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Establishment and validation of a predictive model for lower extremity deep vein thrombosis in patients with traumatic pelvic fractures

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Abstract

Background Patients with traumatic pelvic fracture (TPF) are at high risk for developing deep vein thrombosis (DVT). However, there is still no unified standard on how to distinguish high-risk groups for DVT in patients with TPF and how to accurately use anticoagulants at present.

Objectives This observational study aimed to establish a DVT risk nomogram score (DRNS) model for TPF patients, and to explore the value of the DRNS model as a clinical guideline in the prevention of DVT with low molecular weight heparin (LMWH).

Methods Independent risk factors of lower extremity DVT were screened through Lasso regression and logistic regression. A DRNS model was established per this.

Results The independent risk factors of DVT included combined femoral fractures, age ≥ 40 years old, BMI (body mass index) ≥ 24 kg/m^2, ISS score, fibrinogen concentration, and the minimum concentration of ionized calcium within 48 h after admission. The optimal cutoff value for DRNS was 78.5. In the low-risk population of DVT (DRNS < 78.5), there was no statistical significance of variation about the incidence of DVT progression between the LMWH once a day (qd) group and the LMWH once every 12 h (q12h) group, with $P = 0.323$. In the high-risk population of DVT (DRNS ≥ 78.5), the incidence of DVT progression in the LMWH qd group was significantly higher than that in the LMWH q12h group, with $P = 0.002$.

Conclusions The DRNS model based on independent risk factors of DVT could stratify the risk of DVT for TPF patients, and it was able to provide more precise DVT drug prevention plans for clinicians.

Keywords Pelvic fracture, Deep vein thrombosis, Risk factor, Nomogram, Low molecular weight heparin

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Background

Venous thromboembolism (VTE) refers to a disease in which abnormal blood clots block the lumen of the vein and causes the occlusion of the venous lumen and the obstruction of venous blood reflux, mainly including deep vein thrombosis (DVT) and pulmonary thromboembolism (PTE). In human, the post-fracture hypercoagulable state of blood and other factors, such as limb immobilization and surgery, might increase the risk of DVT [1], and the subsequent occurrence of post-thrombotic syndrome (PTS) would prolong the duration of hospitalization, increase the cost of hospitalization, and seriously decrease the quality of life for patients [2]. Furthermore, once the thrombus adhering to the wall of the deep vein dislodges and blocking the main trunk or branches of the pulmonary artery, it can cause serious adverse events such as PTE, hypoxemia and even sudden death [3, 4]. Patients with traumatic pelvic fractures (TPF) admitted to the emergency intensive care unit (EICU) are often at high risk for lower extremity DVT, as the pelvic ring injury is one of the most prominent risk factors for DVT in trauma patients, and often accompanied by lower extremity injuries, higher injury severity score (ISS), and hemorrhagic shock [5–7].

The anticoagulant treatment for fracture patients has always been a challenge for clinicians, with the main issue being how to minimize the risk of bleeding while preventing DVT [8]. Currently, for fracture patients at high risk of thrombosis without contraindications to bleeding, it is recommended that drug prophylaxis should be initiated within 48 h. However, it is still controversial regarding the dose of prophylactic anticoagulant medications [9, 10]. Despite the use of pharmacological thromboprophylaxis regimens, post-traumatic DVT is still very common in clinical practice, which indicated that the anticoagulation regimens might differ in the pelvic fracture patients with different DVT risks. Early prediction models for DVT risk will probably help clinicians to determine individualized anticoagulation regimens to reduce the incidence of DVT and improve the clinical prognosis of TPF patients.

The aim of this study was to develop a DVT risk nomogram score (DRNS) model for TPF patients at an early stage, which would help clinicians to identify high-risk population for DVT as early as possible, and optimize the administration frequency of low molecular weight heparin (LMWH) prophylaxis per risk stratification of DRNS model.

Methods

In this observational study, retrospective data were retrieved from electronic medical records to develop a DRNS model, and prospective data were collected to validate the clinical value of DRNS model.

Study subjects

In the retrospective study, there were 809 TPF patients who admitted to the EICU of our institute from January 2017 to December 2022. Inclusion criteria: ① TPF patients; ② age≥18 years old; ③ time from injury to admission≤48 h; ④ at least one compression ultrasound (CUS) examination of lower limb vessels performed after admission and before internal fixation surgery. Exclusion criteria: ① pathological fracture; ② pregnancy; ③ receiving anticoagulant or antiplatelet therapy before fracture; ④ former history of tumors or hematological disorders; ⑤ DVT existing before this fracture; ⑥ incomplete clinical data.

In the prospective study, there were 181 TPF patients who admitted to the same unit from January 2023 to December 2023 was conducted. The researchers only observed and recorded the results without intervening in the clinical treatment. All study subjects only discontinued LMWH for one day on the day of internal fixation surgery. Inclusion criteria: ① follow-up until 28 days after internal fixation; ② no contraindications to anticoagulation; ③ treatment with enoxaparin sodium 4000 AXaIU (manufactured by Sanofi-Synthelabo), once daily (qd) or every 12 h (q12h) per the clinician's judgment for the prophylaxis of DVT. Exclusion criteria: ① patients with adverse bleeding during follow-up; ② those who did not complete 28 days of postoperative follow-up; ③ those who did not receive enoxaparin sodium treatment or whose dosage and frequency changed within the observation period of this study. The other inclusion and exclusion criteria were the same as those in the retrospective study section. In this study, clinicians adopted different DVT prevention measures for patients with pelvic and lower limb fractures under their management, based on their own judgment. The researchers did not intervene in clinical treatment, but only selected the population using enoxaparin sodium for prevention, conducted the observational studies, and recorded the progression of DVT.

Data collection

In the retrospective study, a collection of clinical data from research subjects who met the inclusion criteria was conducted, including demographic characteristics, time of injury, injury-causing factors, admission time, previous medical history (diabetes, coronary heart disease, hypertension, atrial fibrillation and cerebral infarction), clinical diagnosis and ISS scores, and laboratory data within 24 h after entering this hospital, which started counting from entering the emergency room. They included the concentrations of the following indicators: white blood cells, red blood cells, platelets, 24-hour minimum hemoglobin, C-reactive protein, ionized sodium, ionized potassium, random blood glucose, lactate dehydrogenase, γ-glutamyl transpeptidase, aspartate aminotransferase, alanine

aminotransferase, alkaline phosphatase, creatinine, urine, troponin I, myoglobin, CKMB, fibrinogen (FIB), D-dimer; Actual bicarbonate, lactate, base excess in arterial blood; And hematocrit, percentage of lymphocytes, percentage of neutrophils, average platelet width, average platelet volume, thrombin time, prothrombin time, partial thromboplastin time, arterial blood pH value, oxygen partial pressure, carbon dioxide partial pressure. The blood transfusion volume, minimum concentration of serum ionized calcium (iCa-min), albumin (Alb-min) within 48 h after admission. Other data included the time and approach of surgery, time and type of DVT formation, and duration of hospitalization.

In the prospective data collection, the patient underwent CUS examination before internal fixation surgery, 1 week after surgery, 2 weeks after surgery, and 4 weeks after surgery to determine the progression of DVT, which was defined as newly developed deep vein thrombosis, muscle thrombosis progressing to deep vein thrombosis, or distal thrombosis progressing to proximal thrombosis. Clinical data of study subjects who met the prospective inclusion criteria were collected, including LMWH administration frequency, CUS at 1, 2, 4 weeks after internal fixation surgery, including time and type of DVT formation. Other clinical data were the same as those in the retrospective study section.

The CUS examiners were all senior attending physicians with over 5 years of work experience, sufficient CUS operation experience, and regularly trained in vascular ultrasound. During each DVT inspection process, the examiner also served as the reviewer. Examination method: The subject has mild thigh abduction and the entire lower limb is in a relaxed state. The examiner inspects the external iliac, common femoral, superficial femoral, deep femoral, and great saphenous veins from top to bottom; afterwards, checks the popliteal vein and calf vein. Blood vessels are displayed in longitudinal and transverse sections. The examiner mainly observes the presence of blood flow in the lumen, as well as the filling defects and blood reflux. The lumen below the site of thrombus obstruction increases, the wall thickens, and homogeneous hypoechogenicity is visible within the lumen.

Statistical analysis

Statistical analysis was performed using R 4.2.3 software, and P value <0.05 was considered as significant difference.

In the retrospective study, univariate logistic regression analysis based on clinical variables was conducted to preliminarily screen variables that would possibly be incorporated in the predictive model. Subsequently, the least absolute shrinkage and selection operator (Lasso) regression analysis were performed to identify the variables of statistical significance. Finally, multivariate logistic regression analysis were performed to determine the independent risk factors for DVT, which were included in the development of DRNS model. The entire study population was divided into a training set and a validation set according to the ratio of 9:1, and a 10-fold cross-validation was performed to evaluate the discrimination of the predictive model by calculating the index of concordance (C-index). The calibration of the DRNS model was evaluated by repeated sampling of 400 times with Bootstrap method, plotting the calibration curve and performing the Hosmer-Lemeshow goodness-of-fit test. The clinical applicability of the DRNS model was further evaluated by decision curve analysis (DCA). Accordingly, the receiver operating characteristic (ROC) curve was plotted to determine the cut-off value for DRNS model by the area under curve (AUC) and the Youden index.

In the prospective study, a cohort study was used, the prospectively enrolled patients were divided into a high- or low-risk group for DVT per the above cut-off value for DRNS model. To compare the incidence of DVT progression at different administration frequencies of LMWH between study subjects within group, the Chi-square ($\chi 2$- test) was performed (corrected $\chi 2$- test for expected frequency <5, and Fisher's exact test for expected frequency <1).

Results

In the retrospective study, a total of 1346 subjects were observed, 537 of whom were excluded due to the following reasons: ① pathological fracture ($n=15$); ② received anticoagulant or antiplatelet therapy before fracture ($n=62$); ③ combined with tumor or blood system disease ($n=36$); ④ fracture to hospitalization time more than 48 h ($n=265$); ⑤ incomplete clinical data ($n=159$). Therefore, 809 TPF patients met the inclusion and exclusion criteria were enrolled into the retrospective study, including 216 in the DVT group and 593 in the non-DVT group, the mean age was 49.6 ± 15.8 years, and 68.6% of patients were male.

In the process of prospective data collection, 220 subjects were observed, of which, 16 patients were excluded due to without or unsustained therapy of LMWH, and 18 patients were excluded for lost to follow-up. In the remained 186 subjects, 147 subjects received LMWH with a frequency of qd, 2 (1.4%) of them stopped due to bleeding events. Meanwhile, 39 subjects received LMWH with a frequency of q12h, and 3 (7.7%) of them stopped due to bleeding events. There was no significant difference in the incidence of bleeding events between the two groups ($P=0.106$), and subsequently, the 5 individuals were excluded from this study(Fig. 1). The baseline data of the research subjects in the retrospective study section were shown in the Table 1.

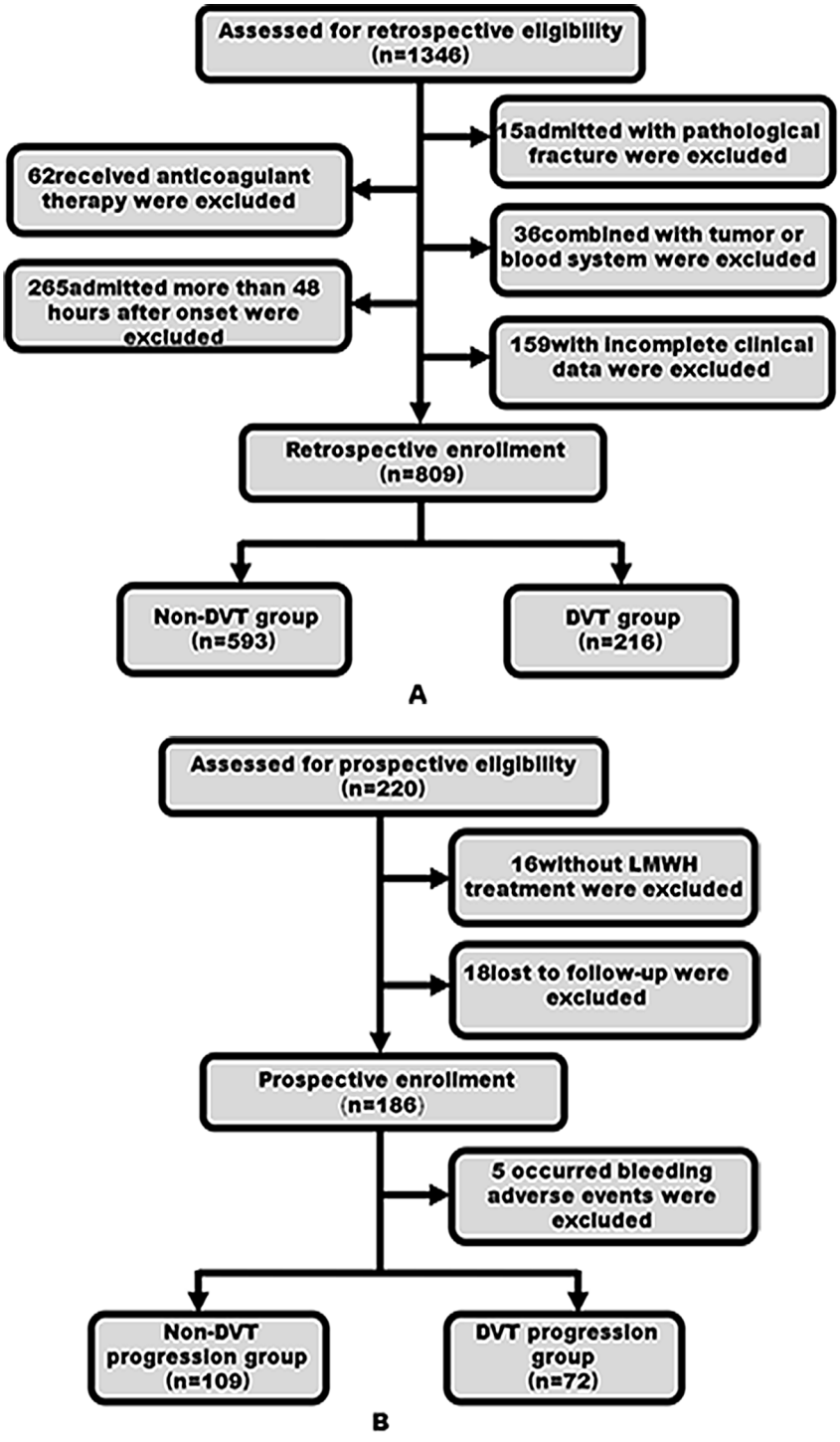

Fig. 1 Flowchart of subjects screening for retrospective (**A**) and prospective (**B**) cohorts in the study

The variables that could be included in the prediction model were initially screened by univariate logistic regression analysis. As illustrated in Fig. 2, Statistically significant variables were screened by Lasso regression, and then the screened variables were incorporated into the multivariate logistic regression analysis for independent risk factors of DVT. Combined femoral fractures (OR=1.533, 95% CI 1.050–2.239, P=0.027), age≥40 years old (OR=2.402, 95% CI 1.565–3.688, P<0.001), BMI≥24 kg/m^2 (OR=1.546, 95% CI 1.101–2.171, P=0.012), ISS score at admission (OR=1.027, 95% CI 1.010–1.045, P=0.002), iCa-min (OR=0.009, 95% CI 0.003–0.033, P<0.001), and FIB concentration at admission (OR=1.186, 95% CI 1.028–13670, P=0.019) were

Table 1 Comparison of baseline between DVT and non-DVT subjects in retrospective research section

Variable	Total($n=809$)	non-DVT($n=593$)	DVT($n=216$)	*P* value
Age(years)	49.59 ± 15.83	48.24 ± 15.96	53.31 ± 14.88	<0.001
Age group(number, %)				<0.001
Age<40 years old	222	186(83.78)	36(16.22)	
Age ≥ 40 years old	587	407(69.34)	180(30.66)	
BMI(kg/m^2)	23.55 ± 3.29	23.41 ± 3.34	23.95 ± 3.10	0.017
BMI group(number, %)				0.003
BMI<24 kg/m^2	467	361(77.30)	106(22.70)	
BMI ≥ 24 kg/m^2	342	232(67.84)	110(32.16)	
ISS	25.45 ± 9.97	24.46 ± 9.67	28.19 ± 10.29	<0.001
ISS group(number, %)				<0.001
ISS<25	371	296(79.78)	75(20.22)	
ISS ≥ 25	438	297(67.81)	141(32.19)	
Gender(number, %)				0.172
Man	553	397(71.79)	156(28.21)	
Woman	256	196(76.56)	60(23.44)	
Injury Factors(number, %)				0.489
Traffic	446	338(75.78)	108(24.22)	
Fall injuries	207	163(78.74)	44(21.26)	
Heavy objects injuries	114	83(72.81)	31(27.19)	
Other	42	36(85.71)	6(14.29)	
Site of fracture(number, %)				0.001
Pelvic fracture without femur	609	465(76.35)	144(23.65)	
Pelvic fracture with femur	200	128(64.00)	72(36.00)	
Use of low molecular weight heparin(number, %)				0.375
No	224	159(70.98)	65(29.02)	
Yes	585	434(74.19)	151(25.81)	
Diabetes mellitus(number, %)				0.711
No	711	566(73.41)	205(26.59)	
Yes	38	27(71.05)	11(28.95)	
Hypertension(number, %)				0.889
No	737	541(73.41)	196(26.59)	
Yes	72	52(72.22)	20(27.78)	
Abdominal surgery(number, %)				0.579
No	770	566(73.51)	204(26.49)	
Yes	39	27(69.23)	12(30.77)	
Chest surgery(number, %)				0.369
No	722	533(73.82)	189(26.18)	
Yes	87	60(68.97)	27(31.03)	
Emergency blood transfusions ≥ 4u(number, %)				0.025
No	674	505(74.93)	169(25.07)	
Yes	135	88(65.19)	47(34.81)	
Pelvic vascular DSA surgery(number, %)				0.012
No	772	573(74.22)	199(25.78)	
Yes	37	20(54.05)	17(45.95)	
Ventilator use(number, %)				0.034
No	757	562(74.24)	195(25.76)	
Yes	52	31(59.62)	21(40.38)	
Concurrent gastrointestinal bleeding(number, %)				0.045
No	793	585(73.77)	208(26.23)	
Yes	16	8(50.00)	8(50.00)	
Length of stay	14.86 ± 8.11	13.68 ± 7.43	18.08 ± 8.98	<0.001

DVT: deep vein thrombosis; BMI: body mass index; ISS: injury severity score

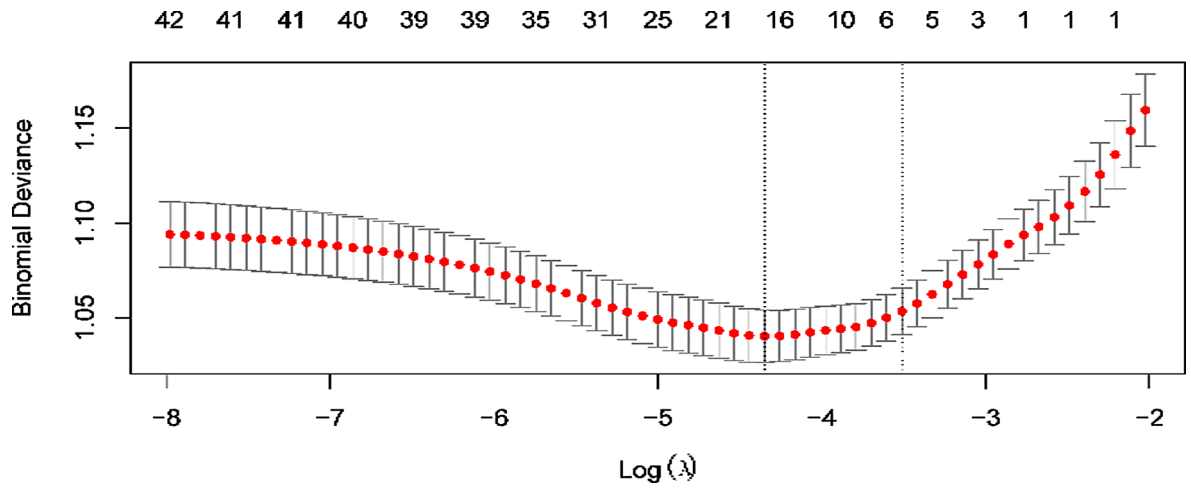

Fig. 2 The potential risk factors selected using the Lasso logistic regression model. The two dashed lines represented specific λ value, in which the left represented the minimum mean square error λ value, the right represented the standard error of the minimum distance mean square error λ value. The present study adopted 0.02984 as λ value

Table 2 Multivariate logistic regression analysis results of DVT risk factors in TPF patients

Variable	OR	95% CI	*P* value
Combined femoral fractures	1.533	1.050 to 2.239	**0.027**
Age ≥ 40 years old	2.402	1.565 to 3.688	**< 0.001**
BMI ≥ 24 kg/m^2	1.546	1.101 to 2.171	**0.012**
ISS score	1.027	1.010 to 1.045	**0.002**
iCa-min	0.009	0.003 to 0.033	**< 0.001**
FIB concentration	1.186	1.028 to 1.367	**0.019**

p values less than 0.05 were bolded. BMI: body mass index; ISS: injury severity score; iCa-min: minimum ionized calcium concentration within 48 h of admission; FIB: fibrinogen

independent risk factors for lower extremity DVT in TPF patients before surgery (Table 2).

In accordance with the results of multivariate logistic regression analysis, with the occurrence of DVT as the dependent variable, and the independent variables including the presence of femoral fractures, age ≥ 40 years old, BMI ≥ 24 kg/m^2, ISS score at admission, iCa-min, and FIB concentration at admission, a nomogram for predicting DVT was plotted, then the DRNS model was constructed (Fig. 3).

Per 10 rounds of repeated sampling and 10-fold cross-validation, the C-index of DRNS model predicting the

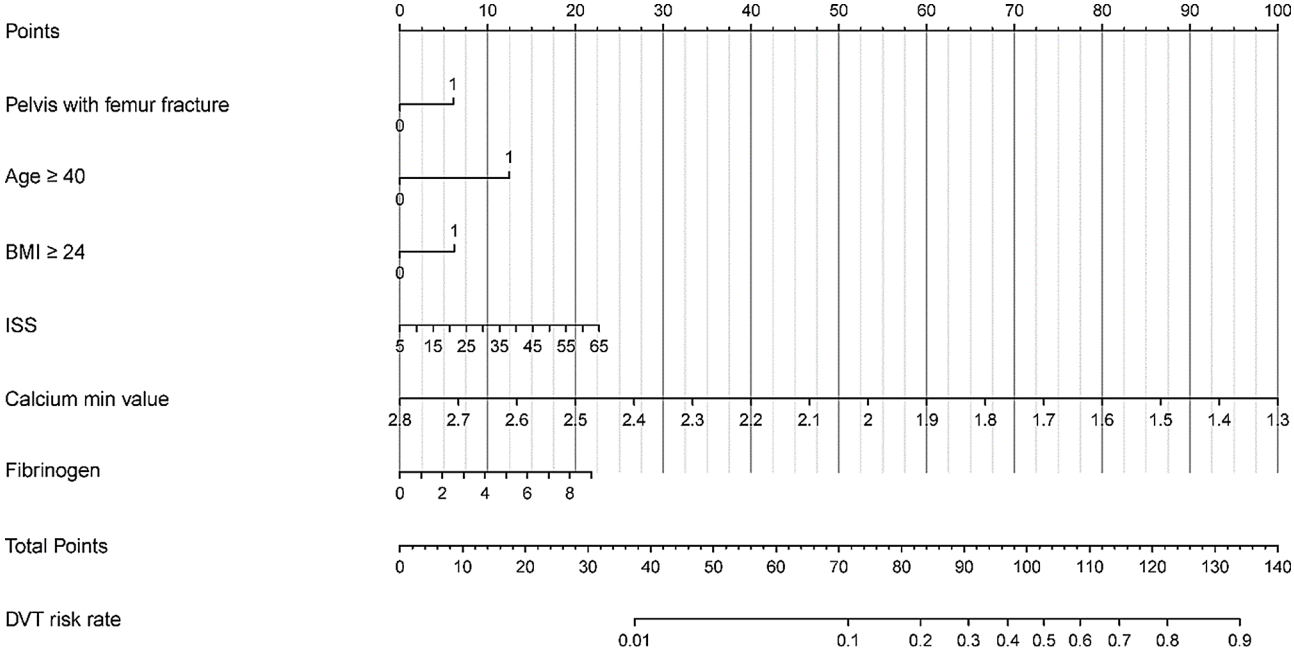

Fig. 3 Nomogram predictive model of lower extremity DVT for TPF patients

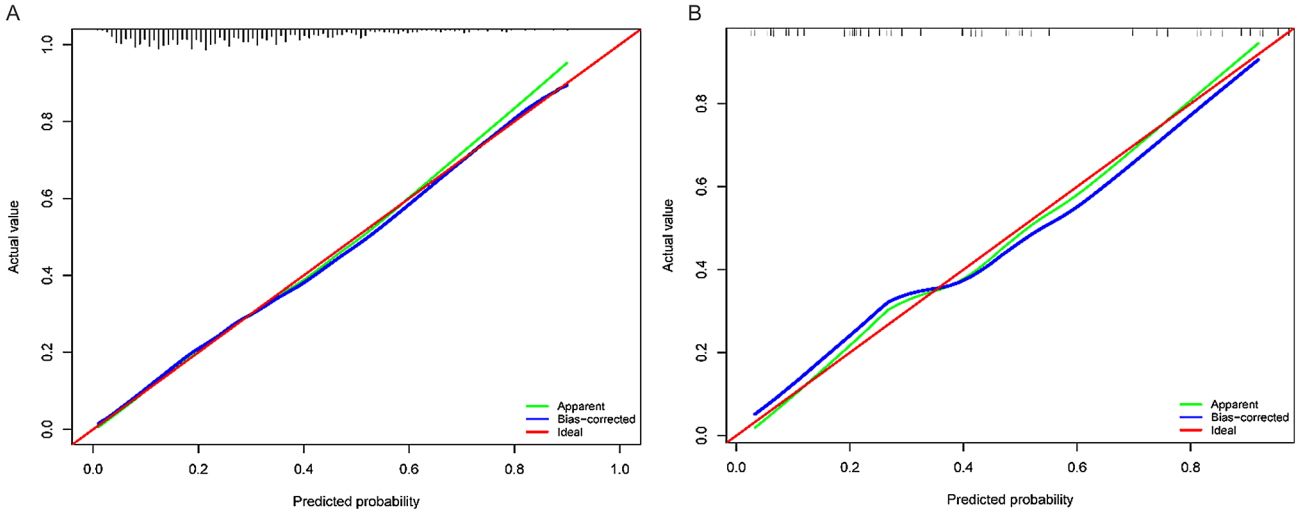

Fig. 4 Calibration curve for internal validation of DRNS model in training (**A**) and validation (**B**) set

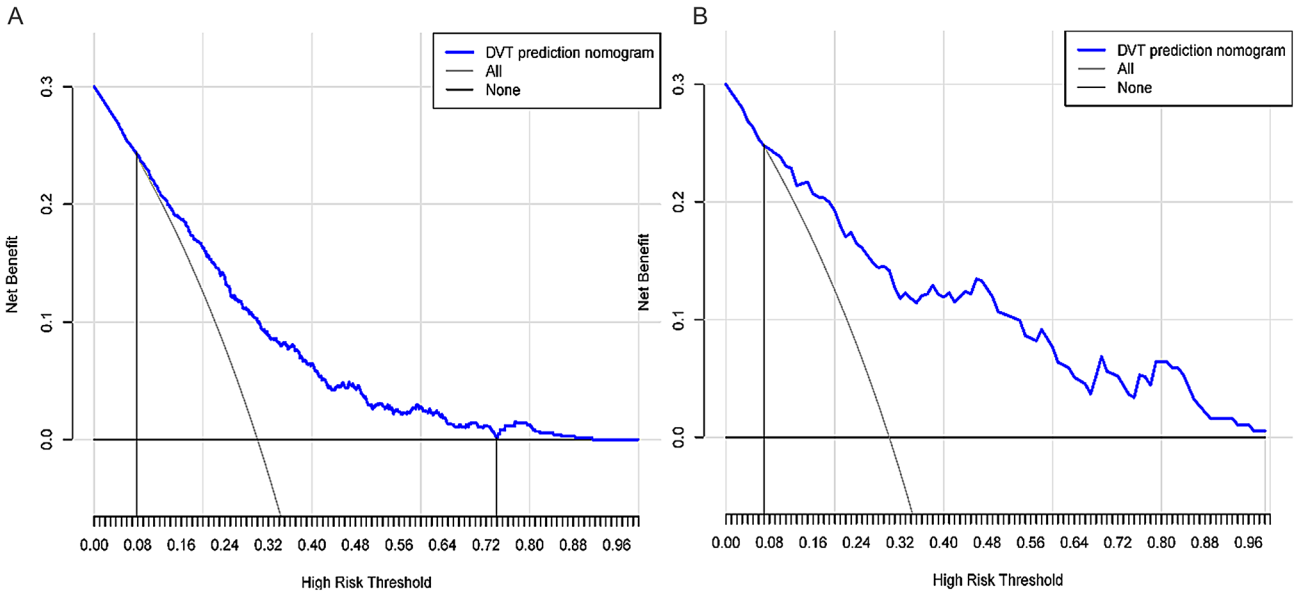

Fig. 5 Decision curve analysis in training (**A**) and validation (**B**) set per DRNS models

occurrence of DVT progression was 0.748 (95% CI 0.710–0.786) and 0.920 (95% CI 0.870–0.969) in the training and validation set, respectively. In training set, the calibration of DRNS model was well indicated by strong consistency between the actual curve and correction curve trajectories (Fig. 4A), as well as the Hosmer-Lemeshow goodness-of-fit test (P=0.239). Similarly, in validation set, the calibration of DRNS model was well repeated by the calibration curve (Fig. 4B) and the Hosmer-Lemeshow goodness-of-fit test (P=0.238).

The decision curve analysis of the DRNS model revealed that the patients would benefited from intervention measures when the probability of DVT ranged from 7 to 72% in the training set (Fig. 5A), and from 6 to 100% in the validation set (Fig. 5B), respectively. The maximum treatment effect in both sets was approximately 0.24.

The ROC curve (Fig. 6) was plotted by using the DRNS model with AUC of 0.785, 95% *CI* 0.706–0.865. When 78.5 was taken as the cut-off value for DRNS model per the Youden index up to maximum value of 0.512, the optimal ability to distinguish high-risk populations of DVT in TPF patients was obtained. Therefore, in TPF pateients, DRNS no less than 78.5 were defined as high risk of DVT. Accordingly, in the prospective population, 101 and 80 patients were included in high- and low-risk groups of DVT, respectively.

In the low-risk group, DVT progression was occurred in 27.0% versus 11.8% (P=0.323) of patients treated with LMWH qd or q12h, respectively. Notably, in the

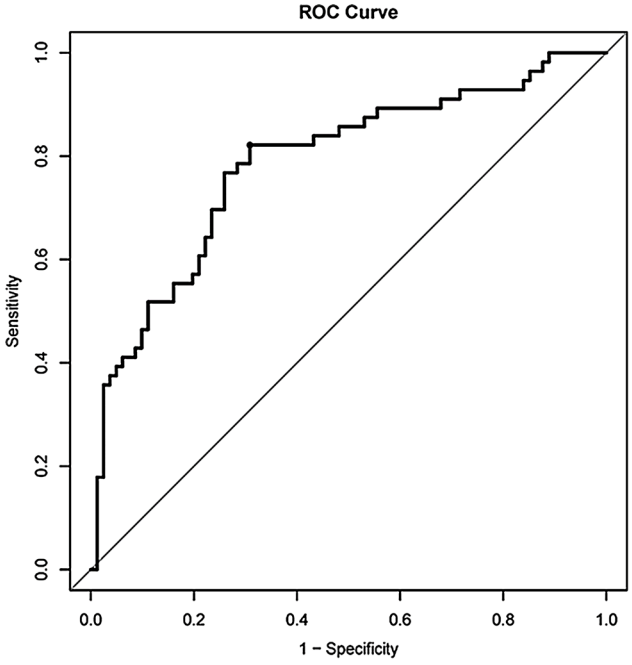

Fig. 6 ROC curve of DRNS model predicting the occurrence of DVT in retrospective study

Table 3 Incidence of DVT progression under different administration frequencies of LMWH

Groups	Non-DVT progression	DVT progression	*P* value
low-risk			0.323
LMWH qd	46 (73.0%)	17 (27.0%)	
LMWH q12h	15 (88.2%)	2 (11.8%)	
high-risk			**0.002**
LMWH qd	33 (40.2%)	49 (59.8%)	
LMWH q12h	15 (78.9%)	4 (21.1%)	

DVT: deep vein thrombosis; LMWH: low molecular weight heparin; qd: once daily; q12h: every 12 h

high-risk group, DVT progression was occurred in 59.8% versus 21.1% (relative risk of 2.838, $P=0.002$) of patients treated with LMWH qd or q12h, respectively (Table 3).

Discussion

Risk factors associated with lower extremity DVT

In the present study, six independent risk factors were identified for predictive model development of DVT in TPF patients, which included combined femoral fractures, age≥40 years, BMI≥24 kg/m^2, ISS, iCa-min, and FIB at admission, and these findings were in accordance with previous reports in general.

The risk of DVT for patients with fracture varies with different fracture location, and the patients with pelvic and femoral fractures usually undertook higher risk of DVT than those with fractures in other parts of the body [11]. The three predominant independent risk factors for DVT were slow blood flow, hypercoagulation and endovascular injury [12], which would explain the increased risk of DVT for patients with combined femoral fractures in the present study. The femur is the longest and thickest tubular bone in human body with high strength and toughness, so the energy of violence causing femoral fractures is usually higher than that causing fractures in other parts of the body. In addition, the intensive zone of blood vessels locates at the distal end of femur, and is easily involved in the endothelial injury of blood vessels when traumas occur. Meanwhile, the venous blood stasis caused by post-traumatic sickbed and immobilization, venous reflux influenced by the edema related to tissues injury and inflammation, and the imbalance between blood coagulation and fibrinolysis systems caused by trauma, synergistically contribute to the post-trauma hypercoagulable state to be prone to DVT [13, 14].

The present study indicated that ISS at admission was an independent risk factor for DVT in TPF patients, which is commonly adopted to evaluate the severity of traumatic patients in clinical practice [15]. The higher ISS is, the more severe a trauma is, and the more likely severe internal environment and coagulation disorder appear [16]. As a result, a large number of inflammatory factors would release into the blood, extensive vessel endothelial injury would occur, and subsequently the progression of DVT would be promoted [17].

The change with age in human body, such as decreased vascular wall elasticity and venous valve function, increased endothelial damage, blood viscosity and procoagulant substances, muscle relaxation and decreased pumping of lower extremity muscles, will increase the risk of DVT after fractures in the elderly [18, 19]. Several studies indicated that older age is an independent risk factor for DVT [20, 21]. However, it was still controversial in the threshold of age for increased DVT risk. It was reported that age>40 years was an independent risk factor of DVT [22], while another study indicated that patients with fractures over the age of 30 had a higher risk of DVT [23]. This study revealed that age≥40 years was an independent risk factor for DVT in TPF patients.

The patients with overweight and obesity who usually suffer from hyperlipidemia and atherosclerosis remain in a chronic inflammatory state for a long time, and are prone to be in a hypercoagulable state after trauma [19, 24]. For these patients, a decrease in venous valve function and hemodynamic abnormalities may be induced by less physical activity, and lower extremity venous blood flow stasis may be exacerbated by higher intra-abdominal pressure [25–27]. Hence, all these factors will increase the risk of post-traumatic DVT in such patients. Currently, several studies had addressed that increased BMI was an important risk factor for DVT [28, 29]. The Chinese guidelines consider BMI ranging from 24.0 to 28 kg/m^2 as overweight, and BMI no less than 28.0 kg/m^2 as obesity [30]. Therefore, in this study, the research

subjects were divided into two groups based on BMI of 24.0 kg/m^2, and the results indicated that BMI no less than 24.0 kg/m^2 was an independent risk factor for DVT in TPF patients, *OR*=1.546, 95% *CI* 1.101–2.171, *P*=0.012. Although people all over the world belong to Homo sapiens, there are still some subtle differences in physical constitutions among people in different regions. Therefore, it is necessary to adopt different BMI thresholds based on the actual situation in different countries.

This study found that iCa-min was an independent risk factor for DVT in TPF patients, *OR*=0.009, 95% *CI* 0.003–0.033, which meant that the level of ionized calcium (iCa) might be inversely associated with DVT. The iCa, also called coagulation factor IV, is involved in almost all stages of the coagulation process and essential for the activation of thrombin and the conversion of prothrombin to thrombin [31–33]. In the endogenous coagulation pathway, iCa could assist in activating factor XI, together with activated factor VIII and factor IX, it activates factor X. In the exogenous coagulation pathway, iCa activates factor X together with factor III and factor VII. In the common pathway, together with activated factor V and factor X, it could convert FIB into fibrin monomers. In addition, iCa can assist in activating factor XIII and continue to assist factor XIII in converting soluble fibrin monomers into stable fibrin polymers. The hypocalcemia caused by the loss of blood components (including iCa) related to traumatic bleeding is associated with coagulation disorders, transfusion volume, and mortality [34]. When a large amount of blood is transfused for bleeding control, the hypocalcemia will be aggravated by the chelation between calcium and citrate which was adopted as anticoagulant in stock blood products [35], which might worsen trauma-induced coagulopathy (TIC) [36]. The main manifestation of TIC can be either hypocoagulable state with haemorrhage or hypercoagulable state with thromboembolism [37]. The hypercoagulable state of TIC might occur in the acute or late stages of trauma, and is triggered by complex mechanism such as stress-induced endothelial damage, tissue damage, inflammatory reactions and excessive release of procoagulant substances. In addition, TIC is often accompanied with high fibrinogen concentration, high platelet reactivity, decreased anticoagulant activity, and fibrinolysis inhibition in lab test [38]. Therefore, the hypercoagulable state of TIC might increase the risk of lower extremity DVT in TPF patients. However, the association among hypocalcemia, TIC and DVT is still to be further verified in the future.

Fibrinogen, also known as coagulation factor I, is a glycoprotein synthesized and secreted in liver cells. As a soluble fibrin precursor, FIB plays a significant role in the coagulation process, and its deficiency or dysfunction would lead to bleeding and thrombotic clinical events [39, 40]. FIB can promote platelet aggregation, as well as the growth, proliferation, and contraction of smooth muscle and endothelial cells, thereby increasing blood viscosity and peripheral resistance [41]. FIB also can accelerate thrombus formation by promoting collagen synthesis, chemotactic migration of monocytes and macrophages to the endometrium [42]. Several studies showed that FIB is associated with venous thrombosis in a concentration-dependent manner, and the early monitoring of FIB is a good predictor of DVT [43, 44]. This study found a positive association between FIB within the acute phase at admission and preoperative lower extremity DVT in TPF patients. Of course, further research is still needed to verify the impact of FIB levels on trauma prognosis.

Clinical value of DRNS model

As mentioned above, according to the six independent risk factors determined by Lasso and multivariate logistic regression analysis, we developed a nomogram for predicting the risk of DVT (DRNS model), in which each risk factor had a corresponding score, and the total score was obtained to predict the probability of DVT for TPF patients.

The DRNS model showed superior performance with C-index (0.748 and 0.920, respectively) in either training or validation set, indicating that the model had moderate discrimination in predicting the probability of DVT. The calibration of DRNS model was also well addressed by the strong consistency between actual and calibration curve in the training and validation sets, respectively, as well as the Hosmer-Lemeshow goodness-of-fit test.

According to the cut-off value of DRNS model determined by ROC curve, in the present study, the prospective population with TPF were divided into low- and high-risk groups of DVT progression. There was no statistical significance in the incidence of DVT progression observed between different administration frequencies (qd or q12h) of LMWH (*P*=0.323) prophylactic treatment within low-risk group, whereas it was observed (*P*=0.002) within high-risk group. Due to the concern of bleeding in clinical practice, we would like to recommend individual administration frequency of LMWH prophylactic treatment for TPF patients according to the risk, which is predicted by some tools such as DRNS model.

Pelvic fracture patients are a high-risk group for DVT, and the usual intervention measures for this group include LMWH anticoagulant therapy and CUS examination. However, anticoagulant therapy and CUS examination will incur certain medical expenses. The CUS examination process may aggravate the pain at the fracture site of the patients. There will be certain medical risks during the transportation when leaving EICU. And anticoagulant therapy may also increase the risk of bleeding in important organs of the patients. Therefore, the

pros and cons should be carefully weighed before anticoagulant therapy and CUS examination are carried out for patients with pelvic fractures. Of course, whether it could reduce the risks and costs in the process of DVT examination and prevention, by using the DRNS model for quantitative analysis of the risk of DVT in the patients, prospective multicenter large sample studies are still needed.

There are several limitations in this study. First, it was a single-center study, and the DRNS model was developed in retrospective population. Second, although CUS has gradually replaced venous angiography and been widely used, this method is not the "golden standard" to detect DVT. Third, the sample size of the prospective cohort was small. Fourth, the controversy still existed in some risk factors for DVT which varied in the present and previous studies.

Conclusions

The present study identified six independent risk factors for DVT in TPF patients, and then develop a DRNS model for DVT risk prediction. The DRNS model might help clinicians to stratify the risk of DVT and determine the administration frequency of prophylactic LMWH for patients with TPF individually, which is worthy of further investigation in prospective clinical studies.

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Author contributions
D. C. S, Y. X. L contributed to study design, writing, review and editing, both of them have the same contribution to the paper. J. M. J. contributed to design, writing, review and funding acquisition. X. G. Z., M. F. L. contributed to data collection and analysis.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval
The studies were conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Sixth People's Hospital Affiliated to Shanghai Jiaotong University School of Medicine, with approval number 2022-KY-010 (K).

Competing interests
The authors declare no competing interests.

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