can affect the occurrence of PTS and have a linear relationship with the Villalta score. This study confirmed that CDT complicating PTS in acute lower extremity DVT is related to a variety of factors, which involve the onset time of acute lower extremity DVT and the relevant indicators of CDT treatment, which is of great significance for effectively identifying high-risk patients in early clinical stage.

Machine learning is a new program and topic in medical research in recent years. It uses computers to learn from research data and statistical information and is an important tool in data mining. Data mining technology can help clinical accurate prediction or decision and guide accurate and personalized diagnosis and treatment. We used six significance indicators as predictors to construct three hybrid machine-learning models, including the nomogram, decision tree, and random forest. It has verified that in practical application, the efficiency of the random forest model in identifying PTS occurred after CDT treatment for acute lower extremity DVT is still better than that of the nomogram and decision tree, and the prediction effect is consistent with its performance in the training set. The AUC, accuracy, sensitivity, recall rate, and F1 values of the random forest model are higher than those of the nomogram and decision tree model. The prediction efficiency of the decision tree model decreased in the verification set. It indicates that the decision tree model has an overfitting phenomenon, and the insufficient training set data may lead to the poor generalization effect of the model. However, there was no significant difference in the AUC values of the three models in the verification set, indicating that the substantial differences in predictive ability between the models were only reflected in the training set data of this study. In contrast, the predictive performance of non-significant differences may be more evident in practical applications. It suggested that clinicians can supplement the random forest, nomogram, and decision tree model according to needs in actual application.

The advantage of this study is that it retrospectively analyzed the clinical information of acute lower extremity DVT patients treated with CDT, which can utilize fewer resources in a short time, cover a wide range of cases, and provide practical clinical information. We can take the occurrence of PTS as the clinical outcome, excavate the differences in various study parameters among patients with different outcomes, and finally highlight the impact factors of PTS and establish a prediction model based on it. However, there are some limitations in this study. We only analyzed compression with elastic bandages or elastic stockings and did not subdivide the types of auxiliary stress therapy, which may ignore the influence of stress treatment methods on the risk of PTS. It is necessary to include these factors in future exploration. In addition, this study is a single-centre retrospective study with small sample size and difficulty in avoiding bias, so further verification with large sample size and prospective randomized controlled studies is needed in the future.

In summary, BMI, onset time, DVT classification, varicose vein history, pressure treatment time, and filter type are closely related to the occurrence of PTS after CDT treatment of acute lower extremity DVT. For patients with acute lower extremity DVT treated with CDT, clinicians should be alert to patients with abnormal indicators to reduce the risk of PTS and improve the prognosis of patients. The machine learning model constructed in this study has good predictive performance. The random forest, the nomogram, and the decision tree model can complement each other and have clinical reference values.

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Ethics approval

This study was approved by the Medical Ethics Committee of Beiliu People's Hospital and and Guigang People's Hospital.

CRediT authorship contribution statement

Yi Zheng: Writing – original draft, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Chunli Cao:** Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Gang Chen:** Validation, Software, Methodology, Formal analysis. **Siming Li:** Validation, Software, Methodology, Formal analysis. **Maolin Ye:** Validation, Software, Methodology, Data curation. **Liang Deng:** Software, Methodology. **Qiyi Li:** Writing – review & editing, Supervision, Resources, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare that no conflict of interest is associated with this work.

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