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Original Article

Non-demographic dependent mechanisms of DVT formation in patients with traumatic limb fractures: an exploratory cohort study based on limited variable matching

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Abstract: Objective: To investigate the non-demographic mechanisms underlying deep vein thrombosis (DVT) formation in patients with traumatic limb fractures, with a focus on the roles of coagulation function and lipid metabolism-related biomarkers. Methods: This retrospective cohort study involved 856 patients who underwent surgical treatment for traumatic limb fractures at Xi'an International Medical Center Hospital from January 2020 to December 2023. Propensity score matching (PSM, 1:1, caliper = 0.02) was applied to control for confounding variables such as age and gender. Multivariate logistic regression analysis identified independent risk factors for DVT. Receiver operating characteristic (ROC) curve analysis was employed to determine optimal cutoff values for fibrinogen (FIB), D-dimer (D-D), triglycerides (TG), and high-density lipoprotein cholesterol (HDL-C). Statistical analyses were conducted using SPSS 27.0 and R 4.3.3. Results: After PSM (530 cases), multivariate analysis revealed that elevated FIB (OR = 5.022, 95% CI: 2.970-8.493), D-D (OR = 10.224, 95% CI: 6.026-17.346), TG (OR = 4.819, 95% CI: 2.893-8.027), and low HDL-C (OR = 0.107, 95% CI: 0.060-0.191) were independent risk factors for DVT (all $P < 0.001$). A history of diabetes was also significantly associated with increased DVT risk (OR = 4.718, $P < 0.001$). Conclusion: Hypercoagulability (elevated levels of FIB and D-D) and dyslipidemia (increased TG and reduced HDL-C) are key non-demographic contributors to DVT development following traumatic limb fractures. Diabetes further exacerbates thrombosis risk, indicating a synergistic effect.

Keywords: Traumatic limb fracture, deep vein thrombosis (DVT), coagulation function, lipid metabolism, propensity score matching (PSM)

Introduction

Traumatic limb fractures, caused by external forces or accidents, are among the most frequently encountered orthopedic conditions in clinical practice, ranging from simple fractures to complex, multi-fragmentary fractures [1, 2]. These fractures are often accompanied by severe pain, functional impairment, and prolonged rehabilitation. Complications such as infections and nerve damage may also occur in certain cases [3]. Surgical intervention is the mainstay of treatment, during which patients may remain bedridden for extended periods or rely on external fixation devices [4]. Deep vein thrombosis (DVT), one of the most common and severe complications following traumatic limb fractures, is a notable concern [5]. DVT not only hinders recovery but may also escalate into life-threatening conditions like pulmonary embolism (PE) [6]. Thus, elucidating the mechanisms of DVT in these patients and identifying effective preventive and therapeutic strategies are critical priorities in orthopedic research.

DVT is characterized by the formation of thrombi within deep veins, particularly of the lower limbs, and is most prevalent in patients with limited mobility or prolonged immobilization [7]. Patients with traumatic limb fractures are at heightened risk for DVT due to extended bed rest, surgical interventions, and venous return obstruction during fracture healing [8]. Thrombus dislodgement may result in PE,

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potentially leading to respiratory failure, cardiac arrest, or even death [9]. Beyond the risk of fatal complications, DVT also delays rehabilitation, extends hospital stay, and significantly increases healthcare costs [10]. Patients with DVT often require extended anticoagulation therapy and monitoring during treatment, significantly raising medical costs and adversely impacting quality of life and functional recovery [11]. Therefore, early risk identification and timely intervention for DVT are essential to prevent severe complications, accelerate the patient's recovery process, and reduce medical expenses.

Over the past decades, numerous studies have investigated traditional demographic factors related to DVT occurrence in patients with traumatic limb fractures, including age, gender, body mass index (BMI), and comorbidities such as hypertension and diabetes [12]. Research has shown that advanced age, higher BMI, and a history of hypertension or diabetes are commonly linked to an increased risk of DVT [13]. For example, elderly patients often experience reduced circulatory efficiency and venous return, predisposing them to thrombus formation [14]. However, despite the predictive value of these demographic factors, a substantial proportion of DVT cases occur in patients without these obvious demographic risks, highlighting the limitations of traditional predictive models and the need to explore additional contributing mechanisms [15].

The innovation of this study lies in its exploration of the non-demographic mechanisms underlying DVT formation in patients with traumatic limb fractures, with a particular focus on the effects of blood biomarkers (such as FIB, D-D, TG, and HDL-C) on DVT occurrence. Unlike traditional studies that primarily relied on demographic factors, this study focused on biomarkers related to coagulation function and lipid metabolism, offering a new perspective for DVT risk assessment. Furthermore, the use of propensity score matching (PSM) enhanced the robustness of our findings by minimizing confounding effects. Additionally, receiver operating characteristic (ROC) curve analysis was used to determine optimal biomarker thresholds, providing clinically applicable tools for early identification of high-risk patients.

Methods and materials

Sample size calculation

The sample size was estimated based on the reported incidence of postoperative DVT. According to a study by Bo et al. [16], the incidence of DVT in patients with traumatic fractures following surgery is approximately 22.7%. Using the standard sample size calculation formula ($N = Z^2 \times [P \times (1\text{-}P)]/E^2$), with a 95% confidence level ($Z = 1.96$), a margin of error of 5% ($E = 0.05$), and a DVT incidence of 22.7% ($P = 0.227$), the minimum sample size per group was calculated to be 270. This study enrolled 856 patients, meeting the minimum sample size requirement.

Sample source

A total of 856 patients who underwent surgical treatment for traumatic limb fractures at a tertiary hospital between January 2020 and December 2023 were included. Clinical and pathological data were retrospectively collected. This study was approved by the Ethics Committee of Xi'an International Medical Center Hospital.

Inclusion and exclusion criteria

Inclusion criteria: Age ≥ 18 years; Radiologically confirmed traumatic limb fractures (via X-ray, CT, or MRI); Complete medical records documenting fracture type, surgery time, Injury Severity Score (ISS), and coagulation/lipid biomarkers (FIB, D-D, TG, HDL-C).

Exclusion criteria: Concomitant head injury, thoracoabdominal organ injury, or severe multiple fractures (ISS score ≥ 30); Use of anticoagulant or antiplatelet agents (e.g., warfarin, aspirin) within 3 months prior to admission; History of malignancies, hereditary coagulopathy, or chronic kidney disease; Pregnant or menstruating women; Incomplete clinical data.

DVT definition

DVT was diagnosed based on the diagnostic criteria outlined in the *Diagnostic Criteria for Lower Limb Deep Vein Thrombosis* [17]. Within 14 days postoperatively, patients were closely monitored for signs suggestive of lower limb vascular compromise. If clinical symptoms such

as swelling, pain, increased skin temperature, skin discoloration, or a positive Homans' sign were observed, a color Doppler ultrasound was performed. A diagnosis of DVT was established if ultrasound showed venous dilation, low intraluminal echogenicity, and absent or deviated blood flow signals, after excluding other conditions such as acute arterial embolism, calf hematoma, or acute lymphangitis.

Patient grouping

Based on the diagnostic findings, patients were divided into two groups: the DVT group (265 patients) and the non-DVT group (591 patients).

Clinical data collection

Clinical data, including demographic variables, clinical characteristics, and biological markers, were collected from patients' electronic medical records.

Demographic information included age (≥ 40 years and < 40 years), gender (male, female), body mass index (BMI: < 22, 22-25, > 25), history of hypertension (yes, no), history of diabetes (yes, no), smoking history (< 10 cigarettes/day, ≥ 10 cigarettes/day), and alcohol consumption history (< 20 g/day, ≥ 20 g/day).

Trauma and treatment-related characteristics included surgery times (≥ 2 hours, < 2 hours), cause of injury (car accident, fall, other), fracture location (upper limb, lower limb, multiple sites), fracture type (open, closed), and injury severity score (ISS: ≥ 25, < 25) [18].

Laboratory indicators included coagulation parameters (prothrombin time [PT], activated partial thromboplastin time [APTT]), and serum biomarkers (fibrinogen [FIB], D-dimer [D-D], triglycerides [TG], total cholesterol [TC], high-density lipoprotein cholesterol [HDL-C], low-density lipoprotein cholesterol [LDL-C], C-reactive protein [CRP]).

All blood samples were collected upon admission, prior to surgery or any pharmacologic interventions, to ensure that baseline biomarker levels were accurately recorded.

Observation indicators

Primary outcomes: Identification of independent risk factors: Univariate and multivariate logistic regression analysis were performed to identify non-demographic independent risk factors for DVT formation in patients with traumatic limb fracture.

Secondary outcomes: Baseline characteristics (e.g., age, gender), clinical characteristics (e.g., surgery time, ISS score, fracture type), and laboratory indicators (e.g., FIB, D-D, TG, HDL-C) were compared between the Non-DVT and DVT patients. Additionally, ROC curve analysis was performed to determine the optimal cutoff values for FIB, D-D, TG, and HDL-C. Binary classification variables were derived accordingly, and their sensitivity, specificity, and area under the curve (AUC) values were calculated to assess discriminative power.

Statistical analysis

Statistical analyses were conducted using SPSS 27.0 and R 4.3.3 software. Kolmogorov-Smirnov test was employed to validate the normality of continuous variables. Data with a normal distribution were expressed as mean ± standard deviation (mean ± SD), and inter-group comparisons were performed using independent sample t-tests. Non-normally distributed data were expressed as median (interquartile range) [M (IQR)], and inter-group comparisons were conducted using the Mann-Whitney U test. Categorical data were described as frequency (percentage) [n (%)], and inter-group comparisons were conducted using the Chi-square (χ^2) test.

Significant variables identified in univariate analysis were entered into multivariate logistic regression (Enter method) to identify independent risk factors, with odds ratios (OR) and 95% confidence intervals (CIs) calculated. Propensity score matching (PSM) was performed using the *MatchIt* package in R, with a 1:1 nearest neighbor matching approach and a caliper width of 0.02. Matching variables included age and gender. Post-matching balance between groups was evaluated using the standardized mean difference (SMD), with SMD < 0.1 indicating acceptable balance.

ROC curve analysis was performed using the *pROC* package to calculate the area under the curve (AUC) and the optimal cutoff values (based on the maximum Youden index). Visualizations were generated using the ggplot2 pack-

Table 1. Comparison of clinical characteristics between DVT and Non-DVT groups in patients with traumatic limb fractures

Index	Total	DVT (n = 265)	Non-DVT (n = 591)	Statistic	*P* Value
Age (years)					
≥ 40	412 (48.13%)	146 (55.09%)	266 (45.01%)	7.455	0.006
< 40	444 (51.87%)	119 (44.91%)	325 (54.99%)		
Gender					
Male	507 (59.23%)	164 (61.89%)	343 (58.04%)	1.123	0.289
Female	349 (40.77%)	101 (38.11%)	248 (41.96%)		
BMI (kg/m^2)					
< 22	178 (20.79%)	66 (24.91%)	112 (18.95%)	10.821	0.004
22-25	491 (57.36%)	130 (49.06%)	361 (61.08%)		
> 25	187 (21.85%)	69 (26.04%)	118 (19.97%)		
History of Hypertension					
Yes	101 (11.80%)	42 (15.85%)	59 (9.98%)	6.050	0.014
No	755 (88.20%)	223 (84.15%)	532 (90.02%)		
History of Diabetes					
Yes	84 (9.81%)	37 (13.96%)	47 (7.95%)	7.466	0.006
No	772 (90.19%)	228 (86.04%)	544 (92.05%)		
Smoking History					
< 10 cigarettes/day	419 (48.95%)	135 (50.94%)	284 (48.05%)	0.611	0.434
≥ 10 cigarettes/day	437 (51.05%)	130 (49.06%)	307 (51.95%)		
Alcohol Consumption History					
< 20 g/day	196 (22.90%)	66 (24.91%)	130 (22.00%)	0.877	0.349
≥ 20 g/day	660 (77.10%)	199 (75.09%)	461 (78.00%)		
Surgery Time					
≥ 2 h	477 (55.72%)	170 (64.15%)	307 (51.95%)	11.047	< 0.001
< 2 h	379 (44.28%)	95 (35.85%)	284 (48.05%)		
Cause of Injury					
Car Accident	421 (49.18%)	132 (49.81%)	289 (48.90%)	0.928	0.629
Fall	224 (26.17%)	64 (24.15%)	160 (27.07%)		
Other	211 (24.65%)	69 (26.04%)	142 (24.03%)		
Fracture Location					
Upper Limb	295 (34.46%)	88 (33.21%)	207 (35.03%)	0.614	0.736
Lower Limb	419 (48.95%)	135 (50.94%)	284 (48.05%)		
Multiple	142 (16.59%)	42 (15.85%)	100 (16.92%)		
Fracture Type					
Open	483 (56.43%)	170 (64.15%)	313 (52.96%)	9.318	0.002
Closed	373 (43.57%)	95 (35.85%)	278 (47.04%)		
ISS Score					
≥ 25	325 (37.97%)	130 (49.06%)	195 (32.99%)	20.041	< 0.001
< 25	531 (62.03%)	135 (50.94%)	396 (67.01%)		
PT (s)	14.30 ± 1.98	14.24 ± 2.07	14.32 ± 1.93	0.520	0.603
APTT (s)	23.52 ± 4.21	23.48 ± 4.28	23.54 ± 4.18	0.211	0.833
FIB (g/L)	2.62 ± 0.96	3.17 ± 0.87	2.38 ± 0.90	-12.077	< 0.001
D-D (μg/mL)	0.77 (0.43)	1.06 (0.39)	0.66 (0.35)	16.151	< 0.001
TG (mmol/L)	1.26 ± 0.32	1.46 ± 0.29	1.17 ± 0.30	-13.192	< 0.001
TC (mmol/L)	3.80 ± 0.91	3.79 ± 0.94	3.81 ± 0.90	0.268	0.789
HDL-C (mmol/L)	1.95 ± 0.46	1.66 ± 0.42	2.08 ± 0.42	13.280	< 0.001

LDL-C (mmol/L)	2.18 (0.49)	2.18 (0.58)	2.18 (0.45)	0.173	0.863
CRP (mg/L)	13.24 ± 3.57	13.31 ± 3.43	13.20 ± 3.64	-0.417	0.677

Note: BMI: Body mass index, PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time, FIB: Fibrinogen, D-D: D-dimer, TG: Triglyceride, TC: Total Cholesterol, HDL-C: High-Density Lipoprotein Cholesterol, LDL-C: Low-Density Lipoprotein Cholesterol, CRP: C-Reactive Protein.

age. The correlation between variables was assessed using the *GGally* package to generate a matrix and calculate Pearson/Spearman correlation coefficients, with strong collinearity defined as $|r| \geq 0.7$. All tests were two-tailed, and $P < 0.05$ was considered statistically significant.

Results

Analysis of factors associated with DVT in patients with traumatic limb fracture

Significant differences were observed between the DVT group and the non-DVT group in terms of age (P = 0.006), BMI (P = 0.004), history of hypertension (P = 0.014), history of diabetes (P = 0.006), surgery time (P < 0.001), fracture type (P = 0.002), ISS score (P < 0.001), FIB (P < 0.001), D-D (P < 0.001), TG (P < 0.001), and HDL-C (P < 0.001). However, no significant differences were observed between the two groups in gender (P = 0.289), smoking history (P = 0.434), alcohol consumption (P = 0.349), cause of injury (P = 0.629), fracture site (P = 0.736), PT (P = 0.603), APTT (P = 0.833), TC (P = 0.789), LDL-C (P = 0.863), and CRP (P = 0.677) (P > 0.05) (**Table 1**).

Correlation analysis of DVT-related variables

Correlation analysis showed that none of the variable pairs had correlation coefficients exceeding 0.3, indicating generally weak linear relationships and the absence of significant multicollinearity. Therefore, all variables were retained for subsequent logistic regression analysis.

The strongest positive correlations were found between D-D and TG (r = 0.197, P < 0.001), FIB and D-D (r = 0.168, P < 0.001), and FIB and TG (r = 0.095, P = 0.005), suggesting moderate association between coagulation and lipid metabolism indicators. The most negative correlations were found between D-D and HDL-C (r = -0.212, P < 0.001), FIB and HDL-C (r = -0.15, P < 0.001), and TG and HDL-C (r = -0.177, P < 0.001), suggesting that HDL-C levels may have a negative correlation with coagulation and lipid-related indicators. The detailed data are shown in **Figure 1**. Overall, the weak correlations support the inclusion of these variables in multivariate analysis.

Univariate logistic regression analysis of DVT in patients with traumatic limb fracture

Variable assignments are detailed in **Table 2**. Univariate logistic regression analysis identified several variables significantly associated with DVT formation: age (P = 0.006, OR = 0.667), history of hypertension (P = 0.015, OR = 0.589), history of diabetes (P = 0.007, OR = 0.532), surgery time (P = 0.001, OR = 0.604), fracture type (P = 0.002, OR = 0.629), ISS score (P < 0.001, OR = 0.511), FIB (P < 0.001, OR = 2.738), D-D (P < 0.001, OR = 150.849), TG (P < 0.001, OR = 26.828), and HDL-C (P < 0.001, OR = 0.093). Specifically, older age (> 40 years), diabetes history, longer surgery time, open fractures, higher ISS score, higher levels of FIB, D-D, TG, and lower HDL-C were significantly associated with increased DVT risk (**Table 3**).

ROC curve analysis of FIB, D-D, TG, and HDL-C

To facilitate multivariate logistic regression analysis, FIB, D-D, TG, and HDL-C were converted into binary categorical variables using cutoff values derived from ROC curve analysis. The ROC curve analysis showed: FIB cut-off value = 2.505, AUC = 0.737, sensitivity = 79.2%, specificity = 56.2%; D-D cut-off value = 0.865, AUC = 0.845, sensitivity = 75.8%, specificity = 78.8%; TG cut-off value = 1.385, AUC = 0.755, sensitivity = 63.8%, specificity = 76.6%; HDL-C cut-off value = 1.725, AUC = 0.755, sensitivity = 63.4%, specificity = 18.1% (**Figure 2**).

Multivariate logistic regression analysis of DVT in patients with traumatic limb fractures

Multivariate logistic regression analysis identified FIB (P < 0.001, OR = 4.589), D-D (P < 0.001, OR = 11.222), TG (P < 0.001, OR =

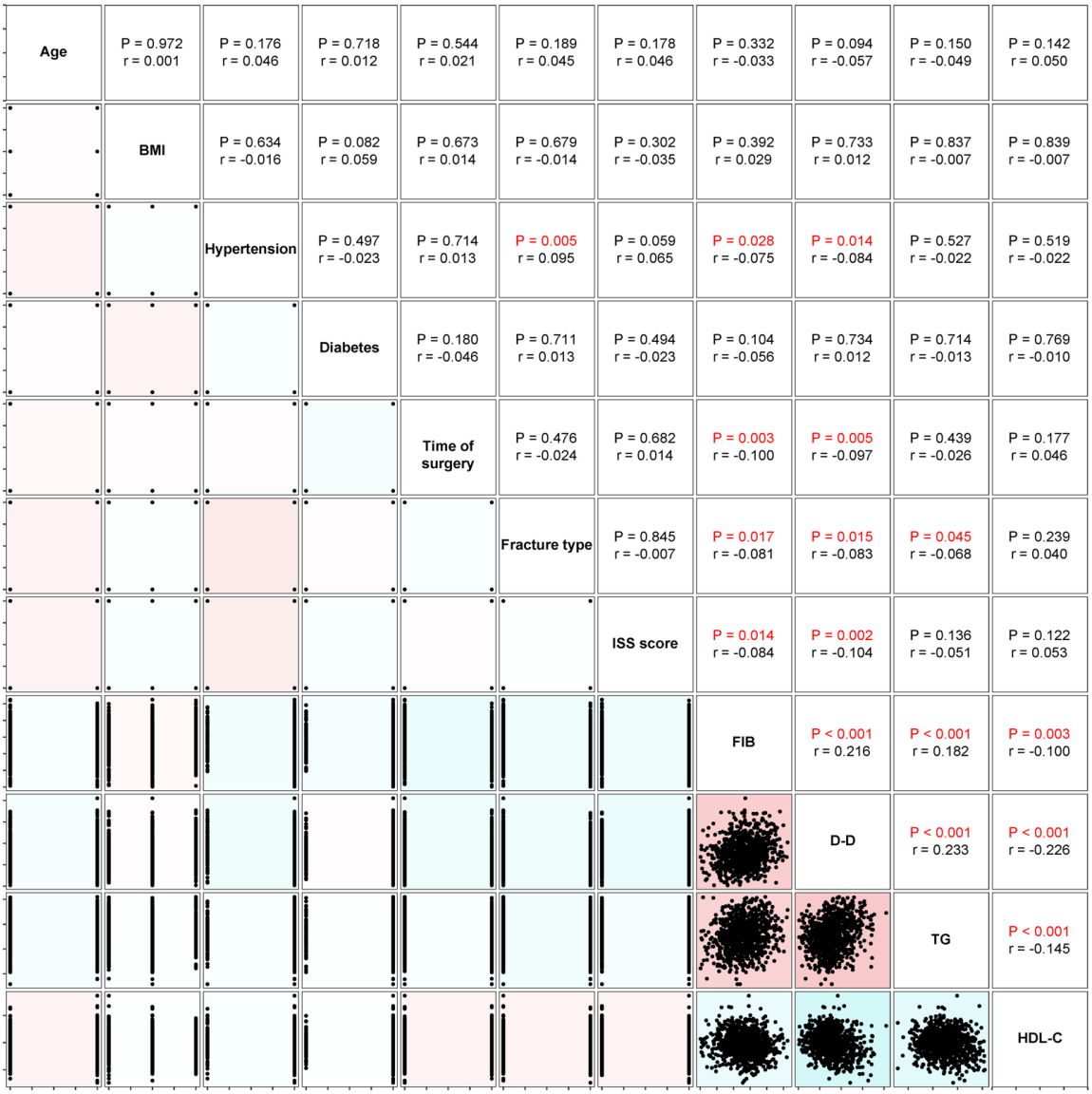


Figure 1. Correlation matrix of relevant variables. Note: BMI: Body Mass Index, ISS: Injury Severity Score, FIB: Fibrinogen, D-D: D-Dimer, TG: Triglyceride, HDL-C: High-Density Lipoprotein Cholesterol.

4.518), and HDL-C ($P < 0.001$, OR = 0.169) as independent predictors of DVT. Specifically, higher levels of FIB, D-D, and TG were significantly associated with an increased risk of DVT, while higher HDL-C levels were protective. Additionally, age ($P = 0.024$, OR = 0.631), diabetes history ($P = 0.002$, OR = 0.356), surgery time ($P = 0.022$, OR = 0.619), and ISS score ($P = 0.004$, OR = 0.557) also remained significantly associated with DVT (**Table 4**).

Propensity score matching (PSM) analysis: balancing DVT risk factors and covariates

To assess the impact of non-demographic mechanisms on DVT risk, PSM was conducted to match for age and gender. Before matching, significant differences in propensity score distributions were observed between the two groups. After matching, the distributions became comparable, indicating that PSM effectively balanced the covariates between the two groups (**Figure 3**). Post-matching evaluation showed that the SMDs for most covariates were close to zero, further confirming adequate balance between groups (**Figure 4**).

Comparison of clinical characteristics between DVT and non-DVT groups after matching

Following PSM, the DVT and non-DVT groups showed significant differences in several vari-

Table 2. Assignment table

Index	Index Type	Assignment
Age	(X)	≥ 40 = 1, < 40 = 2
BMI	(X)	< 22 = 1, 22-25 = 2, > 25 = 3
Hypertension	(X)	Yes = 1, No = 2
Diabetes	(X)	Yes = 1, No = 2
Time of Surgery	(X)	≥ 2 h = 1, < 2 h = 2
Fracture Type	(X)	Open = 1, Closed = 2
ISS Score	(X)	≥ 25 = 1, < 25 = 2
FIB (g/L)	(X)	Continuous variable using raw data
D-D (μg/mL)	(X)	Continuous variable using raw data
TG (mmol/L)	(X)	Continuous variable using raw data
HDL-C (mmol/L)	(X)	Continuous variable using raw data
DVT	(Y)	Yes = 1, No = 2

Note: DVT: Deep Vein Thrombosis, BMI: Body Mass Index, Hypertension, Diabetes, Time of Surgery, Fracture Type, ISS: Injury Severity Score, FIB: Fibrinogen, D-D: D-Dimer, TG: Triglyceride, HDL-C: High-Density Lipoprotein Cholesterol.

Table 3. Results of univariate Logistic regression analysis of DVT in patients with traumatic limb fractures

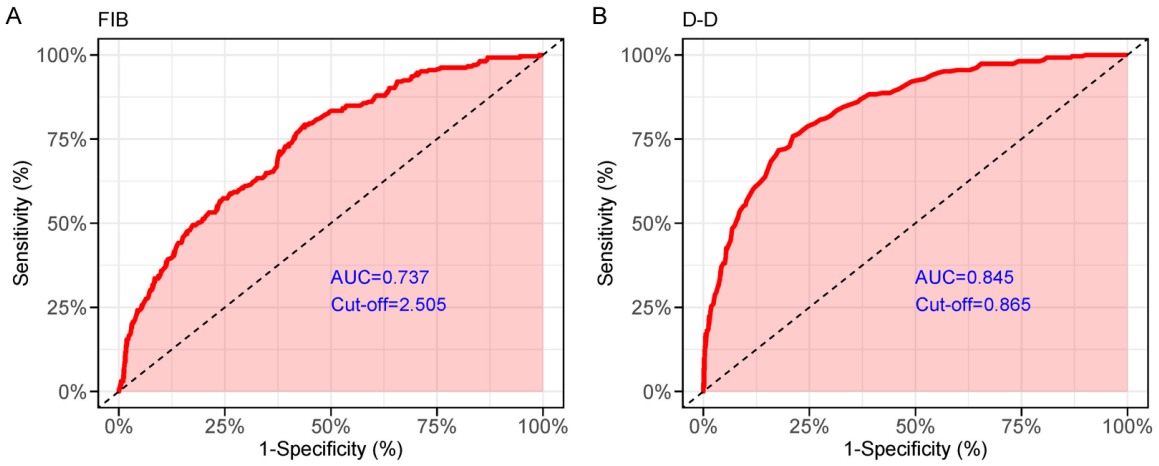
Index	Estimate	Std Error	*P* Value	OR	Lower	Upper
Age	-0.405	0.149	0.006	0.667	0.498	0.892
BMI	0.003	0.113	0.981	1.003	0.803	1.252
Hypertension	-0.530	0.217	0.015	0.589	0.386	0.905
Diabetes	-0.630	0.234	0.007	0.532	0.337	0.845
Time of surgery	-0.504	0.152	0.001	0.604	0.447	0.813
Fracture type	-0.463	0.152	0.002	0.629	0.466	0.847
ISS score	-0.671	0.151	0.000	0.511	0.380	0.687
FIB (g/L)	1.007	0.097	0.000	2.738	2.274	3.328
D-D (μg/mL)	5.016	0.374	0.000	150.849	74.388	322.780
TG (mmol/L)	3.289	0.297	0.000	26.828	15.190	48.815
HDL-C (mmol/L)	-2.374	0.214	0.000	0.093	0.060	0.140

Note: DVT: Deep Vein Thrombosis, BMI: Body Mass Index, ISS: Injury Severity Score, FIB: Fibrinogen, D-D: D-Dimer, TG: Triglyceride, HDL-C: High-Density Lipoprotein Cholesterol.

ables, including BMI (P = 0.030), diabetes history (P = 0.026), surgery time (P = 0.034), ISS score (P < 0.001), FIB (P < 0.001), D-D (P < 0.001), TG (P < 0.001), and HDL-C (P < 0.001). Specifically, the DVT group exhibited a higher prevalence of diabetes, elevated FIB, D-D, and TG levels, and lower HDL-C levels. Furthermore, the DVT group had a higher proportion of patients with an ISS score ≥ 25. Despite balancing for age and gender, these variables remained significantly different between groups, suggesting their strong association with DVT development. In contrast, no significant differences were observed in variables such as age, gender, smoking history, and alcohol consumption (P > 0.05) after matching, implying a limited role of these factors in DVT development (**Table 5**).

Correlation analysis of clinical variables after matching

Post-matching correlation analysis revealed consistently weak associations among clinical variables, with no correlation coefficient exceeding 0.3, indicating the absence of multicollinearity. The strongest positive correlations were observed between FIB and D-D (r = 0.284, P < 0.001), FIB and TG (r = 0.196, P < 0.001), and D-D and TG (r = 0.286, P < 0.001). Negative



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Youden Index	0.354
Accuracy	0.633
Precision	0.448
F1 Score	0.572

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Youden Index	0.547
Accuracy	0.779
Precision	0.617
F1 Score	0.680

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Accuracy	0.727
Precision	0.550
F1 Score	0.591

Parameter.type	Numeric.case
Specificity	0.181
Sensitivity	0.423
Youden Index	-0.396
Accuracy	0.256
Precision	0.188
F1 Score	0.260

Figure 2. ROC curves analysis for FIB, D-D, TG, and HDL-C. A. ROC Curve for FIB and its Classification Criteria. B. ROC Curve for D-D and its Classification Criteria. C. ROC Curve for TG and its Classification Criteria. D. ROC Curve for HDL-C and its Classification Criteria. Note: ROC: Receiver Operating Characteristic Curve, FIB: Fibrinogen, D-D: D-Dimer, TG: Triglyceride, HDL-C: High-Density Lipoprotein Cholesterol.

correlations were found between FIB and HDL-C ($r = -0.155$, $P < 0.001$), D-D and HDL-C ($r = -0.277$, $P < 0.001$), and TG and HDL-C ($r = -0.217$, $P < 0.001$), suggesting a negative correlation between HDL-C and coagulation and lipid-related indicators (**Figure 5**).

Table 4. Multivariate Logistic regression analysis of DVT in patients with traumatic limb fractures

Index	Estimate	Std Error	*P* Value	OR	Lower	Upper
Age	-0.460	0.204	0.024	0.631	0.423	0.940
Hypertension	-0.544	0.298	0.068	0.580	0.324	1.044
Diabetes	-1.033	0.332	0.002	0.356	0.185	0.682
Time of surgery	-0.479	0.210	0.022	0.619	0.409	0.932
Fracture type	-0.364	0.207	0.078	0.695	0.462	1.040
ISS score	-0.585	0.206	0.004	0.557	0.371	0.833
FIB (g/L)	1.524	0.214	0.000	4.589	3.033	7.031
D-D (μg/mL)	2.418	0.214	0.000	11.222	7.449	17.250
TG (mmol/L)	1.508	0.219	0.000	4.518	2.965	7.003
HDL-C (mmol/L)	-1.776	0.230	0.000	0.169	0.107	0.263

Note: DVT: Deep Vein Thrombosis, ISS: Injury Severity Score, FIB: Fibrinogen, D-D: D-Dimer, TG: Triglyceride, HDL-C: High-Density Lipoprotein Cholesterol.

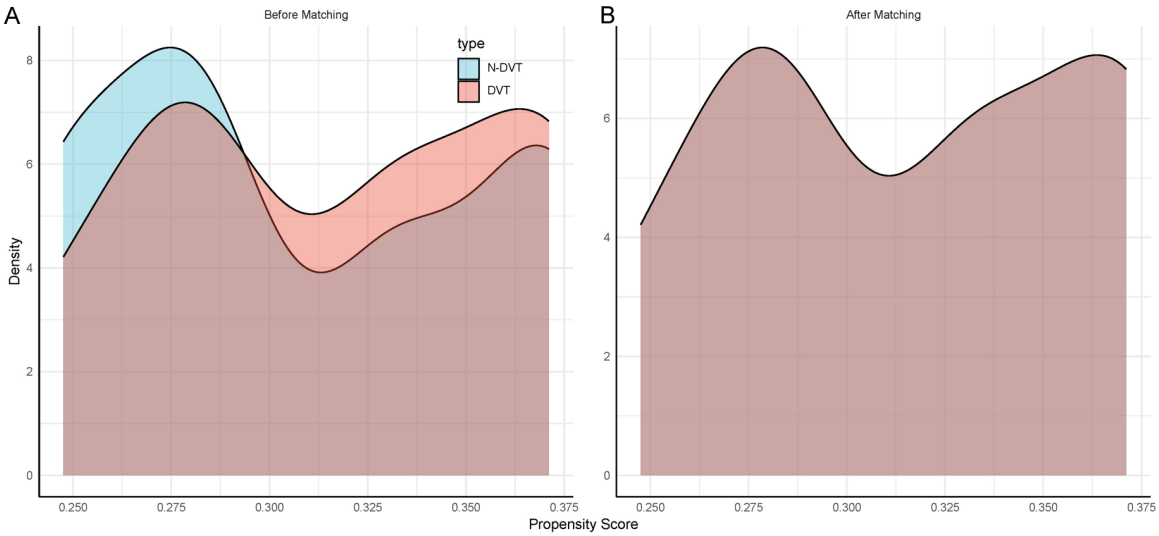


Figure 3. Propensity score distribution before and after PSM between DVT and Non-DVT groups. A. Propensity score distribution before PSM. B. Propensity score distribution after PSM. Note: PSM: Propensity Score Matching.

Univariate logistic regression analysis for DVT after PSM

Post-PSM variable assignments are detailed in **Table 6**. Univariate logistic regression analysis after PSM revealed that several variables remained significantly associated with DVT: diabetes history (P = 0.028, OR = 0.530), surgery time (P = 0.034, OR = 0.686), ISS score (P < 0.001, OR = 0.534), FIB (P < 0.001, OR = 2.994), D-D (P < 0.001, OR = 221.041), TG (P < 0.001, OR = 22.426), and HDL-C (P < 0.001, OR = 0.073). These results demonstrate that diabetes history, prolonged surgery, higher ISS scores, and higher levels of FIB, D-D, TG, and lower HDL-C are significantly related to the occurrence of DVT (**Table 7**).

ROC curve analysis of FIB, D-D, TG, and HDL-C after matching

To facilitate multivariate logistic regression analysis, FIB, D-D, TG, and HDL-C were again converted into binary classification variables using optimal cut-off values obtained from ROC analysis. The ROC curve analysis showed the following results (**Figure 6**): FIB cut-off value = 2.495, AUC = 0.748, sensitivity = 78.9%, specificity = 57.4%; D-D cut-off value = 0.805, AUC = 0.853, sensitivity = 76.2%, specificity = 78.1%; TG cut-off value = 1.385, AUC = 0.743, sensitivity = 63.8%, specificity = 74.7%; HDL-C cut-off value = 1.705, AUC = 0.775, sensitivity = 63.4%, specificity = 18.5%.

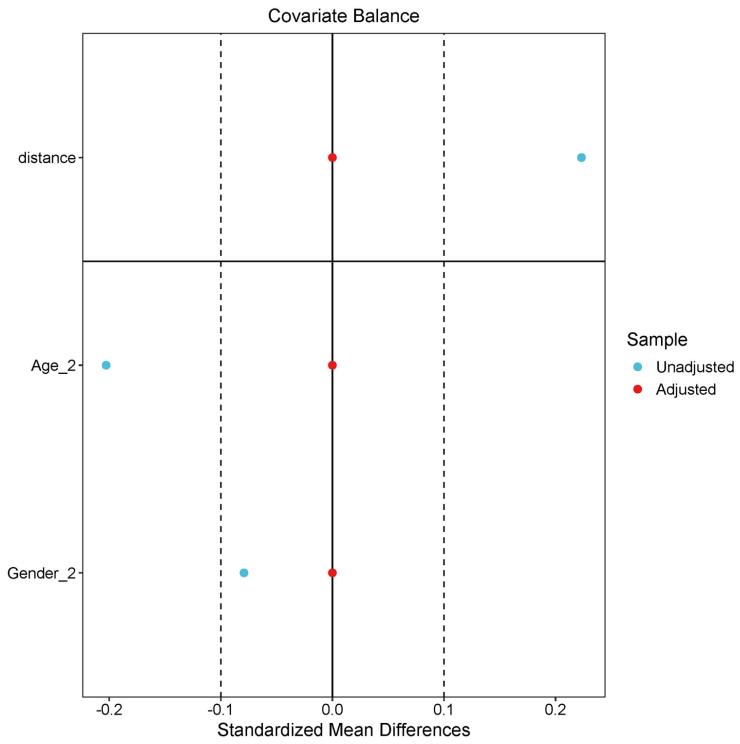


Figure 4. Covariate balance after PSM.

Multivariate logistic regression analysis of DVT after matching

Multivariate logistic regression analysis identified diabetes history ($P < 0.001$, OR = 4.718), FIB ($P < 0.001$, OR = 5.022), D-D ($P < 0.001$, OR = 10.224), TG ($P < 0.001$, OR = 4.819), and HDL-C ($P < 0.001$, OR = 0.107) as independent predictors for DVT. Elevated FIB, D-D, TG levels and decreased HDL-C levels were significantly associated with increased DVT risk. In contrast, surgery time ($P = 0.240$, OR = 1.360) and ISS score ($P = 0.170$, OR = 1.431) did not reach statistical significance in the adjusted model. These results further confirm the prominent role of coagulation dysfunction (FIB, D-D) and lipid metabolism abnormalities (TG, HDL-C) in DVT formation after traumatic limb fractures (**Table 8**).

Discussion

DVT is a globally prevalent condition characterized by the formation of thrombi in the deep venous system, most commonly in the lower extremities [13]. DVT not only causes discomfort and pain but can also lead to severe complications such as pulmonary embolism, posing a serious threat to patient safety. Early identification and effective prevention of DVT are vital in clinical practice, especially for high-risk populations such as trauma patients and those are bedridden for prolonged periods [19]. This study aimed to investigate the role of coagulation dysfunction and lipid metabolism disorders in the pathogenesis of DVT. By incorporating various biomarkers, this research seeks to improve the accuracy of DVT prediction. Through the analysis of relevant metabolic and physiological markers, we sought to deepen the understanding of the mechanistic basis of DVT development.

Coagulation dysfunction plays a critical role in the pathophysiology of DVT [20]. Elevated FIB and D-D reflect an overly active coagulation system and are closely associated with increased thrombotic risk [21]. Procoagulant factors released after trauma-induced tissue damage rapidly activate the extrinsic coagulation pathway, leading to fibrinogen generation and deposition, thereby promoting thrombus formation within the vascular system [22]. Song et al. [23] found a strong correlation between intraoperative and postoperative FIB elevation and DVT occurrence. High FIB levels enhance thrombus stability by facilitating fibrin deposition, enhancing DVT progression [24]. In patients with cervical cancer, elevated FIB levels were similarly associated with increased DVT risk [25].

D-D, a fibrin degradation product, reflects both clot formation and fibrinolysis. Elevated D-D levels are indicative of enhanced fibrin turnover and impaired thrombolysis. Hang et al. [26] found that elevated preoperative D-D levels were an independent risk factor for DVT occurrence. Beyond diagnosis, D-D levels also have prognostic utility in various diseases, such as COVID-19, where they correlate with thromboinflammatory burden and disease severity [27]. Elevated D-D may also indicate impaired thrombus dissolution capacity, contributing to clot persistence and increased embolic risk [28, 29]. Additionally, Navarrete et al. [30] dem-

Table 5. Comparison of clinical characteristics between DVT group and non-DVT group after PSM

Index	Total	DVT (n = 265)	Non-DVT (n = 265)	Statistic	*P* Value
Age (years)					
≥ 40	292 (55.09%)	146 (55.09%)	146 (55.09%)	< 0.001	1.000
< 40	238 (44.91%)	119 (44.91%)	119 (44.91%)		
Gender					
Male	328 (61.89%)	164 (61.89%)	164 (61.89%)	< 0.001	1.000
Female	202 (38.11%)	101 (38.11%)	101 (38.11%)		
BMI (kg/m^2)					
< 22	120 (22.64%)	66 (24.91%)	54 (20.38%)	7.003	0.030
22-25	290 (54.72%)	130 (49.06%)	160 (60.38%)		
> 25	120 (22.64%)	69 (26.04%)	51 (19.25%)		
History of Hypertension					
Yes	70 (13.21%)	42 (15.85%)	28 (10.57%)	3.226	0.072
No	460 (86.79%)	223 (84.15%)	237 (89.43%)		
History of Diabetes					
Yes	58 (10.94%)	37 (13.96%)	21 (7.92%)	4.956	0.026
No	472 (89.06%)	228 (86.04%)	244 (92.08%)		
Smoking History					
< 10 cigarettes/day	264 (49.81%)	135 (50.94%)	129 (48.68%)	0.272	0.602
≥ 10 cigarettes/day	266 (50.19%)	130 (49.06%)	136 (51.32%)		
Alcohol Consumption History					
< 20 g/day	127 (23.96%)	66 (24.91%)	61 (23.02%)	0.259	0.611
≥ 20 g/day	403 (76.04%)	199 (75.09%)	204 (76.98%)		
Surgery Time					
≥ 2 h	316 (59.62%)	170 (64.15%)	146 (55.09%)	4.514	0.034
< 2 h	214 (40.38%)	95 (35.85%)	119 (44.91%)		
Cause of Injury					
Car Accident	263 (49.62%)	132 (49.81%)	131 (49.43%)	2.345	0.310
Fall	141 (26.60%)	64 (24.15%)	77 (29.06%)		
Other	126 (23.77%)	69 (26.04%)	57 (21.51%)		
Fracture Location					
Upper Limb	187 (35.28%)	88 (33.21%)	99 (37.36%)	1.936	0.380
Lower Limb	254 (47.92%)	135 (50.94%)	119 (44.91%)		
Multiple	89 (16.79%)	42 (15.85%)	47 (17.74%)		
Fracture Type					
Open	323 (60.94%)	170 (64.15%)	153 (57.74%)	2.291	0.130
Closed	207 (39.06%)	95 (35.85%)	112 (42.26%)		
ISS Score					
≥ 25	220 (41.51%)	130 (49.06%)	90 (33.96%)	12.434	< 0.001
< 25	310 (58.49%)	135 (50.94%)	175 (66.04%)		
PT (s)	14.28 ± 2.04	14.24 ± 2.07	14.32 ± 2.02	0.415	0.679
APTT (s)	23.45 ± 4.22	23.48 ± 4.28	23.42 ± 4.17	-0.161	0.872
FIB (g/L)	2.76 ± 0.95	3.17 ± 0.87	2.35 ± 0.86	-10.978	< 0.001
D-D (μg/mL)	0.86 ± 0.35	1.07 ± 0.30	0.65 ± 0.26	-16.983	< 0.001
TG (mmol/L)	1.32 ± 0.33	1.46 ± 0.29	1.19 ± 0.30	-10.726	< 0.001
TC (mmol/L)	3.82 ± 0.92	3.79 ± 0.94	3.84 ± 0.91	0.683	0.495
HDL-C (mmol/L)	1.88 ± 0.46	1.66 ± 0.42	2.10 ± 0.39	12.373	< 0.001
LDL-C (mmol/L)	2.19 ± 0.38	2.20 ± 0.41	2.19 ± 0.36	-0.228	0.820

CRP (mg/L)	13.37 ± 3.56	13.31 ± 3.43	13.43 ± 3.70	0.396	0.692

Note: BMI: Body mass index, PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time, FIB: Fibrinogen, D-D: D-dimer, TG: Triglyceride, TC: Total Cholesterol, HDL-C: High-Density Lipoprotein Cholesterol, LDL-C: Low-Density Lipoprotein Cholesterol, CRP: C-Reactive Protein, PSM: Propensity Score Matching.

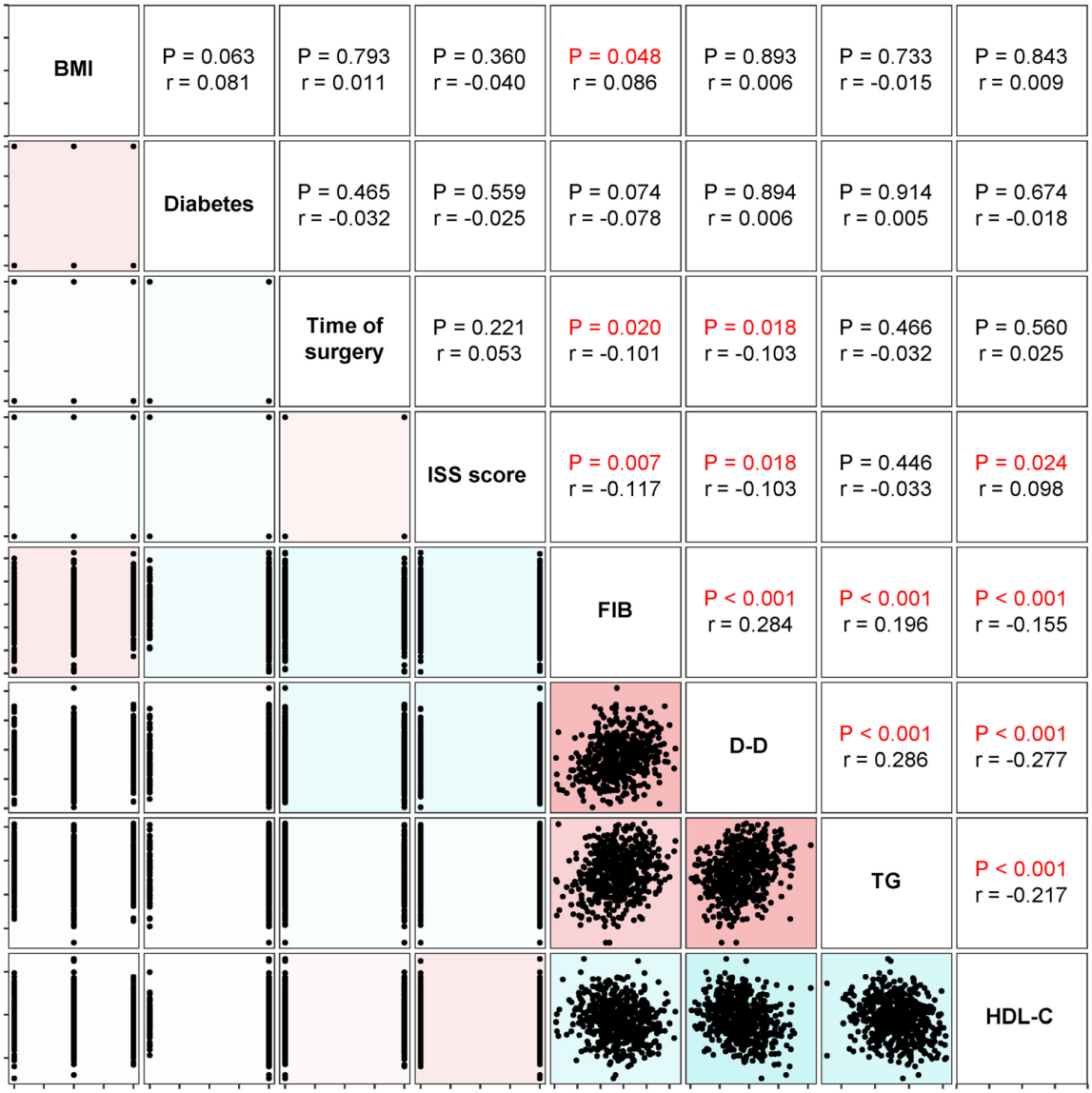


Figure 5. Correlation matrix of clinical variables after PSM. Note: BMI: Body Mass Index, ISS: Injury Severity Score, FIB: Fibrinogen, D-D: D-Dimer, TG: Triglyceride, HDL-C: High-Density Lipoprotein Cholesterol, PSM: Propensity Score Matching.

onstrated that the development of DVT involves platelets and leukocytes activating coagulation through tissue factor expression and neutrophil extracellular traps (NETs), a mechanism consistent with our findings. Moreover, Kaiser et al. [31] showed that procoagulant platelets play a critical role in DVT, and their inhibition can alleviate thrombus formation, providing new cellular-level evidence for coagulation mechanisms. Additionally, literature shows that in patients with spinal fractures, abnormal D-D levels are significantly associated with the risk of DVT [32], suggesting the role of dissolution imbalance.

Table 6. Assignment table (After PSM)

Index	Index type	Assignment content
BMI	(X)	< 22 = 1, 22-25 = 2, > 25 = 3
Diabetes	(X)	Yes = 1, No = 2
Time of surgery	(X)	≥ 2 h = 1, < 2 h = 2
ISS score	(X)	≥ 25 = 1, < 25 = 2
FIB (g/L)	(X)	Continuous variable using raw data
D-D (μg/mL)	(X)	Continuous variable using raw data
TG (mmol/L)	(X)	Continuous variable using raw data
HDL-C (mmol/L)	(X)	Continuous variable using raw data
DVT	(Y)	Yes = 1, No = 2

Note: DVT: Deep Vein Thrombosis, BMI: Body Mass Index, ISS: Injury Severity Score, FIB: Fibrinogen, D-D: D-Dimer, TG: Triglyceride, HDL-C: High-Density Lipoprotein Cholesterol, PSM: Propensity Score Matching.

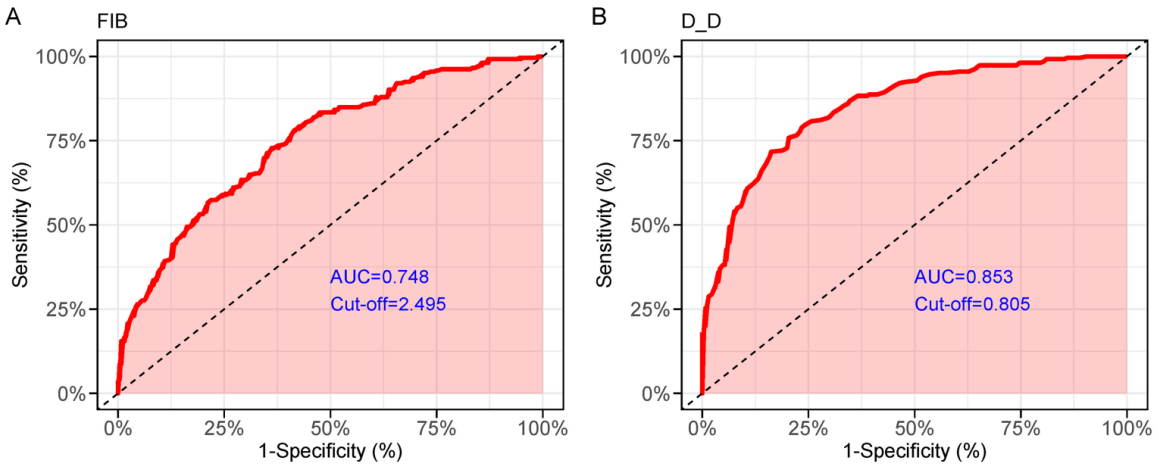
Table 7. Univariate Logistic regression analysis of DVT in patients with traumatic limb fractures (After PSM)

Index	Estimate	Std Error	*P* Value	OR	Lower	Upper
BMI	0.050	0.129	0.699	1.051	0.816	1.355
Diabetes	-0.634	0.288	0.028	0.530	0.297	0.925
Time of surgery	-0.377	0.178	0.034	0.686	0.483	0.971
ISS score	-0.627	0.179	< 0.001	0.534	0.376	0.757
FIB (g/L)	1.097	0.121	< 0.001	2.994	2.380	3.822
D-D (μg/mL)	5.398	0.481	< 0.001	221.041	89.920	593.729
TG (mmol/L)	3.110	0.347	< 0.001	22.426	11.582	45.291
HDL-C (mmol/L)	-2.622	0.269	< 0.001	0.073	0.042	0.121

Note: DVT: Deep Vein Thrombosis, BMI: Body Mass Index, ISS: Injury Severity Score, FIB: Fibrinogen, D-D: D-Dimer, TG: Triglyceride, HDL-C: High-Density Lipoprotein Cholesterol, PSM: Propensity Score Matching.

Lipid metabolism disorders contribute to the pathogenesis of DVT through complex and multifactorial mechanisms [33]. Elevated triglycerides (TG) not only reflect abnormal lipid metabolism but may also promote thrombus formation through multiple mechanisms [34]. First, high TG levels can trigger an inflammatory response, prompting endothelial cells to release procoagulant substances such as prothrombin activator, accelerating the coagulation process [35]. For example, Tang et al. [36] found a significant association between high TG levels and DVT occurrence. In addition, Spasić et al. [37] reported that type IIa hyperlipoproteinemia (hypercholesterolemia) is associated with a nearly double increased risk for DVT (OR 1.99), further highlighting the importance of lipid metabolism disorders in DVT. Furthermore, high TG may induce oxidative stress and endothelial dysfunction, both of which are critical facilitators of thrombus formation. In contrast, low HDL-C levels may weaken its protective effect on the vascular endothelium, making the vessel wall more susceptible to damage, thus promoting thrombus formation and development [38]. Literature also indicates that low HDL-C levels are closely related to an increased risk of DVT in patients with metabolic syndrome [39]. Furthermore, comparative studies have shown that patients with PE exhibit higher TG and lower HDL-C levels compared to those with isolated DVT, implying that lipid metabolism disorders may contribute to different clinical phenotypes of venous thromboembolism [40]. Specifically, in individuals with metabolic dysfunction, diabetes may worsen the coagulation and metabolic dysfunction by increasing insulin resistance, chronic inflammation, and endothelial damage, significantly heightening the risk of DVT [41]. These complex biological interactions underscore the pivotal role that lipid metabolism disorders play in the development of DVT.

After adjusting for age and gender, neither surgery time nor ISS remained significantly associ-



Parameter.type	Numeric.case
Specificity	0.574
Sensitivity	0.789
Youden Index	0.362
Accuracy	0.681
Precision	0.649
F1 Score	0.712

Parameter.type	Numeric.case
Specificity	0.781
Sensitivity	0.762
Youden Index	0.543
Accuracy	0.772
Precision	0.777
F1 Score	0.770

Parameter.type	Numeric.case
Specificity	0.747
Sensitivity	0.638
Youden Index	0.385
Accuracy	0.692
Precision	0.716
F1 Score	0.675

Parameter.type	Numeric.case
Specificity	0.185
Sensitivity	0.400
Youden Index	-0.415
Accuracy	0.292
Precision	0.329
F1 Score	0.361

Figure 6. ROC curve analysis for FIB, D-D, TG, and HDL-C after matching. A. ROC Curve for FIB and its Classification Criteria After Matching. B. ROC Curve for D-D and its Classification Criteria After Matching. C. ROC Curve for TG and its Classification Criteria After Matching. D. ROC Curve for HDL-C and its Classification Criteria After Matching. Note: ROC: Receiver Operating Characteristic Curve, FIB: Fibrinogen, D-D: D-Dimer, TG: Triglyceride, HDL-C: High-Density Lipoprotein Cholesterol.

ated with DVT risk. This finding may be explained by several mechanisms: firstly, the influence of surgery time and ISS score on DVT risk could be partially mediated by confounding factors such as age and gender. For example, elderly patients often experience prolonged surgery

Table 8. Multivariate Logistic regression analysis of DVT in patients with traumatic limb fractures (After PSM)

Index	Estimate	Std Error	*P* Value	OR	Lower	Upper
Diabetes	1.551	0.421	< 0.001	4.718	2.069	10.758
Time of surgery	0.307	0.262	0.240	1.360	0.814	2.271
ISS score	0.358	0.261	0.170	1.431	0.858	2.386
FIB (g/L)	1.614	0.268	< 0.001	5.022	2.970	8.493
D-D (μg/mL)	2.325	0.27	< 0.001	10.224	6.026	17.346
TG (mmol/L)	1.573	0.26	< 0.001	4.819	2.893	8.027
HDL-C (mmol/L)	-2.238	0.296	< 0.001	0.107	0.060	0.191

Note: FIB: Fibrinogen, D-D: D-Dimer, TG: Triglyceride, HDL-C: High-Density Lipoprotein Cholesterol, PSM: Propensity Score Matching.

due to comorbidities, and men are more likely to sustain high-energy trauma, resulting in higher ISS. PSM effectively balanced these confounding variables, eliminating spurious associations between these variables and DVT. For instance, Maheshati et al. [42] found that after adjusting for age and gender, surgery time was no longer a significant independent risk factor for DVT. Furthermore, surgery time and ISS may indirectly increase DVT risk by promoting coagulation dysfunction (e.g., elevated FIB and D-D) and lipid metabolism disorders (e.g., elevated TG and reduced HDL-C). However, after PSM, these biomarkers, particularly D-D (OR = 10.224) directly reflect the downstream effects of surgical and trauma-related stress, thus diminishing the apparent impact of upstream variables such as surgery time and ISS. Similar findings have been observed in other surgical populations. For instance, in patients undergoing lumbar fusion surgery, surgery time was not identified as an independent risk factor for DVT after matching [43]. Although PSM may reduce sample size and statistical power to detect weak effects, the strong association of coagulation and lipid biomarkers with DVT underscore their central mechanistic role. This suggests that DVT development after traumatic fractures relies more on molecular pathways of physiological disorders than on surgery or trauma severity alone. This finding emphasizes the need for clinical monitoring of coagulation and metabolic markers (e.g., D-D ≥ 0.805 mg/L, HDL-C ≤ 1.7 mmol/L) rather than solely relying on traditional indicators like surgery duration or trauma scores for risk assessment.

This study provides actionable guidance for DVT prevention in patients with traumatic limb fractures. Specifically, preoperative/postoperative monitoring of coagulation markers (FIB ≥ 2.495 g/L, D-D ≥ 0.805 μg/mL) and lipid markers (TG ≥ 1.385 mmol/L, HDL-C ≤ 1.705 mmol/L) enables early identification of high-risk individuals. Patients meeting these thresholds - particularly those with diabetes - should receive intensified DVT surveillance (e.g., serial Doppler ultrasounds) and prompt escalation of prophylactic measures (e.g., extended anticoagulation). Implementing this biomarker-driven risk stratification may optimize resource allocation and reduce DVT incidence by implementing targeted interventions, ultimately improving post-trauma outcomes.

Despite the novel contributions in exploring the multifactorial mechanisms of coagulation dysfunction and lipid metabolism disorders in DVT, there are still several limitations that should be recognized. First, the retrospective single-center design, based on electronic medical records, may introduce information bias, particularly due to the incomplete documentation of latent thrombus events. Second, while PSM balanced traditional demographic factors such as age and gender, other unmeasured confounders may still influence the results. Additionally, the analysis was limited to a 14-day postoperative period, potentially missing delayed thrombus events and lacking dynamic monitoring of coagulation/metabolic markers before and after surgery. Therefore, future research should adopt a multicenter prospective design, expanding the sample to include different ethnicities and medical settings to validate the external generalizability and robustness of the model. Future studies should focus on exploring the molecular crosstalk between coagulation and lipid metabolism.

Randomized controlled trials (RCTs) should be conducted to assess the efficacy of lipid-lowering drugs or novel anticoagulants in DVT prevention. Furthermore, the development of diagnostic tools enabling real-time biomarker monitoring may facilitate timely intervention and support the implementation of personalized thromboprophylaxis strategies in trauma populations.

Conclusion

Coagulation disorders and lipid abnormalities are independent risk factors for DVT in patients with traumatic limb fractures. Additionally, a history of diabetes further increases the risk. Propensity score matching reinforces their predictive value, highlighting the importance of early identification and targeted monitoring to guide DVT prevention in high-risk patients.

Disclosure of conflict of interest

None.

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