Development of an Integrated Nomogram for Predicting Postoperative Deep Vein Thrombosis Risk in Trauma Patients: Combining Thrombosis Risk Assessment Profile Score and Thrombosis Biomarkers

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AIM: This study aims to evaluate the effectiveness of combining the risk assessment profile for thromboembolism (RAPT) score with thrombotic biomarkers in predicting postoperative deep vein thrombosis (DVT) in patients with traumatic fractures and to create a nomogram model for risk assessment.

METHODS: This retrospective cohort study recruited 329 traumatic fracture patients from Shouxiang Community Health Service Center of Yinhu Street between September 2021 and September 2024. Patient data were randomly assigned to a training set (n = 230, 70%) and a test set (n = 99, 30%) for model development and validation. In the training set, patients were stratified based on DVT state into a DVT group (n = 110) and a non-DVT group (n = 120). The RAPT score and thrombotic biomarker levels were compared between the two groups. Multivariate logistic regression analysis was conducted to identify independent risk factors for postoperative DVT. Based on these factors, a nomogram model was developed, and its diagnostic performance was assessed through receiver operating characteristic (ROC) curve analysis, calibration curve analysis, and clinical decision curve analysis.

RESULTS: The DVT group exhibited significantly higher levels of RAPT score (7.00 [5.00, 9.00] vs. 4.00 [2.00, 7.00]), D-dimer (D-D) (874.12 ± 77.16 vs. 841.37 ± 86.94), fibrinogen (FIB; 4.00 [3.90, 4.30] vs. 4.00 [3.70, 4.20]), and thrombin-antithrombin complex (TAT; 16.60 [14.43, 18.38] vs. 15.40 [14.10, 16.90]) relative to non-DVT group ($p < 0.05$). Multivariate logistic regression analysis identified the RAPT score, D-D, FIB, and TAT as independent risk factors for postoperative DVT, with odds ratios (ORs) of 1.209, 1.006, 3.625, and 1.246, respectively ($p < 0.05$). Using these factors, a nomogram model was constructed. In both the training and test sets, the fitting degree of this nomogram model was good. ROC curve analysis revealed that the area under the curve (AUC) of 0.7714 (0.7107–0.832) and 0.7066 (0.603–0.8103) for predicting the occurrence of lower extremity DVT in the training set and the test set, respectively. The calibration curve demonstrated excellent agreement between the predicted probabilities and the observed outcomes. Decision curve analysis (DCA) demonstrated that the nomogram yielded a higher net benefit than the "treat all" or "treat none" strategies across a threshold probability range of 0.055–0.755 in the training set and 0.095–0.805 in the testing set.

CONCLUSIONS: The integration of the RAPT score with thrombotic biomarkers (D-D, FIB, and TAT) offers a feasible and effective approach for predicting postoperative DVT in patients with traumatic fractures, guiding targeted prophylactic strategies and enhancing perioperative management and patient outcomes.

Keywords: thrombosis risk assessment profile; deep vein thrombosis; nomogram model; traumatic fracture; risk prediction

Introduction

Deep vein thrombosis (DVT) refers to the formation of thrombi within deep veins, most commonly in the lower extremities [1,2]. This condition is associated with significant morbidity and mortality and may lead to severe complications, including pulmonary embolism (PE) [3,4]. Clinically, DVT typically presents with lower extremity swelling, pain, skin redness, and warmth [5]. In patients with traumatic fractures, the postoperative incidence of DVT ranges from 0.3% to 30%, influenced by factors such as prolonged bed rest (immobilization), reduced mobility, and increased blood viscosity [6–8]. If not timely diagnosed and treated, DVT can progress to chronic venous insufficiency, persistent lower extremity edema, skin hyperpigmentation, and, in severe cases, long-term functional impairment [9].

Currently, the management of postoperative DVT in patients with traumatic fractures primarily involves anticoagulation therapy, low-molecular-weight heparin (LMWH) injections, intermittent pneumatic compression, and early mobilization [6,10], all of which help reduce the incidence and progression of DVT. However, given the often insidious and atypical clinical manifestation of DVT, traditional diagnostic approaches, including clinical assessment and ultrasonography, may fail in enabling early detection.

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Therefore, developing effective strategies for the early diagnosis or accurate prediction of DVT is crucial for reducing its incidence, alleviating patient suffering, and improving overall clinical outcomes.

The risk assessment profile for thromboembolism (RAPT) is a scoring tool designed to evaluate DVT risk based on patients' clinical characteristics and predisposing risk factors [11]. This scoring system not only assists clinicians in the early identification of high-risk patients but has also demonstrated significant efficacy in predicting postoperative DVT in patients with multiple trauma by incorporating variables such as age, postoperative mobility limitations, type of surgical procedure, and medical history [12]. Furthermore, RAPT scores can guide the implementation of individualized preventive measures, including anticoagulant therapy or mechanical prophylaxis, to reduce thrombosis risk [13]. Although integrating RAPT scoring with clinical evaluation and imaging enhances the early diagnosis of DVT, the system has some limitations: it may be unable to fully capture patients' physiological changes, can lead to misclassification in asymptomatic cases, relies heavily on clinical judgment, and is subject to variability due to physician experience. Hence, integrating RAPT scoring with other complementary diagnostic approaches is essential for optimal risk stratification and management.

Additionally, D-dimer (D-D) represents an effective alternative biomarker for thrombosis [14]. Fibrinogen (FIB), a key factor involved in the blood coagulation process, plays a crucial role in thrombus formation [15]. The thrombin-antithrombin complex (TAT) has been recognized as a biomarker for early coagulation activation, reflecting thrombin generation and the transition to a prothrombotic state [16].

Therefore, in this study, we combined the RAPT score with these thrombosis-associated biomarkers (D-D, FIB, and TAT) to predict postoperative DVT in the lower extremity of patients with traumatic fracture, aiming to provide a more precise and evidence-based tool for rapid clinical risk assessment.

Materials and Methods

Study Population

This study recruited 329 patients with traumatic fractures treated at our hospital between September 2021 and September 2024. Patients were randomly divided into a training set (n = 230) and a test set (n = 99) at a 7:3 ratio.

The inclusion criteria for patient selection were as follows: (1) patients diagnosed with secondary traumatic fractures by X-ray and computed tomography (CT) imaging; (2) fractures requiring surgical intervention; (3) age >18 years; (4) those with complete clinical data available; and (5) absence of other relevant comorbidities.

Exclusion criteria included: (1) cardiac, hepatic, or renal dysfunction; (2) malignancies; (3) systemic infections or autoimmune diseases; (4) psychiatric or cognitive disorders; (5) coagulation disorders; and (6) long-term anticoagulant therapy before enrollment. The flowchart of study design and patient selection is depicted in Fig. 1.

Diagnosis of DVT

All postoperative patients underwent vascular ultrasound examinations within 3 days after surgery to assess for DVT. The diagnosis of DVT was independently confirmed by two experienced ultrasonologists, with no discrepancies found. Vascular imaging was conducted using a PHILIPS 5500 Doppler ultrasound system (model L12-5, Philips, Amsterdam, Netherlands). Doppler data were processed and displayed as color-coded overlays to visualize blood flow direction and velocity.

DVT was diagnosed based on the following ultrasonographic criteria [17]: (1) thickened venous walls with hypoechoic thrombi occupying the lumen and absence of blood flow signals, indicating acute thrombus formation; (2) elevated echogenicity of the thrombus accompanied by punctate or columnar blood flow in the occluded lumen, suggesting subacute or delayed DVT; and (3) a combination of hyperechoic and hypoechoic thrombi with intermittent blood flow signals, valvular insufficiency, substantial wall thickening, and obliteration of vein septa, indicating advanced DVT. Based on the presence of DVT, patients in the training set were assigned to the DVT group (n = 110) and the non-DVT group (n = 120), while patients in the test set were also divided into the DVT group (n = 47) and the non-DVT group (n = 52).

Observational Indicators

Baseline Characteristics

Baseline characteristics of patients with traumatic fractures were collected, including gender, age, body mass index (BMI), smoking history, time from injury to surgery, fracture site (upper limb, lower limb, or other), comorbidities (hypertension, diabetes, or other), causes of fracture (fall, traffic accident, high fall, or other), white blood cell (WBC) count, red blood cell (RBC) count, neutrophil count, and C-reactive protein (CRP) levels. Fasting peripheral venous blood samples (5 mL) were collected the day before surgery. WBC, RBC, and neutrophil counts were measured using a BC-760 CS automated cell counter (Mindray, Shenzhen, China). CRP levels were determined using enzyme-linked immunosorbent assay (ELISA, EK194, Linc-Bio, Hangzhou, China).

RAPT Scoring

The RAPT score was used to evaluate the risk of venous thromboembolism in all postoperative patients [18]. Two senior orthopedic physicians independently assessed the RAPT scores for each patient, and any discrepancies were resolved by a senior consultant to determine the final score.

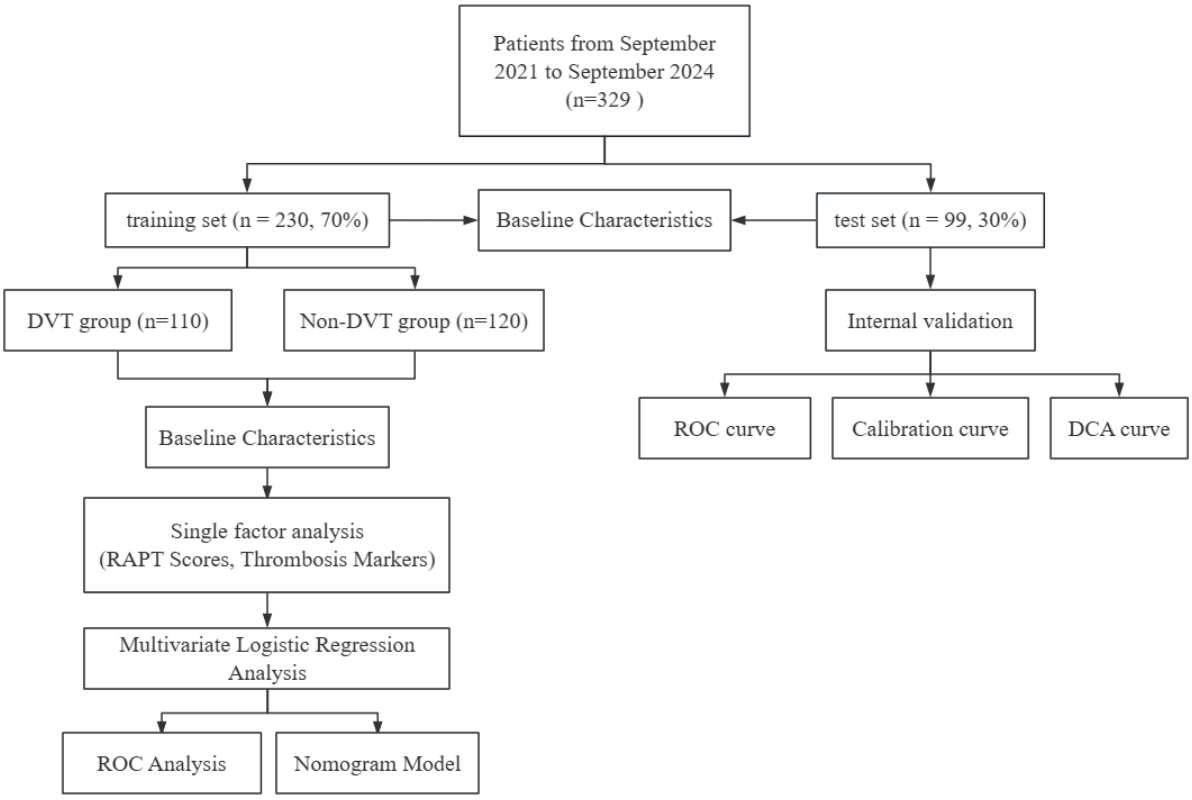

Fig. 1. A flowchart of study design and patient recruitment. DVT, deep vein thrombosis; ROC, receiver operating characteristic; RAPT, risk assessment profile for thromboembolism; DCA, decision curve analysis.

Thrombosis Biomarkers

At 48 hours after surgery, fasting peripheral venous blood samples (5 mL) were collected from all patients. Levels of FIB (D711412, Sangon Biotech, Shanghai, China), D-D (E-EL-H6145, Elabscience, Wuhan, China), TAT (D711235, Sangon Biotech, Shanghai, China), soluble thrombomodulin (sTM; ml038102, Mlbio, Shanghai, China), and tissue plasminogen activator-inhibitor complex (tPAIC; ab269559, Abcam, Cambridge, UK) were measured using ELISA kits. Prothrombin time (PT) and activated partial thromboplastin time (APTT) were evaluated with a PUN-2048 automatic coagulation analyzer (Pulang New Technology, Beijing, China).

Model Development and Validation

The cohort of 329 patients was randomly divided into a training set (DVT (n = 110); Non-DVT (n = 120)) and a test set (DVT (n = 47); Non-DVT (n = 52)) at a 7:3 ratio. A logistic regression-based risk prediction model was developed using the lrm function from the rms package in R. Independent variables included the RAPT score, D-D, FIB, and TAT, with DVT status (DVT or Non-DVT) as the dependent variable. Calibration curves were plotted using the calibrate function in the rms package (parameters: 1000 resampling iterations, sample size of 80 per iteration). In these plots, the "Ideal" line represents perfect agreement between predicted and observed outcomes, whereas the 'Apparent' and 'Bias-corrected' lines indicate internal validation outcomes. The proximity of these lines to the Ideal line suggests minimal risk of model overfitting. Decision curve analysis (DCA) was conducted using the rmda package in R to assess the clinical significance of the model.

Sample Size Calculation

The sample size for developing the multivariate predictive model was determined following the Events Per Variable (EPV) criterion. A minimum EPV of 10 is commonly recommended to ensure model stability and minimize the risk of overfitting [19]. Using DVT as the primary outcome and an initial set of approximately 5 candidate predictor variables, at least 50 DVT events were required. In this retrospective cohort of 329 patients, 157 DVT events were observed, yielding an EPV of 31.4 (157/5), thereby meeting and exceeding the methodological requirement.

Statistical Analysis

Statistical analysis was performed using SPSS 26.0 (IBM Corp., Armonk, NY, USA). Data normality was evaluated with the Kolmogorov-Smirnov test. Normally distributed continuous variables were presented as mean ± standard deviation ($\bar{x} \pm s$) and compared using independent-sample *t*-tests. However, non-normally distributed continuous

Table 1. Comparison of baseline characteristics between the two groups.

Factors	Training set (n = 230)	Test set (n = 99)	$t/Z/\chi^2$	p-value
Group [n (%)]			0.003	0.953
Non-DVT Group	120 (52.17)	52 (52.53)		
DVT Group	110 (47.83)	47 (47.47)		
Gender [n (%)]			0.106	0.689
Male	124 (53.91)	51 (51.52)		
Female	106 (46.09)	48 (48.48)		
Age (years)	51.00 (48.00, 55.00)	52.00 (49.00, 55.00)	–0.730	0.465
BMI (kg/m^2)	22.50 (21.50, 24.08)	22.80 (20.85, 24.50)	–0.053	0.958
Smoking history [n (%)]			0.046	0.831
No	163 (70.87)	69 (69.70)		
Yes	67 (29.13)	30 (30.30)		
Time from injury to operation (days)	6.00 (6.00, 7.00)	6.00 (6.00, 7.00)		
Fracture site [n (%)]			1.634	0.442
Upper Limb	72 (31.30)	36 (36.36)		
Lower Limb	62 (26.96)	29 (29.29)		
Other	96 (41.74)	34 (34.34)		
Comorbidities [n (%)]				
Hypertension	85 (36.96)	28 (28.28)	2.309	0.129
Diabetes	68 (29.57)	27 (27.27)	0.177	0.674
Others	62 (26.96)	25 (25.25)	0.103	0.748
Fracture cause [n (%)]			3.161	0.357
Fall	124 (53.91)	56 (56.57)		
Traffic Accident	57 (24.78)	19 (19.19)		
High Fall	47 (20.43)	21 (21.21)		
Other	2 (0.87)	3 (3.03)		
WBC count (10^9/L)	8.13 ± 3.35	8.43 ± 3.35	–0.735	0.463
RBC count (10^{12}/L)	5.17 ± 1.26	5.28 ± 1.32	–0.772	0.441
Neutrophil count (10^9/L)	4.75 ± 1.94	4.93 ± 1.68	–0.798	0.426
CRP (mg/L)	10.72 ± 2.66	10.52 ± 2.69	0.612	0.541
RAPT score (points)	6.00 (3.00, 8.00)	5.00 (3.00, 7.50)	–1.055	0.292
PT (s)	12.00 (11.25, 13.00)	13.00 (12.00, 13.00)	–0.798	0.425
APTT (s)	22.00 (20.00, 23.00)	22.00 (20.00, 23.00)	–0.225	0.822
FIB (g/L)	4.00 (3.80, 4.20)	4.00 (3.80, 4.20)	–0.079	0.937
D-D (μg/L)	857.03 ± 83.85	865.77 ± 85.83	–0.861	0.390
TAT (ng/mL)	15.80 (14.20, 17.50)	16.20 (15.00, 17.85)	–1.896	0.058
sTM (TU/mL)	8.20 (7.60, 9.10)	8.50 (7.80, 9.00)	–1.380	0.168
tPAIC (ng/mL)	5.80 (4.90, 6.58)	5.80 (4.80, 6.85)	–0.222	0.824

Abbreviation: DVT, deep vein thrombosis; BMI, body mass index; CRP, C-reactive protein; WBC, white blood cell; RBC, red blood cell; RAPT, risk assessment profile for thromboembolism; PT, prothrombin time; APTT, activated partial thromboplastin time; FIB, fibrinogen; D-D, D-dimer; TAT, thrombin-antithrombin complex; sTM, soluble thrombomodulin; tPAIC, tissue plasminogen activator-inhibitor complex.

variables were expressed as medians (interquartile range) [M (P25, P75)] and analyzed using the Mann-Whitney U test. Furthermore, categorical variables were reported as frequencies or proportions and compared using the chi-square test. The multivariate logistic regression analysis included only significant variables ($p < 0.05$) in the regression model based on the result of the univariate analysis. Multivariate analysis was conducted employing logistic regression analysis, with multi-collinearity assessed through the variance inflation factor (VIF). The diagnostic performance of the model was assessed using receiver operating characteristic (ROC) curve analysis, with the area under the curve (AUC) also determined. A p-value < 0.05 was considered statistically significant.

Results

Comparison of Baseline Characteristics Between the Two Study Groups

As shown in Table 1, no significant differences were found between the training and test sets in terms of gender, age,

Table 2. Comparison of baseline characteristics between the Non-DVT and DVT groups within the training set.

Factors	Non-DVT group (n = 120)	DVT group (n = 110)	$t/Z/\chi^2$	*p*-value
Gender [n (%)]			1.973	0.163
Male	70 (58.33)	54 (49.09)		
Female	50 (41.67)	56 (50.91)		
Age (years)	52.15 ± 5.27	50.76 ± 5.48	1.956	0.052
BMI (kg/m^2)	22.80 ± 2.19	22.49 ± 2.06	1.114	0.266
Smoking history [n (%)]			0.782	0.377
No	82 (68.33)	81 (73.64)		
Yes	38 (31.67)	29 (26.36)		
Time from injury to operation (days)	6.00 (6.00, 7.00)	6.00 (6.00, 7.00)	–1.465	0.143
Fracture site [n (%)]			1.089	0.580
Upper limb	38 (31.67)	34 (30.91)		
Lower limb	29 (24.17)	33 (30.00)		
Other	53 (44.17)	43 (39.09)		
Comorbidities [n (%)]				
Hypertension	43 (35.83)	42 (38.18)	0.136	0.712
Diabetes	40 (33.33)	28 (25.45)	1.711	0.191
Others	28 (23.33)	34 (30.91)	1.673	0.196
Fracture cause [n (%)]			4.476	0.179
Fall	60 (50.00)	64 (58.18)		
Traffic accident	35 (29.17)	22 (20.00)		
High fall	25 (20.83)	22 (20.00)		
Other	0 (0.00)	2 (1.82)		
WBC count (10^9/L)	8.46 ± 3.76	7.78 ± 2.80	1.558	0.121
RBC count (10^{12}/L)	5.18 ± 1.21	5.15 ± 1.32	0.132	0.895
Neutrophil count (10^9/L)	4.60 (3.18, 6.43)	4.80 (3.50, 5.68)	–0.005	0.996
CRP (mg/L)	10.89 ± 2.97	10.53 ± 2.26	1.036	0.301

BMI, smoking history, time from injury to surgery, fracture site, comorbidities, cause of fracture, WBC count, RBC count, neutrophil count, CRP levels, or RAPT scores, and thrombotic markers (all $p > 0.05$), indicating that the two groups were comparable.

Patients in the training set were classified based on the presence of DVT into a DVT group (n = 110) and a non-DVT group (n = 120). As detailed in Table 2, gender, age, BMI, smoking history, time from injury to operation, fracture site, comorbidities, cause of fracture, WBC count, RBC count, neutrophil count, or CRP levels demonstrated no statistically significant differences between the DVT (n = 110) and non-DVT (n = 120) groups (all $p > 0.05$).

Comparison of RAPT Scores and Thrombosis Markers Between the Two Groups

Furthermore, we investigated differences in RAPT scores and thrombosis-associated markers between the DVT and non-DVT groups within the training set. As shown in Table 3, the RAPT scores were significantly higher in the DVT group compared to the non-DVT group (7.00 (5.00, 9.00) vs. 4.00 (2.00, 7.00), $p < 0.001$). Moreover, the DVT group showed substantial increases in FIB (4.00 [3.90, 4.30] vs. 4.00 [3.70, 4.20]), D-D (874.12 ± 77.16 vs. 841.37 ± 86.94), TAT (16.60 [14.43, 18.38] vs. 15.40 [14.10, 16.90]), and tPAIC (6.04 ± 1.38 vs. 5.57 ± 1.31) compared to the non-DVT group (Table 3, $p < 0.05$). However, no significant differences were observed in PT, APTT, or sTM levels between the two groups (Table 3, all $p > 0.05$).

Multivariate Logistic Regression Analysis and ROC Analysis of Postoperative DVT in Patients With Traumatic Fracture

In the training set, multivariate logistic regression analysis was performed to identify independent risk factors for postoperative DVT in traumatic fracture patients. RAPT scores, D-D, FIB, and TAT levels were identified as independent risk factors for DVT, with odds ratios (ORs) of 1.209, 1.006, 3.625 and 1.246., respectively (Table 4, all $p < 0.05$).

To further assess the clinical diagnostic performance of these factors, ROC curve analysis was conducted. The results demonstrated that RAPT scores (cut off: 4.500), FIB (cut off: 3.850), D-D (cut off: 823.900), TAT (cut off: 17.350), and the combination of these four indicators showed significant predictive performance for postoperative DVT, with AUC values of 0.698, 0.586, 0.596, 0.610, and 0.771, respectively (Table 5, Fig. 2, $p < 0.05$).

Table 3. Comparison of RAPT scores and thrombotic-associated markers between the Non-DVT and DVT groups within the training set.

Factors	Non-DVT group (n = 120)	DVT group (n = 110)	*t*/*Z*	*p*-value
RAPT score (points)	4.00 (2.00, 7.00)	7.00 (5.00, 9.00)	–5.194	<0.001
PT (s)	12.00 (11.00, 13.00)	13.00 (12.00, 14.00)	–1.926	0.054
APTT (s)	21.00 (20.00, 23.00)	22.00 (20.00, 23.00)	–0.899	0.369
FIB (g/L)	4.00 (3.70, 4.20)	4.00 (3.90, 4.30)	–2.255	0.024
D-D (μg/L)	841.37 ± 86.94	874.12 ± 77.16	–3.011	0.003
TAT (ng/mL)	15.40 (14.10, 16.90)	16.60 (14.43, 18.38)	–2.892	0.004
sTM (TU/mL)	8.25 ± 0.95	8.34 ± 1.10	–0.646	0.519
tPAIC (ng/mL)	5.57 ± 1.31	6.04 ± 1.38	–2.635	0.009

Table 4. Multivariate logistic regression model parameters for postoperative DVT formation in patients with traumatic fractures.

Factors	*b*	S_b	Wald χ^2	*p*-value	*OR*	*OR* 95% *CI*
RAPT score	0.189	0.048	15.724	<0.001	1.209	1.101–1.327
FIB	1.288	0.420	9.386	0.002	3.625	1.590–8.262
D-D	0.006	0.002	10.488	<0.001	1.006	1.002–1.010
TAT	0.220	0.069	10.180	0.001	1.246	1.088–1.425
tPAIC	0.194	0.114	2.860	0.091	1.214	0.970–1.519
Constant	–16.273	3.076	27.985	<0.001	—	—

Note: Related variable assignments were 0 = Non-DVT Group, and 1 = DVT Group. RAPT scores, D-D, FIB, TAT, and tPAIC were quantitative data, which were directly incorporated into the multivariate logistic regression model analysis.
Abbreviation: OR, odds ratio; CI, confidence interval.

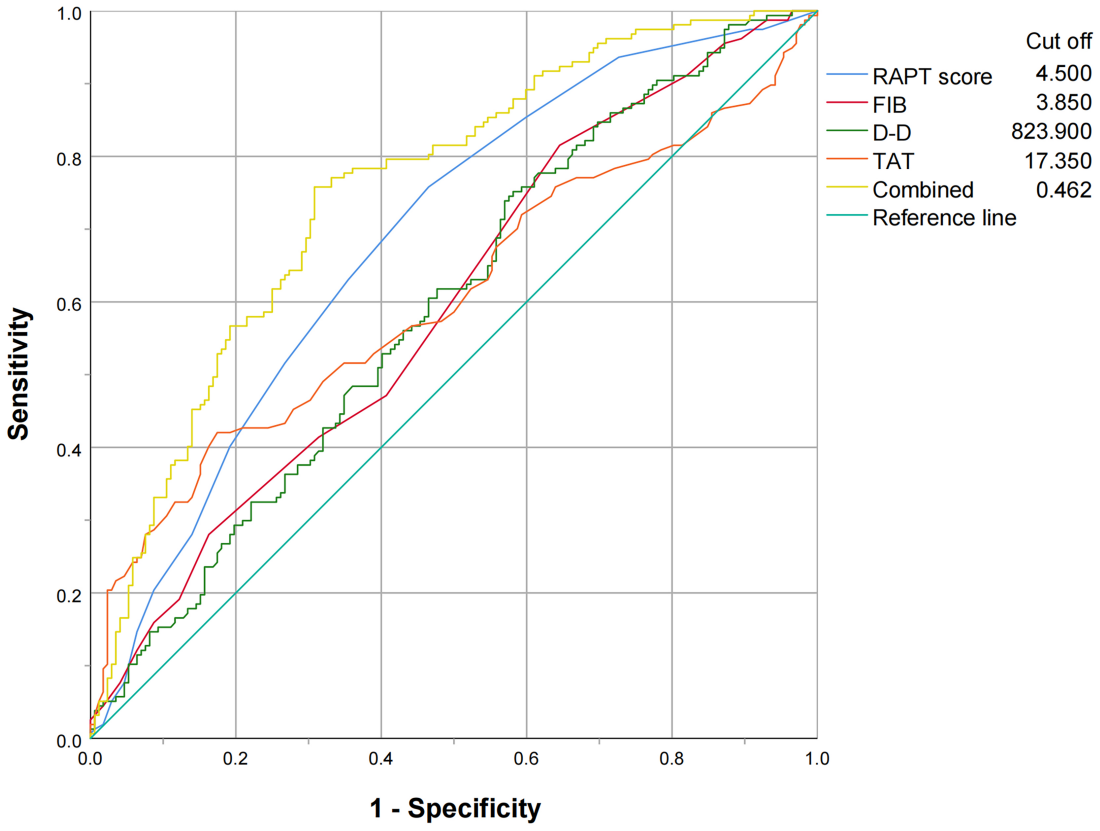

Fig. 2. Receiver operating characteristic (ROC) curve of risk assessment profile for thromboembolism (RAPT) score, fibrinogen (FIB), D-dimer (D-D), thrombin-antithrombin complex (TAT).

Table 5. ROC curve parameters for postoperative DVT in patients with traumatic fractures.

Factors	AUC	95% *CI*	*p*-value	Sensitivity	Specificity	Positive predictive value
RAPT score	0.698	0.630–0.765	<0.001	0.773	0.533	0.603
FIB	0.586	0.512–0.659	0.025	0.818	0.358	0.539
D-D	0.596	0.523–0.669	0.012	0.764	0.442	0.556
TAT	0.610	0.536–0.685	0.004	0.418	0.833	0.697
Combined detection	0.771	0.711–0.832	<0.001	0.782	0.683	0.694

Abbreviation: ROC, receiver operating characteristic; AUC, area under the curve; CI, confidence interval; FIB, fibrinogen; D-D, D-dimer; TAT, thrombin-antithrombin complex.

Table 6. Line chart score-risk comparison.

Total points	122.04	147.68	164.72	178.69	191.51	204.32	218.29	235.33	260.97
Risk	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9

Nomogram Model for Predicting Postoperative DVT in Traumatic Fracture Patients

The constructed nomogram is illustrated in Fig. 3. Based on the model derivation, a score of 191.51, corresponding to a risk probability greater than 0.5, was identified as a potential threshold for high risk (Table 6). To evaluate the stability and predictive performance of the nomogram model, ROC analysis was performed. The model yielded an AUC of 0.7714 (0.7107, 0.832), demonstrating discriminative ability and predictive performance for assessing postoperative DVT risk in traumatic fracture patients (Fig. 4A). Furthermore, calibration curve analysis showed that both the Apparent and Bias-corrected curves closely aligned with the Ideal curve, indicating the model fits well in internal resampling validation and that the predicted and observed values are highly consistent (Fig. 4B). DCA curve analysis further confirmed the clinical application of the model, with the net benefit curve positioned above the "None" and "All" within the probability range of 0.055–0.755, indicating reliable performance within this range (Fig. 4C).

Validation of Risk Prediction Models

The predictive model was further validated using the test set. ROC curve analysis yielded an AUC of 0.7066 (0.603, 0.8103), demonstrating good stability and predictive performance (Fig. 4D). Calibration curve analysis showed that both the Apparent and Bias-corrected curves closely aligned with the Ideal curve, indicating the model fits well in internal resampling validation and that the predicted and observed values are highly consistent (Fig. 4E). DCA curve analysis demonstrated that the net benefit curve remained above the two ineffective lines of "None" and "All" within the probability range of 0.095–0.805, implying robust clinical performance of the model within this range (Fig. 4F).

Discussion

D-dimer (D-D) is a specific fibrin degradation product released during fibrinolysis, the process by which the body breaks down blood clots [20]. During thrombosis, the fibrin network is degraded, generating D-D to enter the bloodstream [21]. Elevated D-D levels are a significant clinical biomarker of thrombosis, especially in conditions such as DVT and PE [22,23]. Combining D-D and ultrasonography improves the effective detection of asymptomatic venous thromboembolism [24]. FIB, a precursor of fibrin in the coagulation cascade, plays a key role in thrombosis by forming the basic framework of thrombi [25]. Increased FIB levels promote thrombosis and are frequently observed in patients experiencing acute trauma, surgical interventions, infections, or cardiovascular diseases [26]. TAT, generated during thrombin activation, reflects ongoing coagulation activity [27]. Elevated TAT levels indicate enhanced coagulation and are closely associated with thrombosis, particularly in acute conditions such as DVT and PE [28].

Consistent with previous results, our study revealed upregulation of D-D, FIB, and TAT in DVT patients. Further multivariate analysis identified RAPT scores, along with D-D, FIB, and TAT, as independent risk factors for postoperative DVT in traumatic fracture patients, highlighting their clinical diagnostic value. These findings suggest that combining RAPT scores with thrombosis biomarkers offers a more comprehensive risk assessment, facilitating early identification of high-risk patients and enabling timely interventions to reduce DVT incidence and improve clinical outcomes. Although TAT is a sensitive marker of coagulation activation that promotes the model's predictive performance, its measurement is not routinely available in all healthcare settings. This limited accessibility may restrict the immediate clinical utility and widespread implementation of our current model in resource-limited settings. Future studies should investigate whether more readily available clinical or laboratory parameters could serve as effective substitutes or consider developing simplified predictive models for settings lacking advanced biomarker testing, thereby expanding the model's utility.

Furthermore, while our analysis identified several statistically significant predictors, some demonstrated relatively modest differences, with AUC of individual metrics (e.g., FIB = 0.586, D-D = 0.596) only slightly exceeding 0.5, ap-

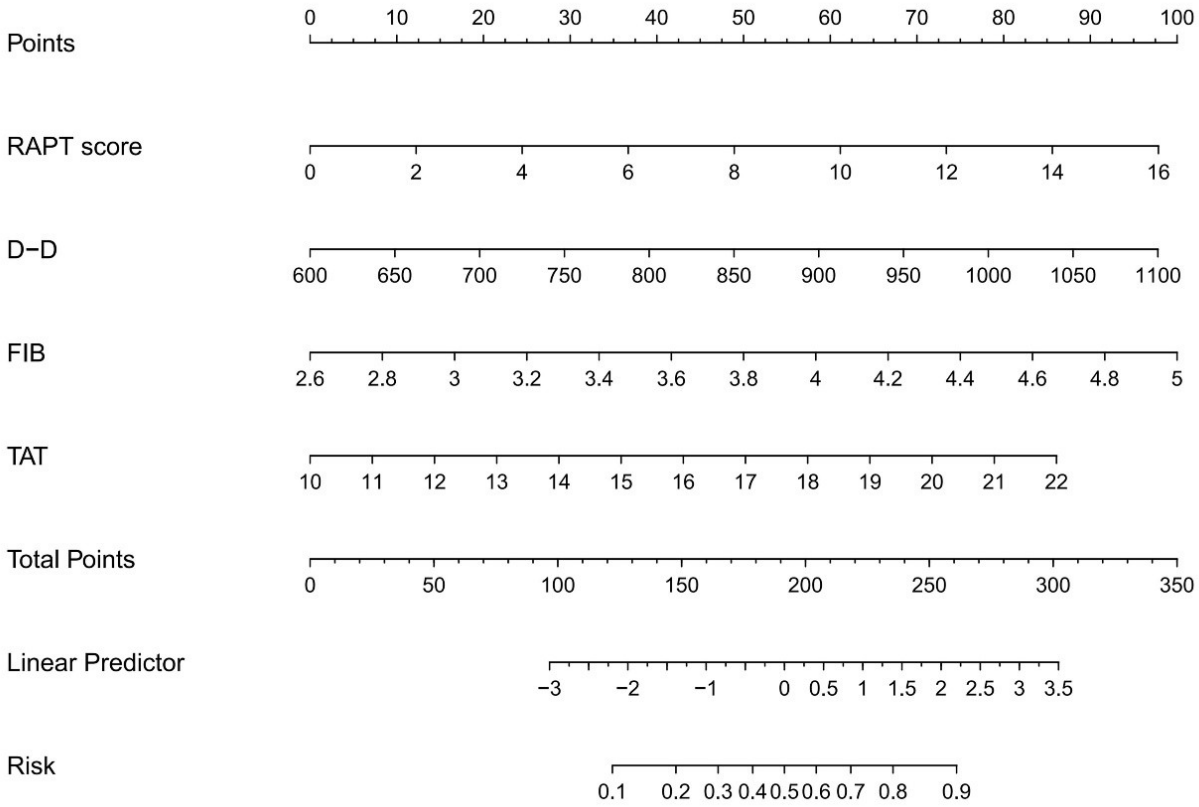

Fig. 3. Nomogram model for predicting the occurrence of postoperative DVT in traumatic fracture patients.

proaching the level of random chance. Therefore, the clinical interpretation of these effect sizes necessitates caution, as their individual utility may be limited. Notably, when combined within a multivariate nomogram, even predictors with small individual effects can act synergistically, enhancing the overall discriminatory ability for risk stratification and supporting more personalized clinical decision-making. Nonetheless, the modest effect sizes of some components highlight that their contributions are primarily manifested within the context of the multivariate model.

Nomograms are valuable tools for individualized risk prediction, integrating multiple predictive variables, including clinical characteristics, physiological parameters, and laboratory findings, to estimate the likelihood of disease occurrence, progression, or clinical outcomes [29,30]. By integrating the effects of multiple factors, nomograms provide a visual and intuitive approach for clinical decision-making. Previous studies have combined thrombotic molecular indicators with the postoperative Caprini score, demonstrating their potential to predict DVT risk in patients after traumatic fracture surgery. Among them, the combination with thrombomodulin (TM) has reported the highest predictive performance (AUC = 0.869) [31]. The Caprini scoring system is a tool used for assessing venous thromboembolism risk [32]; however, its predictive accuracy can vary among different surgical populations, and a single threshold may not be equally applicable to all patients.

The RAPT model was specifically developed for trauma patients [18] and has been found to link strongly with the risk of venous thromboembolism in this cohort, regardless of the mechanism of injury, making it a valid risk assessment tool [33]. RAPT score, though trauma-specific, primarily captures mechanical and physiological aspects of trauma; it may not fully reflect the underlying biochemical thrombotic state. In the current study, we developed a nomogram model integrating RAPT scores with D-D, FIB, and TAT to predict postoperative DVT in traumatic fracture patients. Subsequent analyses demonstrated the model's high stability and strong predictive performance in clinical settings. However, the nomogram was developed from a relatively small, single-institution cohort, which may introduce selection bias. Moreover, patients with cardiac, hepatic or renal insufficiency, malignancies, and other comorbidities were excluded, potentially limiting the generality of the results, as comorbidities are common among trauma patients and may interact with the observed risk factors. Further studies with larger and more diverse patient populations are required to validate and optimize the model, ensuring its applicability across wider trauma cohorts. Collectively, these findings underscore the clinical significance of thrombosis risk factor-based nomograms for preventing and managing DVT in traumatic fracture patients, offering robust support for rapid and accurate diagnosis decision-making.

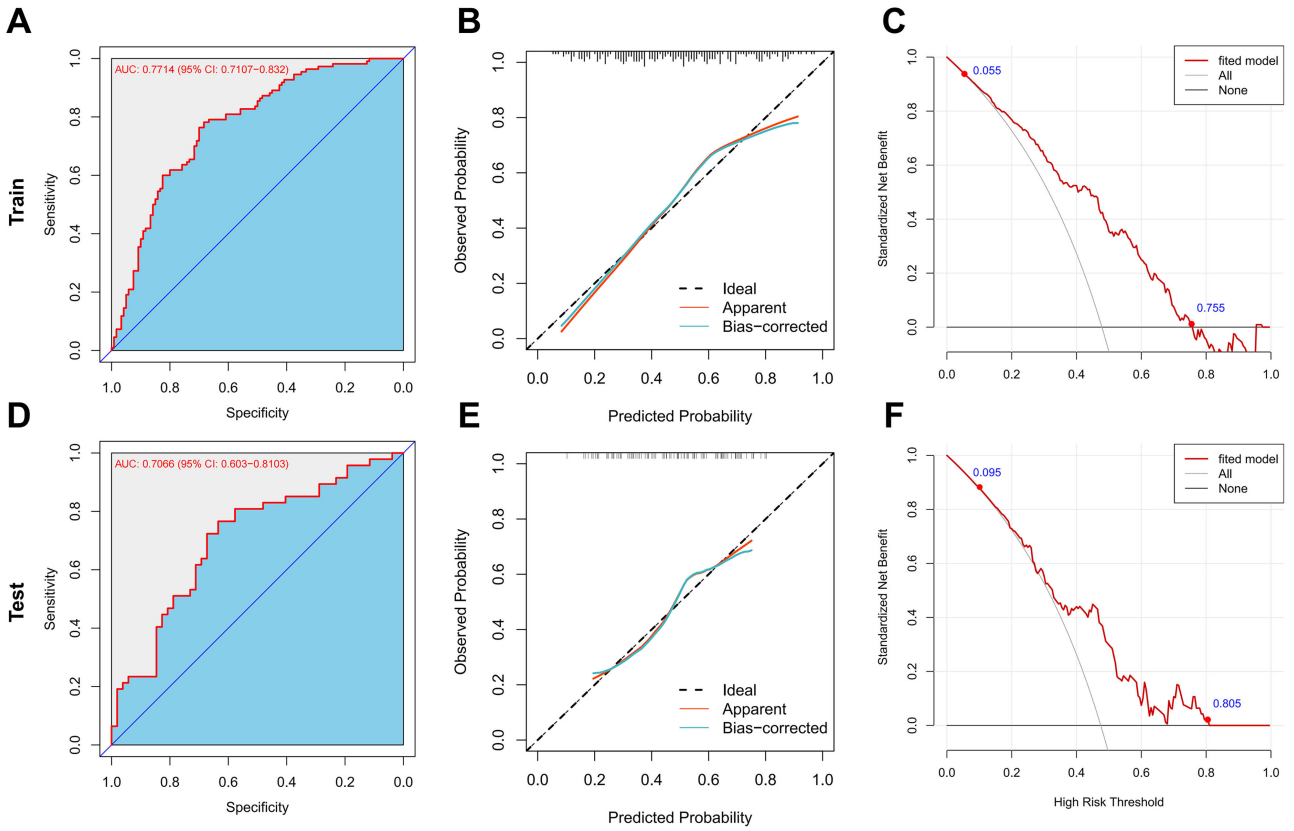

Fig. 4. Performance evaluation of the nomogram model for predicting postoperative DVT in traumatic fracture patients. (A,D) ROC curve of the nomogram model for predicting postoperative DVT in traumatic fracture patients in the training set (A) and the test set (D). (B,E) Calibration curve of the nomogram model for predicting postoperative DVT in traumatic fracture patients in the training set (B) and the test set (E). (C,F) Clinical DCA for the nomogram model predicting postoperative DVT in traumatic fracture patients in the training set (C) and the test set (F).

Additionally, the duration of RBC storage has been associated with increased incidence of DVT and higher in-hospital mortality among patients with traumatic injuries [34]. RBC transfusions are also correlated with changes in circulating coagulation factors, including FIB chains [35]. The PI3K-Akt signal transduction pathway has been speculated to mediate the regulatory effects of small nucleolar host gene 12 (SNHG12)/miR-424-5p in DVT development, and the combination of SNHG12 and D-D has been reported to improve the diagnostic sensitivity and specificity for DVT [36]. Targeting inflammatory mediators has been indicated as a potential approach to alleviate thrombus burden and treat DVT [37]. Moreover, factors such as the severity of trauma may influence outcomes, underscoring the possibility of confounders that warrant further investigation. Future studies could explore defining optimized cut off values adjusted for variables such as age, injury severity, or other clinical factors to enhance diagnostic accuracy. However, while unmeasured confounders cannot be fully excluded, they are unlikely to completely negate the observed association between combining the RAPT score with thrombosis biomarkers and postoperative DVT, underscoring the robustness of our findings. Further research is needed to elucidate this association and to guide targeted strategies using the combined RAPT score with the thrombosis biomarkers approach for DVT prediction in trauma patients.

However, it is crucial to note that, to isolate the relationship between the biomarkers and postoperative DVT, we applied strict inclusion criteria, excluding patients with significant comorbidities such as cardiac, hepatic, or renal dysfunction, malignant tumors, and immune disorders. While this approach enhances the internal validity of our findings by minimizing potential confounders, it consequently creates an “idealized” patient population that may not fully represent the broader, more complex population of trauma patients, who often present with such comorbidities. Therefore, the generalizability of our nomogram may be limited to a relatively healthier subgroup of trauma fracture patients. Clinicians should exercise considerable caution when interpreting these results or applying this predictive tool to patients with significant underlying medical conditions.

Despite these advances, our study has several limitations. First, the study was conducted at a single center with a relatively small sample size, and the validation was per-

formed through an internal random split of the available data. While this method helps assess internal performance, it cannot substitute validation in a truly independent, external cohort from a different center or population, which is essential to confirm the model's robustness and clinical utility. Future prospective, larger-scale, multicenter studies are required to verify the predictive accuracy and clinical applicability of the constructed nomogram model. Second, the diagnosis of DVT was limited to the immediate postoperative period (within 3 days after surgery) during hospitalization. Consequently, late-onset DVT occurring after discharge was not captured, potentially leading to an underestimation of overall DVT incidence and limiting comparability with studies involving longer follow-up periods. Finally, many critical confounding factors, including clinical randomization, the type of surgery, anesthesia method, and postoperative anticoagulant use, were not considered, which may influence DVT risk and potentially lead to residual confounding.

Conclusions

In conclusion, this study demonstrates the clinical utility of combining the RAPT score with thrombosis biomarkers, including FIB, D-D, and TAT, to predict postoperative DVT in patients with traumatic fractures. Multivariate logistic regression confirmed these factors as independent risk predictors, forming the basis for a nomogram that exhibits good predictive performance, as evidenced by decision curve analysis. These results provide a practical tool for individualized risk assessment, which may aid in the early identification of high-risk patients, inform targeted prophylactic strategies, and contribute to improved perioperative management and patient outcomes.

Availability of Data and Materials

The data used and analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

XJ, FJ and YPL designed the research study. YPL and YJZ performed the research. YJZ and XJ provided help and advice on the ELISA experiments. YJZ analyzed the data. FJ drafted this manuscript. All authors contributed to the critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study followed a retrospective cohort design. This study was approved by Shouxiang Community Health Service Center of Yinhu Street (Approval No. 2025-LL0109-01), and written informed consent was obtained from all participants. Furthermore, the study design adhered to the principles outlined in the Declaration of Helsinki.

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Conflict of Interest

The authors declare no conflict of interest.

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