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Development and validation of preoperative proximal and distal lower limb deep vein thrombosis nomograms in geriatric hip fracture patients

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Abstract. – OBJECTIVE: This study aimed to develop and validate a risk nomogram for preoperative proximal and distal deep vein thrombosis (DVT) in geriatric patients with hip fractures.

PATIENTS AND METHODS: The 970 collected geriatric hip fracture patients were randomly divided into a training set (70%, n=682) and a validation set (30%, n=288). Multivariate logistic regression analyses were used to optimize the predictive risk variables for proximal and distal preoperative lower extremity DVT in the training set, respectively, and the selected variables were finally incorporated to establish preoperative DVT nomogram prediction models. Receiver operating characteristic curves (ROC), calibration plots, and decision curve analysis (DCA) were performed to validate the nomograms in the training and validation sets, respectively.

RESULTS: Among the 970 patients, 125 (12.88%) were diagnosed with preoperative DVT. The area under the curve (AUC) for predicting preoperative proximal DVT was 0.888 in the training and 0.792 in the validation sets. The AUC for predicting preoperative distal DVT was 0.907 in the training and 0.790 in the validation sets. The calibration plots and decision curve analysis for preoperative proximal DVT performed well in the training set and slightly worse in the validation set. The calibration plots and decision curve analysis for preoperative distal DVT performed well in both the training and validation sets.

CONCLUSIONS: To construct nomograms for predicting the risk of proximal and distal preoperative lower extremity DVT in geriatric hip fracture patients. For patients at high risk, as assessed by this model, clinicians should intervene and treat them promptly before surgery.

Key Words:
Hip fracture, Geriatric, Deep vein thrombosis, Nomogram.

Introduction

Hip fracture is a common orthopedic traumatic disease among the geriatric population[1]. According to epidemiological studies[2], the absolute number of hip fractures is currently increasing and is expected to reach 21 million cases by 2050. Due to the poor prognosis of hip fractures causes great inconvenience to patients' quality of life, and the mortality rate can reach between 22% and 30% within one year[3].

The high mortality rate associated with hip fractures is primarily attributed to the occurrence of related complications, among which venous thromboembolism (VTE) is a severe complication of hip fractures and is significantly associated with the incidence, recurrence risk, and mortality rate of pulmonary embolism (PE)[4]. According to reports[5], approximately 70% of patients who experience acute VTE events mainly develop lower limb DVT, while 30% of patients experience PE. Therefore, accurately understanding the risk factors for DVT and implementing early prevention of VTE is crucial in clinical practice. Previous studies[6] have indicated that 70% of VTE cases can be prevented with early intervention in clinical practice. Deep vein thrombosis (DVT) is not effectively controlled in the clinical outcomes of hip fracture patients due to various risk factors not being adequately considered, and clinicians' experience varies[7]. Therefore, to prevent the occurrence of DVT more effectively, literature has been focused on developing and establishing risk prediction models for DVT. Lately, most efforts have been concentrated on developing predictive models for postoperative DVT in hip fracture patients, while only a few studies[8,9] have focused on developing predictive models for preoperative DVT. However, these studies lack a defined and stratified approach to thrombus sites.

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Lower limb DVT can be classified into proximal deep vein thrombosis (PDVT) and distal deep vein thrombosis (DDVT) based on the location of thrombus formation[10]. Compared to PDVT, the incidence of adverse events is significantly lower in DDVT cases[11-13]. Research reports[5,14,15] suggest that anticoagulant therapy effectively prevents pulmonary embolism (PE) during hospitalization in PDVT patients, while it is unnecessary for DDVT patients. As only a minority of DDVT patients risk developing PDVT or PE, current guidelines recommend cessation of anticoagulation as the preferred strategy for DDVT patients[16,17]. However, none of the previous prediction models for DVT differentiate between thrombus sites, resulting in clinical practitioners not knowing whether the predicted thrombus is proximal or distal, thus generating incorrect clinical interventions for treatment.

In this study, we improved this deficiency by dividing preoperative lower extremity DVT into proximal and distal and establishing their nomograms separately, aiming to develop and validate a predictive model for preoperative DVT in geriatric hip fractures in a more comprehensive stratified manner, providing a valid reference for clinicians to identify and intervene early in preoperative DVT.

Patients and Methods

Patients

A total of 1,246 patients with hip fractures were diagnosed in our hospital from February 2016 to February 2023. Inclusion criteria were as follows: (1) age ≥60 years; (2) unilateral hip fracture diagnosed by clinical symptoms and imaging [including X-ray, computed tomography (CT), or magnetic resonance imaging (MRI)] or surgery by an orthopedic surgeon; (3) first surgery for ipsilateral hip fracture; and (4) perioperative ultrasound examination. Exclusion criteria were as follows: (1) age <60 years; (2) multiple fractures; (3) pathological or open fractures; (4) readmission or hospitalization less than two days; (5) lack of documented perioperative ultrasound examination of lower extremity veins; and (6) previous peripheral vascular disease and use of anticoagulant drugs before admission. Based on the above criteria, 276 patients were excluded. Finally, 970 patients were included in our study. The admission flow chart is shown in Figure 1.

This retrospective study was performed according to the guideline of Strengthening the Reporting of Cohort Studies in Surgery (STROCS) and following the Declaration of Helsinki of 1964 and its later amendments. The institutional review boards of the ethics committees approved this study.

Diagnosis of Preoperative DVT

Color Doppler ultrasonography is the gold standard for determining whether DVT has occurred in the lower extremity[18]. The lower extremity vessels screened were all lower extremity deep veins from the inguinal ligament to the ankle, with PDVT defined as thrombosis occurring in the iliac, femoral, or popliteal veins and DDVT defined as thrombosis occurring in the posterior or anterior tibial, gastrocnemius, peroneal or flounder veins[15]. All patients with hip fractures underwent routine ultrasound within 24 hours of admission and every 3-5 days while awaiting surgery. Experienced sonographers used color Doppler ultrasound to examine the lower extremity vessels and made a diagnosis based on imaging features, which was reviewed by a senior sonographer. Specific diagnostic criteria include: (1) the presence of abnormal echogenicity; (2) obstruction of the lumen or stenosis of an incompressible vein; (3) the absence of significant blood flow signal in the obstructed segment of the lumen; and (4) decreased blood flow distally compared to the proximal end of the obstructed lumen. According to the standard treatment protocol for hip fracture patients at our institution, all patients need to have the affected limb elevated upon admission to increase blood return and avoid thrombotic events. For patients diagnosed with preoperative DVT, the American College of Chest Physicians guidelines (ACCP: 2016, 10th edition)[19] were followed, and low-molecular heparin sodium (e.g., enoxaparin sodium, 100 IU/kg twice daily) is the drug of choice; for geriatric patients at high risk of thrombosis, we routinely use low-molecular heparin sodium (e.g., enoxaparin sodium, 4,000 IU once daily) for prophylaxis 24 hours after admission; for other general patients, we usually instruct patients to move the affected limb, drink plenty of fluids, and use intermittent pneumatic compression devices if necessary to prevent thrombosis.

Data Collection

Comparing the literature, 40 risk factors associated with lower extremity DVT were collected. Demographic characteristics included age, gender, whether smoking or drinking, hypertension, diabetes, cardiovascular disease, stroke, intracranial hemorrhage, chronic liver disease, chronic kidney disease, history of deep venipuncture, history of

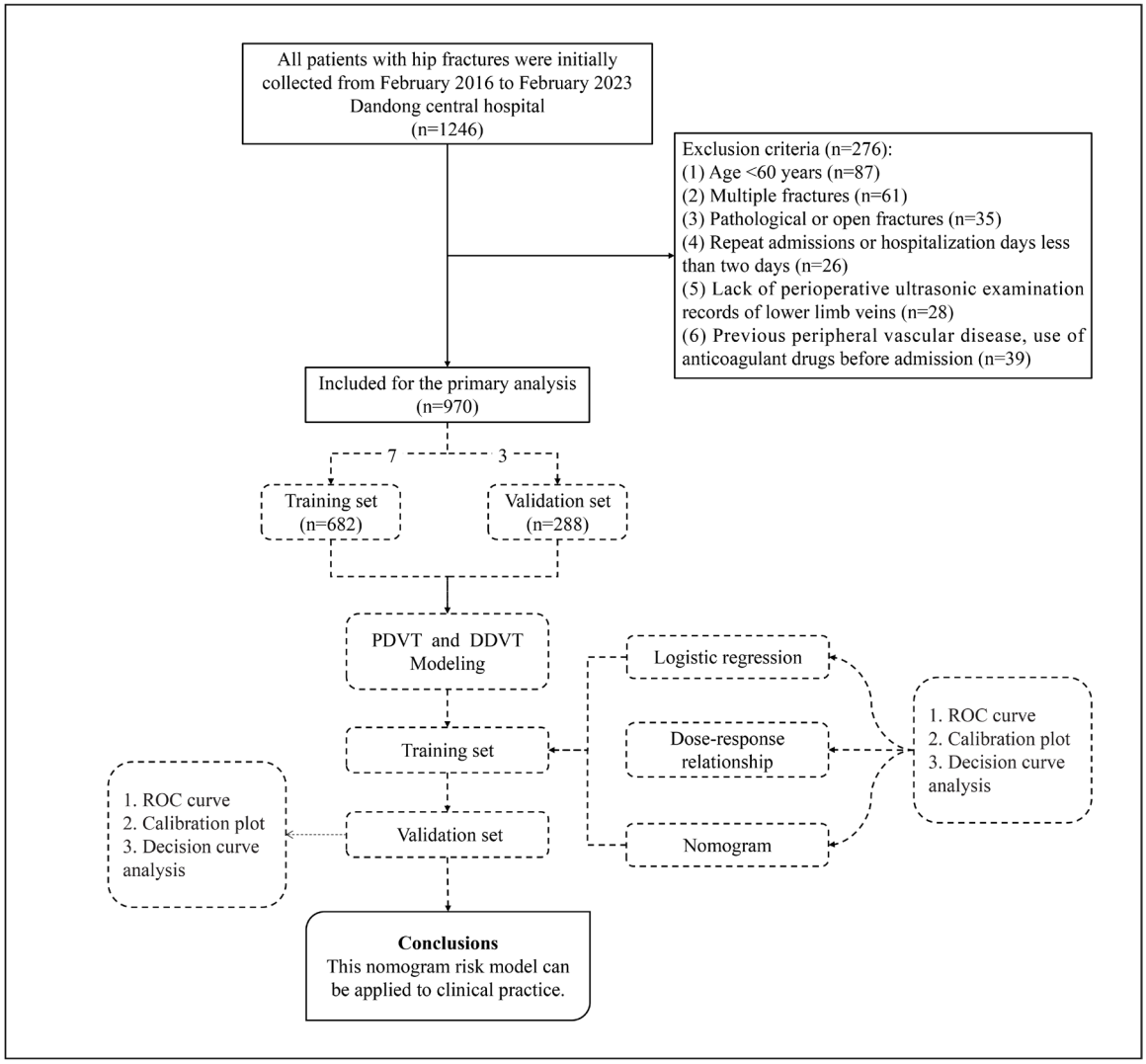

Figure 1. Flow chart of enrollment.

VTE, history of tumor, and readmission. The surgery-related indicators were fracture type, admission time, bedridden time, and American Society of Anesthesiologists physical status classification (ASA), where admission time was the time from injury to hospital admission, and bedridden time was the time from admission to surgery. Laboratory indices included red blood cell count, white blood cell count, platelet count, hemoglobin count, mean platelet volume, red blood cell distribution width, glucose value, creatinine, glutamate transaminase, glutamic oxalacetic transaminase, total protein, albumin, cholesterol, low-density lipoprotein, high-density lipoprotein, and triglycerides. Hematological indicators include fibrinogen, activated partial thromboplastin time, prothrombin time, thrombin time, and D-dimer.

To minimize interference with the patient's physiology due to medication or treatment measures after admission, all measurements were conducted within 24 hours of admission. Three rigorously trained researchers (WY, WYT, and WW) collected all data for this study from the institution's orthopedic clinical information database. Any discrepancies during the data collection process were resolved through discussions or by senior researchers (QML and WBD).

Statistical Analysis

Firstly, the dataset was randomly divided into a training set (70%, n=682) and a validation set (30%, n=288). The lower limb DVT was further classified into PDVT and DDVT. Categorical variables were presented as numbers and percentages

(%), and the Chi-square test was used to compare the groups. The Shapiro-Wilk test was used to assess the normality of continuous variables. Normally distributed continuous variables were expressed as mean ± standard deviation, and an independent samples *t*-test was used for between-group comparisons. Non-normally distributed continuous variables were presented as median ± interquartile range (IQR), and the Mann-Whitney U test was used for between-group comparisons. Two-sided *p*-values of less than 0.05 were considered statistically significant. Multiple imputation was used to handle missing values for all variables. Secondly, univariate logistic regression analysis was conducted for data reduction and variable selection. In the univariate logistic regression, confounding factors for PDVT and DDVT were adjusted ($p>0.1$), and variables with $p<0.10$ were selected for inclusion in the multivariate logistic regression. The multivariate logistic regression analysis established the final predictive model using variables with $p<0.05$. In our study, all selected variables were included in the model. Additionally, we analyzed the dose-effect relationships of crucial independent risk factors (D-dimer and bedridden time) with PDVT and DDVT. Finally, we assessed the accuracy of the two predictive models using the training and validation sets. ROC curves were plotted, and the area under the curve (AUC) was calculated to evaluate the discriminative ability and predictive accuracy of the nomograms. Calibration plots were generated to evaluate the calibration of the nomogram models. The clinical utility of the nomograms was evaluated through decision curve analysis (DCA). All statistical analyses were performed using SPSS software version 24.0 (IBM Corp, Armonk, NY, USA) and R software (version 4.0.3, R Foundation for Statistical Computing, USA).

Results

Characteristics of Patients

The study ultimately included 970 geriatric patients with hip fractures (365 males and 605 females). Among them, 125 patients (12.88%) had preoperative DVT. According to the 7:3 random allocation principle, the training set consisted of 682 patients (270 males and 412 females), and the validation set consisted of 288 patients (95 males and 193 females). All patients were divided into the DVT group and the non-DVT group. In the PDVT training set, patients in both groups were statistically significant regarding age, diabetes, chronic kidney disease, history of deep venipuncture, readmission, bedridden time, blood glucose level, and D-dimer. In the DDVT training set, patients in both groups were statistically significant regarding smoking, hypertension, diabetes, stroke, history of deep venipuncture, history of VTE, bedridden time, blood glucose level, and D-dimer. All data and clinical characteristics of the patients in both groups are shown in Table I.

Variables Selection in the Training Set

In the variable selection process for PDVT, based on a training set of 682 patients, we identified 9 potential predictors from 40 variables by univariate logistic regression analysis and then included these 9 predictors in the multivariate logistic regression, with 5 variables finally retained (Table II). Multivariate logistic regression analysis showed that diabetes (OR=3.34, 95% CI 1.21-9.27), readmission (OR=3.57, 95% CI 1.46-8.73), bedridden time (OR=1.13, 95% CI 1.02-1.25), glucose value (OR=1.14, 95% CI 1.03-1.28), and D-dimer (OR=1.08, 95% CI 1.01-1.15) were independent risk factors for preoperative PDVT formation in geriatric hip fracture patients (Table III).

Similarly, in the variable selection process for DDVT, we identified 10 potential predictors from 40 variables by univariate logistic regression analysis, and then 5 variables were finally retained by multivariate logistic regression analysis (Table IV). Multivariate logistic regression analysis showed that smoking (OR=2.87, 95% CI 1.38-5.97), diabetes (OR=2.58, 95% CI 1.16-5.73), history of VTE (OR=5.73, 95% CI 2.56-12.86), bedridden time (OR=1.24, 95% CI 1.14-1.35) and D-dimer (OR=1.18, 95% CI 1.12-1.24) were independent risk factors for preoperative DDVT formation in geriatric hip fracture patients (Table IV).

Figure 2 shows the dose-effect relationship between D-dimer and bedridden time with PDVT and DDVT. In PDVT, the incidence of PDVT in patients increased with increasing D-dimer (reference value: 3.7 mg/L) and bedridden time (reference value: 5 days) (Figure 2A and C). The predicted probability and observation rate of PDVT increased according to baseline D-dimer values and bedridden time (Figure 2B and D). Similarly, patients were at increased risk of DDVT with D-dimer values >3.8 mg/L and bedridden time >5 days (Figure 2E and G). The predicted and observed probability of DDVT increased according to baseline D-dimer values and bedridden time (Figure 2F and H).

Table I. Baseline data on risk factors for proximal and distal preoperative deep vein thrombosis in the training set.

Variables	PDVT			DDVT		
	Patients without DVT (n=654)	Patients with DVT (n=28)	*p*-value	Patients without DVT (n=621)	Patients with DVT (n=61)	*p*-value
Demographic						
Age, × years [median (IQR)]	76.00 (16.00)	79.00 (10.50)	0.038	76.00 (16.50)	77.00 (13.00)	0.419
Male gender (n, %)	263 (40.20)	7 (25.00)	0.107	241 (38.80)	29 (47.50)	0.183
Smoking (n, %)	129(19.70)	5 (17.90)	0.808	109 (17.60)	25 (41.00)	<0.001
Alcohol (n, %)	81 (12.40)	4 (14.30)	0.766	75 (12.10)	10 (16.40)	0.330
Hypertension (n, %)	348 (53.20)	13 (46.40)	0.481	330 (53.10)	41 (67.20)	0.035
Diabetes (n, %)	116 (17.70)	19 (67.90)	<0.001	141 (22.70)	32 (52.50)	<0.001
Cardiovascular disease (n, %)	182 (27.80)	9 (32.10)	0.619	195 (31.40)	20 (32.80)	0.824
Stroke (n, %)	171 (26.10)	10 (35.70)	0.262	157 (25.30)	24 (39.30)	0.018
Intracerebral hemorrhage (n, %)	34 (5.20)	2 (7.10)	0.652	29 (4.70)	4 (6.60)	0.512
Chronic liver disease (n, %)	36 (5.50)	1 (3.60)	0.658	34 (5.50)	3 (4.90)	0.855
Chronic kidney disease (n, %)	35 (5.40)	8 (1.20)	0.046	36 (5.80)	3 (4.90)	0.778
History of deep venipuncture (n, %)	8 (1.20)	4 (14.30)	0.011	7 (1.10)	3 (4.90)	0.019
History of VTE (n, %)	54 (8.30)	4 (14.30)	0.263	52 (8.40)	19 (31.10)	<0.001
Tumor (n, %)	57 (8.70)	1 (3.60)	0.339	53 (8.50)	5 (8.20)	0.928
Readmission (n, %)	177 (27.10)	18 (64.30)	<0.001	201 (32.40)	23 (37.70)	0.397
Operation						
Fracture type (n, %)						
Femoral neck fracture	348 (53.20)	19(69.9)	0.186	338 (54.40)	29 (47.50)	0.522
Intertrochanteric fracture	276 (42.20)	7 (25.00)		255 (41.10)	28 (45.90)	
Subtrochanteric fracture	30 (4.60)	2 (7.10)		28 (4.50)	4 (6.60)	
Admission time (n, %)						
<6h	334 (51.10)	16 (57.10)	0.302	325 (52.30)	25 (41.00)	0.165
6-24h	95 (14.50)	6 (21.40)		88 (14.20)	13 (21.30)	
>24h	225 (34.40)	6 (21.40)		208 (33.50)	23 (37.70)	
Bedridden time, ×days [median (IQR)]	5.00 (4.00)	9.00 (4.50)	<0.001	5.00 (4.00)	7.00 (4.00)	<0.001
ASA (n, %)						
III-IV	381 (58.30)	21 (75.00)	0.078	360 (58.0)	42 (68.90)	0.099
I-II	273 (41.70)	7 (25.00)		261 (42.0)	19 (31.10)	
Laboratory findings [median (IQR)]						
RBC count, × 10^9/L	3.94 (0.89)	4.07 (1.01)	0.372	3.95 (0.88)	3.89 (1.00)	0.929
WBC count, × 10^9/L	8.42 (3.53)	8.70 (2.85)	0.434	8.40 (3.45)	8.90 (3.70)	0.210
PLT count, × 10^9/L	193.00 (88.00)	200.00 (76.25)	0.793	194.00 (85.50)	186.00 (100.50)	0.942
HGB count, × g/L	121.00 (26.00)	120.50 (22.75)	0.695	121.00 (26.00)	121.00 (27.00)	0.686
MPV, × fl	8.50 (1.20)	8.50 (1.03)	0.800	8.50 (1.20)	8.80 (1.15)	0.270
RDW, × %	13.60 (1.20)	13.40 (1.08)	0.387	13.60 (1.20)	13.80 (1.25)	0.221
Blood glucose, × mmol/L	6.10 (2.20)	9.15 (8.03)	<0.001	6.00 (2.20)	8.40 (4.55)	<0.001
Cr, × μmol/L	62.00 (25.00)	69.50 (43.50)	0.157	62.00 (24.00)	66.00 (38.50)	0.065
ALT, × U/L	15.00 (10.00)	16.00 (8.00)	0.663	15.00 (10.00)	15.00 (14.00)	0.973
AST, × U/L	19.00 (10.00)	19.50 (6.00)	0.290	19.00 (9.00)	19.00 (10.50)	0.939
TP, × g/L	65.00 (8.00)	64.50 (12.50)	0.585	65.00 (9.00)	65.00 (8.00)	0.595
ALB, × g/dL	38.00 (6.00)	37.00 (6.75)	0.126	38.00 (6.00)	38.00 (5.00)	0.921
Cholesterol, × mmol/L	4.48 (1.48)	4.89 (1.53)	0.408	4.51 (1.41)	4.39 (1.72)	0.621
LDL, × mmol/L	2.73 (1.24)	2.90 (1.70)	0.462	2.74 (1.28)	2.75 (1.20)	0.748
HDL, × mmol/L	1.19(0.48)	1.20 (0.40)	0.970	1.19 (0.46)	1.18 (0.52)	0.926
TG, × mmol/L	1.20 (0.71)	1.34 (0.85)	0.155	1.20 (0.71)	1.21 (0.73)	0.589

(Table continued)

Table I *(continued)*. Baseline data on risk factors for proximal and distal preoperative deep vein thrombosis in the training set.

Variables	PDVT			DDVT		
	Patients without DVT (n=654)	Patients with DVT (n=28)	*p*-value	Patients without DVT (n=621)	Patients with DVT (n=61)	*p*-value
Hematology indicators [median (IQR)]						
FIB, × g/L	3.53 (1.26)	3.66 (1.07)	0.839	3.55 (1.22)	3.52 (1.31)	0.961
APTT, × sec	30.60 (5.15)	31.00 (6.35)	0.856	30.60 (5.10)	29.90 (5.60)	0.086
PT, × sec	12.40 (1.80)	12.65 (1.98)	0.280	12.40 (1.80)	12.60 (1.90)	0.521
TT, × sec	14.70 (2.30)	15.45 (3.05)	0.053	14.80 (2.20)	15.00 (3.60)	0.219
D-Dimer, × mg/L	3.62 (4.80)	9.45 (10.51)	<0.001	3.37 (4.80)	9.00 (15.04)	<0.001

The *p*-value indicates whether the difference between two sets of data for a certain indicator is statistically significant. DVT, Deep Vein Thrombosis; PDVT, Proximal Deep Vein Thrombosis; DDVT, Distal Deep Vein Thrombosis; IQR, Interquartile Range; ASA, American Society of Anesthesiologists physical status classification; RBC, Red blood cell; WBC, White blood cell; PLT, Platelet; HGB, Hemoglobin; MPV, Mean platelet volume; RDW, Red cell distribution width; Blood glucose, Blood glucose level; Cr, Creatinine; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; TP, Total protein; ALB, Albumin; Cholesterol, Cholesterol; LDL, Low-density lipoprotein; HDL, High-density lipoprotein; TG, Triglycerides; FIB, Fibrinogen; APTT, Activated partial thromboplastin time; PT, Prothrombin time; TT, Thrombin time.

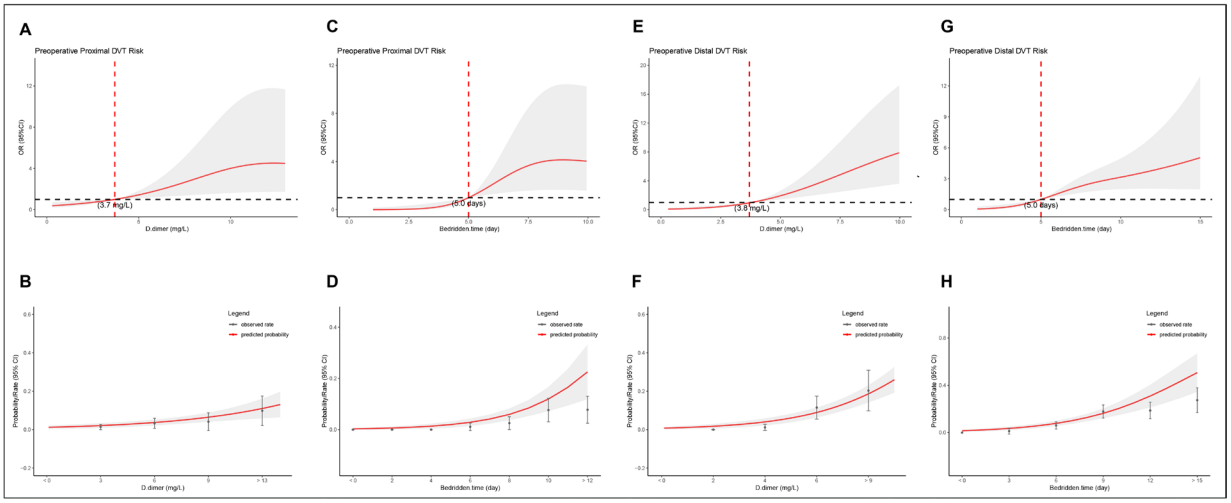

Figure 2. Multivariable adjusted odds ratio (OR) for preoperative PDVT according to levels of D-dimer (**A**), and bedridden time (**C**) on a continuous scale. Predicted probabilities and the observed rate of preoperative PDVT: Relationship between D-dimer (mg/L) and preoperative PDVT (**B**); Relationship between bedridden time (day) and preoperative PDVT (**D**). Multivariable adjusted odds ratio (OR) for preoperative DDVT according to levels of D-dimer (**E**), and bedridden time (**G**) on a continuous scale. Predicted probabilities and the observed rate of preoperative DDVT: Relationship between D-dimer (mg/L) and preoperative DDVT (**F**); Relationship between bedridden time (day) and preoperative DDVT (**H**). Solid red lines are multivariable-adjusted odds ratios, with a grey area showing 95% confidence intervals derived from restricted cubic spline regressions. The black dashed line indicates reference lines for no association at an odds ratio of 1.0.

Nomogram Model Development

Predictive models for PDVT and DDVT in geriatric hip fracture patients were developed based on the 7 predictable factors obtained from multivariate logistic regression analysis in Table IV and represented as nomograms (Figure 3A and C). For example, geriatric hip fracture patients admitted for the first time with diabetes mellitus, with no previous history of smoking or venous thromboembolism, with an admission measured glucose value of 5.2 mmol/L, a D-dimer value of 8.0 mg/L, and 6 days of preoperative bed rest, had a corresponding predicted risk of PDVT of 2.47% and a total score of 105 (Figure 3B); the predicted risk of DDVT was 8.60% and a total score of 106 points (Figure 3D).

Nomogram Model Validation

To assess the discriminative ability of the nomogram models, we calculated the area under

Table II. Multivariate analysis of preoperative PDVT.

	Univariate			Multivariate		
Characteristics	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**
Age, × years	1.04	1.00-1.09	0.043	1.01	0.95-1.06	0.861
Male gender	0.50	0.21-1.18	0.114			
Smoking	0.89	0.33-2.37	0.808			
Alcohol	1.18	0.40-3.49	0.766			
Hypertension	0.76	0.36-1.63	0.483			
Diabetes	9.79	4.32-22.19	<0.001	3.34	1.21-9.27	0.020
Cardiovascular disease	1.23	0.55-2.77	0.619			
Stroke	1.57	0.71-3.47	0.265			
Intracerebral hemorrhage	1.40	0.32-6.16	0.654			
Chronic liver disease	0.64	0.08-4.81	0.661			
Chronic kidney disease	2.95	0.97-8.96	0.057	2.68	0.73-9.85	0.139
History of deep venipuncture	6.21	1.26-30.71	0.025	3.91	0.44-34.64	0.220
History of VTE	1.85	0.62-5.53	0.270			
Tumor	0.39	0.05-2.91	0.357			
Readmission	4.85	2.20-10.71	<0.001	3.57	1.46-8.73	0.005
Fracture type	1.46	0.73-2.94	0.288			
Admission time	0.78	0.51-1.22	0.279			
Bedridden time, × days	1.24	1.14-1.35	<0.001	1.13	1.02-1.25	0.015
ASA	1.88	1.11-3.18	0.019	1.20	0.64-2.26	0.564
RBC count, × 10^9/L	1.47	0.83-2.61	0.191			
WBC count, × 10^9/L	1.10	0.97-1.24	0.150			
PLT count, × 10^9/L	1.00	0.99-1.00	0.615			
HGB count, × g/L	1.01	0.99-1.03	0.551			
MPV, × FL	1.06	0.76-1.49	0.723			
RDW, × %	0.88	0.66-1.17	0.377			
Blood glucose, × mmol/L	1.30	1.20-1.41	<0.001	1.14	1.03-1.28	0.014
Cr, × μmol/L	1.00	0.99-1.01	0.293			
ALT, × U/L	0.98	0.94-1.02	0.314			
AST, × U/L	0.97	0.93-1.02	0.228			
TP, × g/L	0.99	0.94-1.05	0.754			
ALB, × g/dL	0.95	0.87-1.02	0.160			
Cholesterol, × mmol/L	1.11	0.80-1.53	0.528			
LDL, × mmol/L	1.12	0.76-1.65	0.582			
HDL, × mmol/L	0.74	0.25-2.19	0.584			
TG, × mmol/L	1.06	0.72-1.54	0.777			
FIB, × g/L	0.94	0.65-1.36	0.744			
APTT, × sec	1.03	0.99-1.07	0.115			
PT, × sec	1.05	0.99-1.12	0.135			
TT, × sec	1.01	0.96-1.06	0.675			

ASA, American Society of Anesthesiologists physical status classification; RBC, Red blood cell; WBC, White blood cell; PLT, Platelet; HGB, Hemoglobin; MPV, Mean platelet volume; RDW, Red cell distribution width; Blood glucose, Blood glucose level; Cr, Creatinine; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; TP, Total protein; ALB, Albumin; Cholesterol, Cholesterol; LDL, Low-density lipoprotein; HDL, High-density lipoprotein; TG, Triglycerides; FIB, Fibrinogen; APTT, Activated partial thromboplastin time; PT, Prothrombin time; TT, Thrombin time.

the ROC curve (AUC). The AUC values for the PDVT and DDVT training sets were 0.888 and 0.907, respectively (Figure 4A and B). In the validation set, the AUC values were 0.792 for PDVT and 0.790 for DDVT (Figure 4C and 4D). These results indicate that both models have good predictive ability. The calibration plots for the PDVT and DDVT training sets demonstrate strong agreement between the predicted probabilities from the nomogram models and the actual probabilities (Figure 4E and F). This consistency between predicted and observed probabilities also exists in the validation set, although the range of predicted probabilities is narrower for PDVT compared to DDVT (Figure 4G and H). In the training set, the DCA of the nomogram model showed a net benefit in predicting the risk of PDVT using the nomogram model compared with no intervention

Table III. Multivariate analysis of risk factors for proximal and distal preoperative deep vein thrombosis in the training set.

DVT type	Variables	OR	95% CI	*p*-value
PDVT	Diabetes	3.34	1.21-9.27	0.020
	Readmission	3.57	1.46-8.73	0.005
	Bedridden time	1.13	1.02-1.25	0.015
	Blood glucose	1.14	1.03-1.28	0.014
	D-dimer	1.08	1.01-1.15	0.020
DDVT	Smoking	2.87	1.38-5.97	0.005
	Diabetes	2.58	1.16-5.73	0.020
	History of VTE	5.73	2.56-12.86	<0.001
	Bedridden time	1.24	1.14-1.35	<0.001
	D-dimer	1.18	1.12-1.24	<0.001

The *p*-value is used to determine whether a variable has statistical significance for the occurrence of DVT; DVT, Deep Vein Thrombosis; PDVT, Proximal Deep Vein Thrombosis; DDVT, Distal Deep Vein Thrombosis.

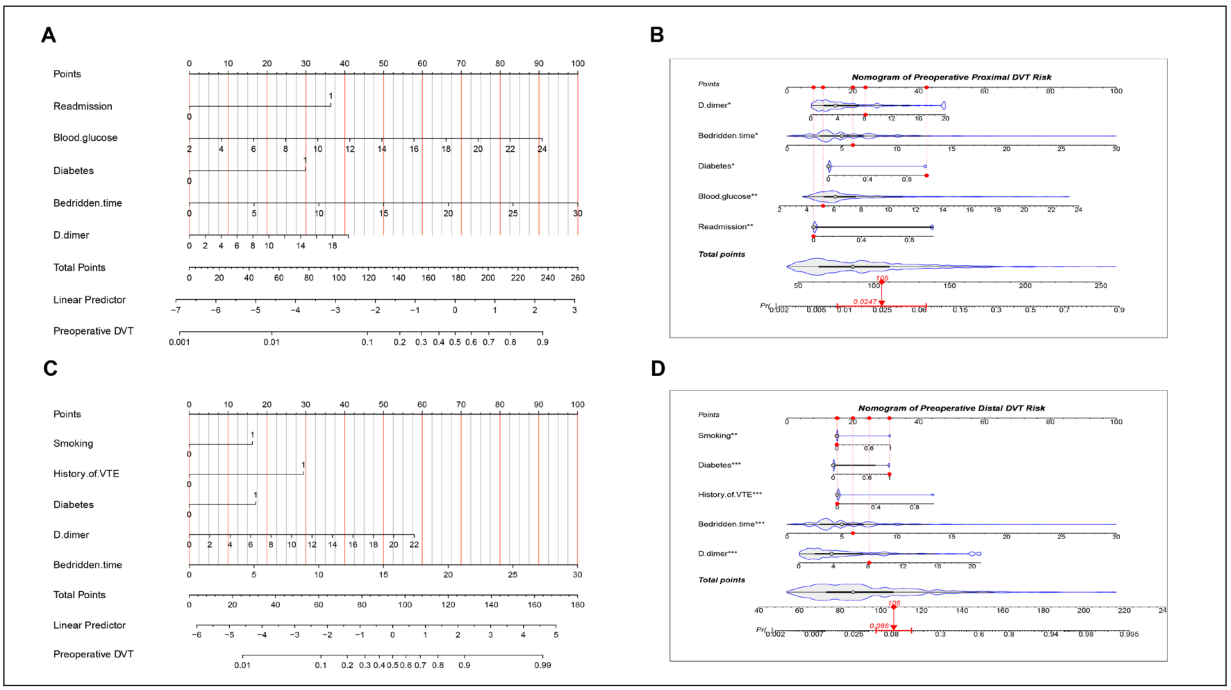

Figure 3. Nomogram for predicting preoperative PDVT in geriatric patients with hip fracture: Five variables were included in the nomogram prediction model, namely: readmission, blood glucose, diabetes, bedridden time, D-dimer (**A**); Dynamic nomogram as an example (**B**). Nomogram for predicting preoperative DDVT in geriatric patients with hip fracture: Five variables were included in the nomogram prediction model, namely: smoking, history of VTE, diabetes, bedridden time, D-dimer (**C**); Dynamic nomogram as an example (**D**).

when the threshold probability was in the range of 3-68% (Figure 4I); and a net benefit in predicting the risk of DDVT using the nomogram model compared with no intervention when the threshold probability was in the range of 9-78% (Figure 4J). In the validation set, patients with PDVT benefited from the nomogram when the threshold probability was 3-34% (Figures 4K); patients with DDVT benefited from the nomogram when the threshold probability was 9-92% (Figures 4L).

Discussion

With the continuous improvement of medical technology, the incidence of DVT is decreasing, but the risk of DVT in geriatric patients with hip fractures has not been reduced. Unlike previous studies[20-23] that focused on the risk factors for postoperative DVT, in recent years, more and more researchers have begun to pay more attention to the mechanisms and risk factors of preoperative

Table IV. Multivariate analysis of preoperative DDVT.

	Univariate			Multivariate		
Characteristics	**OR**	**95% CI**	***p*-value**	**OR**	**95% CI**	***p*-value**
Age, × years	1.01	0.98-1.04	0.435			
Male gender	1.43	0.84-2.42	0.185			
Smoking	3.26	1.88-5.66	<0.001	2.87	1.38-5.97	0.005
Alcohol	1.43	0.70-2.93	0.332			
Hypertension	1.81	1.04-3.16	0.037	1.08	0.53-2.21	0.829
Diabetes	3.29	1.93-5.63	<0.001	2.58	1.16-5.73	0.020
Cardiovascular disease	1.07	0.61-1.87	0.824			
Stroke	1.92	1.11-3.31	0.019	1.17	0.56-2.44	0.670
Intracerebral hemorrhage	1.43	0.49-4.22	0.514			
Chronic liver disease	0.89	0.27-3.00	0.855			
Chronic kidney disease	0.84	0.25-2.81	0.778			
History of deep venipuncture	4.54	1.14-18.02	0.032	2.59	0.40-16.78	0.320
History of VTE	4.95	2.69-9.13	<0.001	5.73	2.56-12.86	<0.001
Tumor	0.96	0.37-2.49	0.928			
Readmission	1.27	0.73-2.18	0.398			
Fracture type	0.78	0.51-1.20	0.257			
Admission time	1.21	0.91-1.60	0.202			
Bedridden time, × days	1.29	1.20-1.38	<0.001	1.24	1.14-1.35	<0.001
ASA	1.23	0.84-1.80	0.285			
RBC count, × 10^9/L	1.02	0.69-1.50	0.941			
WBC count, × 10^9/L	1.05	0.96-1.16	0.265			
PLT count, × 10^9/L	1.00	0.99-1.00	0.561			
HGB count, × g/L	1.00	0.99-1.01	0.667			
MPV, × FL	1.05	0.82-1.33	0.713			
RDW, × %	1.03	0.87-1.22	0.713			
Blood glucose, × mmol/L	1.23	1.15-1.32	<0.001	1.10	0.99-1.22	0.054
Cr, × μmol/L	1.00	0.99-1.00	0.979			
ALT, × U/L	1.00	0.99-1.01	0.944			
AST, × U/L	1.00	0.98-1.01	0.706			
TP, × g/L	0.99	0.96-1.03	0.763			
ALB, × g/dL	1.00	0.94-1.06	0.969			
Cholesterol, × mmol/L	0.98	0.78-1.23	0.842			
LDL, × mmol/L	1.08	0.82-1.41	0.604			
HDL, × mmol/L	1.37	0.69-2.71	0.368			
TG, × mmol/L	0.92	0.66-1.28	0.610			
FIB, × g/L	1.02	0.80-1.29	0.905			
APTT, × sec	0.94	0.89-1.00	0.049	0.96	0.90-1.02	0.210
PT, × sec	0.98	0.87-1.10	0.681			
TT, × sec	1.01	0.97-1.05	0.709			
D-Dimer, × mg/L	1.19	1.14-1.24	<0.001	1.18	1.12-1.24	<0.001

ASA, American Society of Anesthesiologists physical status classification; RBC, Red blood cell; WBC, White blood cell; PLT, Platelet; HGB, Hemoglobin; MPV, Mean platelet volume; RDW, Red cell distribution width; Blood glucose, Blood glucose level; Cr, Creatinine; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; TP, Total protein; ALB, Albumin; Cholesterol, Cholesterol; LDL, Low-density lipoprotein; HDL, High-density lipoprotein; TG, Triglycerides; FIB, Fibrinogen; APTT, Activated partial thromboplastin time; PT, Prothrombin time; TT, Thrombin time.

DVT[24-26]. However, no studies have stratified the location of the thrombus. Since PDVT is more harmful to patients and more likely to progress to PE, early anticoagulant therapy is meaningful[15]. As for DDVT, the American College of Chest Physicians (ACCP) suggests monitoring through continuous imaging instead of anticoagulant therapy[11,27]. Currently, most predictive models for preoperative DVT cannot determine whether the DVT is proximal or distal, leading to the overuse of anticoagulant therapy and imposing a more significant medical burden on patients. Therefore, stratified research on the location of the thrombus is necessary for clinical practice.

This study divided preoperative DVT into PDVT and DDVT and included more coagulation and immune-inflammatory response indicators. We used univariate logistic regression and

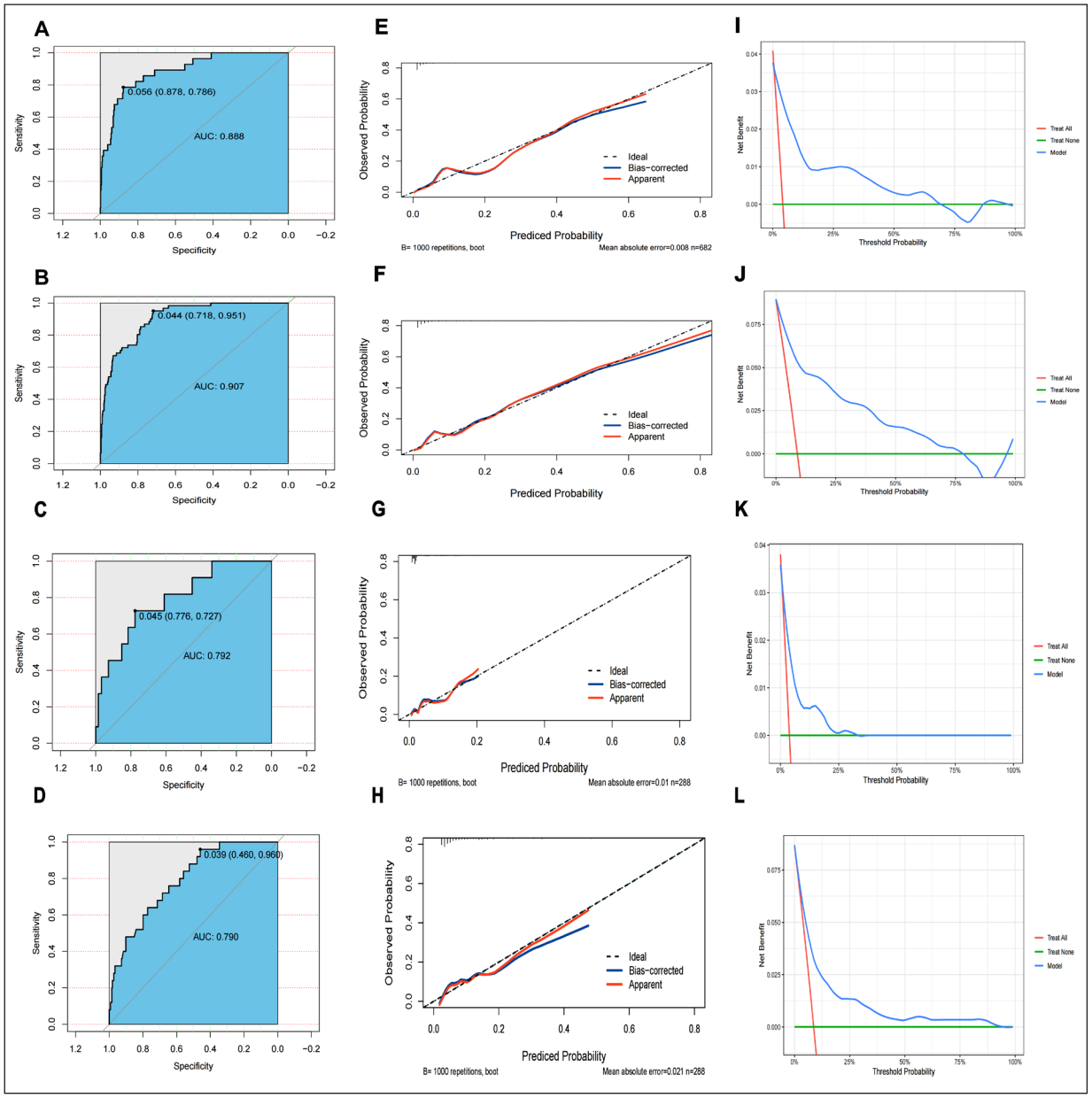

Figure 4. Receiver operating characteristic curves (ROC) for the nomogram in the preoperative PDVT (**A**) and preoperative DDVT training set (**B**). Calibration plot of the nomogram in the preoperative PDVT (**E**) and preoperative DDVT training set (**F**). Decision curve analysis of the nomogram in the preoperative PDVT (**I**) and preoperative DDVT training set (**J**). Receiver operating characteristic curves (ROC) for the nomogram in the preoperative PDVT (**C**) and preoperative DDVT validation set (**D**). Calibration plot of the nomogram in the preoperative PDVT (**G**) and preoperative DDVT validation set (**H**). Decision curve analysis of the nomogram in the preoperative PDVT (**K**) and preoperative DDVT validation set (**L**).

multivariate logistic regression analysis to identify predictive risk factors. According to the results of multivariate logistic regression, seven factors were identified as independent risk factors for preoperative DVT in geriatric hip fracture patients. Diabetes, readmission, blood glucose levels, bedridden time, and D-dimer were independently associated with PDVT, while diabetes, smoking, history of VTE, bedridden time, and D-dimer were independently associated with DDVT. Common factors between the two types of DVT were diabetes, bedridden time, and D-dimer.

Diabetes Mellitus

Hyperglycemia and insulin resistance are significant metabolic abnormalities in diabetes and have been implicated as antecedent states leading to thrombosis in diabetic patients[3]. Many studies[28,29]

have reported that diabetes is an independent risk factor for DVT formation; Jiao et al[28] observed that diabetic patients have a dramatically increased risk of DVT after surgery; Mraovic et al[29] reported a 3.2-fold increased risk of PE in diabetic patients compared to non-diabetic patients. The mechanisms by which diabetes contributes to the formation of DVT are diverse. Some studies[30] suggest that diabetes can cause endothelial dysfunction, induce inflammatory reactions, and promote a procoagulant state, leading to thrombus formation. Other research[28] indicates that diabetes exacerbates hemodynamic abnormalities, resulting in venous stasis and platelet adhesion. In patients with fractures, the inflammatory response inherent in the trauma, combined with the long-term exposure of vascular endothelial cells to elevated blood glucose, predisposes to apoptosis, which leads to DVT formation[31].

Bedridden Time

The pumping action of calf muscles plays an important role in lower extremity venous return; therefore, patients who are bedridden for a long time after hip fracture have significantly slower blood circulation and lower extremity venous return and reduced pumping function of lower extremity muscles, which increases the risk of DVT[32-34]. In the present study, the incidence of both PDVT and DDVT was significantly increased in patients who were bedridden for >5 days by dose-effect relationship, which is consistent with previous studies[32-34]. Overall, the risk of preoperative DVT increases with the duration of bed rest. Since bedridden time is an essential risk factor for preoperative DVT[33,34], prompt access to medical care to reduce bedridden time is critical.

D-dimer

As a degradation product of cross-linked fibrin, D-dimer is currently a practical biomarker used in the clinical diagnosis of adult disseminated intravascular coagulation (DIC) and VTE[35]. The diagnostic capability of D-dimer for DVT and PE has been extensively studied[36-38]. Lower levels of D-dimer may help exclude the formation of acute thrombi in a clinical setting. Surgical trauma patients are often tested for D dimer after admission to the hospital levels, and DVT is excluded when D-dimer levels are <500 ng/ml, with a negative predictive value of 98-99%[39]. Our study found that patients are at increased risk of preoperative PDVT and DDVT when D dimer levels are >3.7 mg/L. Therefore, attention should be paid to D-dimer admission monitoring in the clinic, and timely management decisions should be made.

Smoking

The contribution of smoking to DVT formation remains a controversial issue. Smoking increases oxidative stress and inflammation, promotes endothelial cell activation, alters endothelium-mediated control of vascular tone, increases hypercoagulability and platelet activation, and reduces fibrinolysis[40-42]. In contrast, Blondon et al[40] did not support a direct biological effect of smoking on the risk of thrombotic events. However, a recent large multicenter randomized study[41] confirmed the relationship between smoking and venous thrombotic events. In this regard, we believe that in our clinical work, we should distinguish between over-smoking and smoking, previous smoking that has been quit, and long-term smoking, and should focus on patients who are over-smokers and long-term smokers.

Readmission and History of VTE

There does not appear to be a clear correlation between readmission and DVT, but combining a history of VTE with readmission reveals that patients are at increased risk of VTE on readmission[43,44]. Patients with a previous history of VTE are more likely to develop a hypercoagulable state in a traumatic stress state, leading to a risk of DVT recurrence, as has been confirmed by several studies[45-47]. Combining a patient's medical history with other risk predictors can better predict the occurrence of preoperative DVT.

Blood Glucose Values

In this study, blood glucose values were an independent risk factor for preoperative PDVT. A recent retrospective study[48] also found that hyperglycemia was associated with the development of preoperative DVT. A sustained hyperglycemic state can lead to vascular endothelial cell damage, platelet adhesion and aggregation on damaged endothelial cells, and elevated fibrinogen levels, which disrupt the balance of the fibrinolytic-coagulation system, resulting in increased blood viscosity and blood in a hypercoagulable state[49]. Controlling the blood glucose level in admitted patients is beneficial in reducing the probability of thrombotic events.

Accurate identification of preoperative lower extremity DVT in elderly hip fracture patients through the use of nomograms can effectively improve patient prognosis and enable clinicians to be more vigilant for such diseases. Currently,

researchers are exploring the management of preoperative DVT in hip fracture patients, recognizing the importance of controlling preoperative DVT through enhanced screening, perioperative care, and timely surgery[50,51]. Additionally, several studies[52,53] have proposed an etiologic pathway for preventing hip fracture events, emphasizing fall prevention and improved balance in older adults. A recent study highlighted the potential of using a physical therapy robot to reduce the incidence of hip fractures by training older adults to improve endurance, perform daily activities independently, and prevent falls[54]. Accurate prognosis and identification of preoperative DVT can greatly facilitate communication between physicians and patients, particularly when involving the patient's family.

Limitations

The nomogram is a new, non-invasive visual prediction model widely used in clinical settings. Our study built a prediction model based on a training set and was successfully validated in a validation set. Compared with conventional prediction models based on laboratory indicators, all variables in this nomogram model are more readily available, facilitating clinicians' risk assessment of preoperative DVT in newly admitted patients. Based on the assessment results, interventions can be implemented for high-risk patients. This study also has several limitations: firstly, the number of thrombotic events in the validation set of PDVT was relatively small, which resulted in a suboptimal validation of the predictive model fitted in the training set. Secondly, this was a single-center retrospective study, and selection bias could only be avoided partially. Thirdly, although the nomogram model was validated in the validation set, the patient population may differ among different hospitals and regions, which may limit the generalizability of the nomogram to a few hospitals. Fourthly, our external validation was based on internally randomized data. We plan to collaborate with multiple hospitals to increase the sample size and optimize the nomogram model.

Conclusions

We developed and validated nomogram models for PDVT and DDVT with high accuracy to help orthopedic surgeons promptly assess the risk of preoperative DVT in geriatric hip fracture patients upon admission and improve early screening and intervention. For patients with PDVT, early use of anticoagulation therapy, and for patients with DDVT, continuous imaging monitoring is more effective than anticoagulation therapy.

Ethics Approval

The Institutional Review Board of Dandong Central Hospital approved the study (No. DDZX-20221201), which followed the principles of the Declaration of Helsinki of 1964 and its later amendments. The study exclusively collected clinical data while ensuring the exclusion of personal or identifiable information.

Informed Consent

Hence, considering the study's design and data characteristics, the IRB waived the necessity of obtaining informed consent.

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None.

Conflict of Interests

The authors declare no conflicts of interest.

Availability of Data and Materials

All data can be obtained from the corresponding author by reasonable request.

Authors' Contributions

Study concept: Q.-M. Lv and W.-B. Ding. Study design: All authors. Acquisition, analysis, or interpretation of data: W. Yao, W.-Y. Tang, and W. Wang. Statistical analysis: W. Yao. Drafting of the manuscript: W. Yao and W.-Y. Tang. Critical revision of the manuscript for important intellectual content: All authors.

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