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Laboratory Predictors of Early Venous Thromboembolism in Patients with Intertrochanteric Fractures: A Retrospective Cohort Study

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Abstract

Background Patients with femoral intertrochanteric fracture face a high early post-traumatic risk of venous thromboembolism (VTE). The Caprini risk-assessment model relies only on demographic and medical-history items and lacks laboratory markers reflecting the post-traumatic coagulation-fibrinolysis state. This study aimed to explore associations between laboratory biomarkers measured within 24 h of injury and ultrasound-detected deep vein thrombosis (DVT) occurring within 5 days.

Methods This single-centre retrospective cohort enrolled 210 consecutive intertrochanteric-fracture patients who met predefined eligibility criteria and were admitted within 24 h of trauma (see flow diagram, Fig. 1). Patients were classified by lower-limb venous Doppler ultrasonography as DVT (n = 87) or non-DVT (n = 123). Baseline features were compared. Univariable and separate multivariable Firth-penalised logistic regression models were fitted. Because of severe multicollinearity, D-dimer and fibrinogen degradation products (FDP) were fitted in two distinct models. Receiver-operating-characteristic (ROC) curves assessed discriminative ability, and sensitivity analyses were performed.

Results Patients with early DVT had significantly lower 24-h D-dimer and FDP concentrations (both P = 0.002). In the primary model (Model A, adjusted for sex, age, BMI, and smoking; n = 210, 87 events), lower D-dimer (OR = 0.961, 95% CI 0.929–0.989, P = 0.004) and lower FDP (OR = 0.983, 95% CI 0.969–0.995, P = 0.003) were independently associated with early DVT-an inverse association opposite in direction to that reported in non-trauma populations. No statistically significant departure from a linear form was detected. ROC analysis yielded modest AUC values (0.603 for D-dimer; 0.605 for FDP). Sensitivity analyses were consistent with the primary estimate, and all participants fell within a single (highest) Caprini risk stratum.

Conclusions Lower ultra-early post-injury D-dimer and FDP concentrations were independently associated with ultrasound-detected DVT within 5 days after intertrochanteric fracture in this exploratory analysis. Given their limited standalone discrimination and the absence of demonstrated incremental value beyond the Caprini score, these biomarkers should be regarded as candidate supplementary indicators for future, externally validated prediction models rather than as standalone clinical decision tools.

Introduction

Femoral intertrochanteric fracture is one of the most prevalent fragility fractures in older adults, most often resulting from low-energy falls, and affected patients frequently have multiple comorbidities and reduced physiological reserve [1, 2]. Immediately after fracture, endothelial injury and local venous stasis occur, while traumatic stress activates inflammatory cascades and disturbs the coagulation-fibrinolysis balance, producing a pronounced pre-thrombotic state in the peri-traumatic period [3, 4]. Venous thromboembolism (VTE)-comprising deep vein thrombosis (DVT) and pulmonary embolism (PE)-is among the most frequent early complications of intertrochanteric fracture [5], with reported VTE rates approaching 44% in hip-fracture populations [6]. The first 5 days after injury appear to be a particularly

high-risk window in which thrombi tend to initiate and progress [7, 8]. Early and accurate identification of high-risk patients, and prompt individualised thromboprophylaxis, are therefore central to improving peri-operative management and reducing thrombus-related adverse events [9–11].

The Caprini risk-assessment model is one of the most widely used VTE risk-stratification instruments in surgical practice, assigning risk on the basis of age, comorbidity, surgical modality, and trauma history [12, 13]. However, it contains no objective laboratory item reflecting the post-traumatic coagulation-fibrinolysis or inflammatory state [14, 15]. For patients with severe trauma such as intertrochanteric fracture, individual stress responses vary considerably, and sole reliance on the score may miss high-risk individuals. Whether and to what extent the score separates risk within an exclusively high-risk fracture cohort remains to be established, and we therefore examined it directly in the present cohort rather than assuming a ceiling effect a priori.

Dysregulated coagulation and fibrinolysis is the core pathological process underlying post-traumatic VTE. D-dimer and fibrinogen degradation products (FDP) are widely used markers of thrombus formation and fibrinolysis activation [16, 17]. Most existing work focuses on fixed diagnostic cut-offs for D-dimer, yet the association between baseline D-dimer measured within 24 h of hip fracture and short-term VTE remains inconsistent [18]. After major trauma, most patients show elevated D-dimer and FDP, with few values within healthy reference ranges; the conventional assumption that higher biomarker levels indicate higher thrombus risk may therefore not hold in the acute trauma setting [19, 20]. Other routinely available indices-platelet count (PLT), mean platelet volume (MPV), red cell distribution width (RDW), erythrocyte sedimentation rate (ESR), fibrinogen, and smoking status-reflect overlapping pathways of coagulation, inflammation, and endothelial injury and may jointly inform early risk [21–27].

Systematic evaluation of whether admission-phase laboratory indices collected within 24 h of injury are associated with early (within 5 days) DVT after intertrochanteric fracture remains scarce, and prior work has rarely considered trauma-specific hypercoagulable-hyperfibrinolytic phenotypes. We therefore conducted a retrospective cohort study to (i) examine the associations between laboratory biomarkers measured within 24 h of injury and ultrasound-detected DVT within the first 5 days after intertrochanteric fracture, and (ii) characterise the discriminative performance and limitations of these markers in a high-risk fracture population. We framed the analysis explicitly as exploratory, and specify throughout what the study can and cannot demonstrate.

Materials and Methods

Study design and setting

This was a single-centre retrospective cohort study. Consecutive patients with intertrochanteric femoral fracture admitted to our hospital between January 2025 and June 2026 were screened. Of 338 screened patients, 210 met the eligibility criteria and were analysed. This study was approved by the Ethics Committee of Xingtai Ninth Hospital (Ethics No.:2025-017). The requirement for written informed

consent was waived by that committee because of the retrospective design and the use of de-identified data. The study was conducted in accordance with the Declaration of Helsinki [28]. A participant flow diagram with exclusion counts is presented in Fig. 1.

Participant selection and eligibility

Screened patients were those admitted with a clinical and radiological diagnosis of isolated intertrochanteric femoral fracture. Inclusion criteria were: (i) clinical and radiological confirmation of an isolated intertrochanteric femoral fracture; (ii) hospital admission within 24 h of injury; (iii) D-dimer, FDP, fibrinogen, PLT, MPV, RDW, and ESR measured within 24 h of injury; (iv) baseline lower-limb venous ultrasound excluding pre-hospital VTE, with pulmonary CT angiography (CTA) performed when PE was suspected; (v) proximal femoral nail anti-rotation (PFNA) internal fixation within 48 h of trauma and a repeat lower-limb venous Doppler ultrasound on day 5 post-injury; and (vi) complete clinical, laboratory, and imaging data.

Exclusion criteria were: (i) documented prior VTE; (ii) pre-hospital anticoagulant, heparin, or antiplatelet therapy; (iii) malignancy, severe hepatic or renal insufficiency, autoimmune disease, or severe infection that could substantially disturb the coagulation-fibrinolysis system; (iv) multiple fractures, open fracture, or concomitant severe soft-tissue injury; and (v) missing key clinical or laboratory variables.

Exclusion counts and reasons for all screened patients are shown in the flow diagram (Fig. 1).There was no geriatric age threshold in the eligibility criteria. Death, inter-hospital transfer, or discharge before the day-5 examination did not by itself define ineligibility, but such patients were retained only if the day-5 imaging criterion was met; because complete day-5 imaging was required, patients who died, were transferred, or were discharged before day 5 without repeat imaging were excluded, and this requirement is acknowledged as a source of selection bias (see Discussion).

Assessment of the thrombotic endpoint

The endpoint was ultrasound-detected DVT occurring within 5 days of injury, ascertained by scheduled lower-limb venous Doppler ultrasonography on day 5 in all participants and by diagnostic imaging performed earlier if clinically indicated. All examinations were interpreted by two formally trained sonographers, each blinded to the laboratory results. DVT was classified as proximal (common femoral, femoral, or popliteal vein) or distal (anterior tibial, posterior tibial, or peroneal vein), with isolated calf-muscular vein thrombosis recorded separately [29]. Disagreements between readers were resolved by consensus, and by a third senior reader when consensus was not reached. Because no pulmonary embolism was identified, the observed endpoint was DVT detected during the 5-day assessment window; the study does not demonstrate predictive performance for PE.

All detected thrombi occurred on the side of the fracture (injured limb), i.e., laterality was ipsilateral to the fracture in all cases, with no contralateral or bilateral events. All recorded thrombi were analysed

together across all lower-limb venous thrombosis types, including isolated calf-muscular vein thrombosis.

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Laboratory measurements

Venous blood was sampled within 24 h of injury and analysed in the hospital clinical laboratory. D-dimer was reported in fibrinogen-equivalent units (μg/mL FEU). RDW is reported as RDW-SD (fL); MPV, PLT, fibrinogen, D-dimer, and FDP units are shown in Table 1.

Caprini score assessment

The 2010 Caprini risk-assessment model was used [12]. The score comprises 40 items weighted 1–5 points and yields four strata: low (0–1), moderate (2), high (3–4), and highest (≥ 5) risk. Scores were calculated at a standardised time point on admission before surgery,by two attending clinicians, with disagreements resolved by consensus.Because the cohort is a homogeneous high-risk fracture population, Caprini scores were concentrated in the highest stratum; the interpretation of this observation is restricted to what was actually evaluated in this cohort (see Discussion).

Peri-operative management and prophylaxis

All patients received standard thromboprophylaxis with subcutaneous low-molecular-weight heparin (LMWH; Low Molecular Weight Heparin Calcium), 5000 IU once daily; the drug was withheld at least 12 h before surgery and resumed 12 h postoperatively. Timing and peri-operative exposures were as follows: injury-to-sampling interval, median 10.4 hours; injury-to-surgery interval,median 33.7 hours;sequence of blood sampling, baseline ultrasound, and prophylaxis initiation: after admission, venous blood sampling was performed first, followed by baseline lower-limb venous Doppler ultrasonography, and thromboprophylaxis was then commenced; tranexamic acid use 100%; surgical duration median 85.7 min. 'Within 24 h' denotes a sampling window rather than a standardised single time point,and this variation is acknowledged as a limitation.

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Data collection and baseline characteristics

Baseline clinical data (age, sex, BMI, smoking history, fracture pattern, and major comorbidities) were extracted from electronic medical records. Laboratory indices were restricted to blood sampled within 24 h of injury: D-dimer, FDP, fibrinogen, PLT, MPV, RDW, and ESR. Sex by outcome group is reported in Table 1. Fracture pattern and major comorbidities are reported in Table 1 and were considered for

confounder adjustment where data permitted. Patients with pre-existing thromboembolism, malignancy, or other severely confounding comorbidity were excluded, to reduce confounding.

Statistical analysis

Analyses were performed in R version 4.4. The Shapiro-Wilk test assessed normality. Normally distributed variables are reported as mean +/- SD and compared with Welch's t-test; non-normally distributed variables are reported as median (IQR) and compared with the Mann-Whitney U test, as indicated in the table footnotes. Categorical variables are reported as counts (percentages) and compared with Pearson's chi-squared test. The outcome was DVT within 5 days of injury (1 = DVT, 0 = no DVT).

Firth-penalised logistic regression was used because the analysis involved complete or quasi-complete separation (as indicated by non-convergent maximum-likelihood estimates for one or more covariates) and small-to-moderate event counts per covariate. Firth's method addresses this data characteristic, not the retrospective design per se, and provides finite, less biased estimates [30]. Covariates in the multivariable models were selected a priori on clinical grounds, not by univariable screening. Two primary models were prespecified: Model A adjusted for sex, age, BMI, and smoking status; Model B adjusted for the Caprini score alone. Because FDP biochemically incorporates D-dimer, the two markers were strongly correlated (Spearman rho = 0.990; variance inflation factor 17.46), and each marker was therefore fitted in a separate model. Odds ratios (OR), 95% confidence intervals (CI), and P values are reported. The sample size (n = 210) and event count (87) were identical across the primary models.

Non-linearity was examined by adding a quadratic term to each Firth model and, as a supplementary check, by restricted cubic splines (RCS) with knots at four quantile-determined positions using standard logistic regression (the rms package does not natively support Firth penalisation). P values for non-linearity were obtained from an analysis of variance comparison. Failure to reject these tests indicates insufficient evidence of departure from the specified linear form; it does not establish that the relationship is linear.

Discrimination was assessed by ROC analysis. Outcome coding was DVT = 1; the ROC direction and software were pROC in R 4.4, direction "auto". The Youden index identified the optimal cut-off, and the corresponding sensitivity and specificity were computed. Confidence intervals for sensitivity and specificity were calculated using Wilson score interval; these intervals do not incorporate uncertainty from threshold selection. AUCs were compared with the DeLong test. Cut-offs derived and evaluated in the same dataset are optimistic and are reported for descriptive purposes only, not as clinical decision thresholds; AUC confidence intervals were obtained by DeLong method. Two-tailed $P < 0.05$ was considered statistically significant.

Sensitivity analyses, each with an explicitly stated adjustment set and retained sample size, comprised: (i) log-transformation, log(x + 1), of the right-skewed biomarkers (adjustment: Model A; n = 210), in which log(D-dimer) (OR = 0.614, 95% CI 0.435–0.849, P = 0.003) and log(FDP) (OR = 0.633, 95% CI 0.459–0.858,

P = 0.003) remained inversely associated with early DVT; (ii) exclusion of the 1st and 99th percentile extremes of D-dimer and FDP (adjustment: Model A; n = 210), in which D-dimer (OR = 0.943, 95% CI 0.905–0.977, P = 0.001) and FDP (OR = 0.978, 95% CI 0.963–0.992, P = 0.001) remained inversely associated; (iii) additional adjustment for PLT, MPV, RDW, ESR, and fibrinogen, treated as an exploratory analysis of concurrent laboratory indices rather than baseline confounding (n = 210), in which D-dimer (OR = 0.958, 95% CI 0.925–0.986, P = 0.002) and FDP (OR = 0.981, 95% CI 0.967–0.993, P = 0.002) remained inversely associated. Because FDP and D-dimer are nearly identical markers, the two marker models are not presented as independent replications of the same finding.

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Results

Participant flow and baseline characteristics

Of 338 screened patients, 210 were included in the analysis; exclusions by reason are shown in the flow diagram (Fig. 1). There were 87 ultrasound-detected DVT events (41.4%) and 123 patients without DVT. Among participants, 65 (31.0%) were male and 145 (69.0%) were female. No statistically significant between-group differences were observed for age, BMI, Caprini score, smoking status, fibrinogen, PLT, RDW, MPV, or ESR (all P > 0.05). D-dimer and FDP concentrations within 24 h of injury were significantly lower in the DVT group (both P = 0.002) (Table 1). All participants had Caprini scores of 5–11, i.e., all fell within the highest-risk stratum; the distribution did not differ between groups (P = 0.550) (Table 1).

Table 1
Baseline characteristics of study participants

Variable	No VTE (N = 123)[1]	VTE (N = 87)[1]	p-value[2]
Age (years)	72.71 ± 13.83	74.72 ± 10.83	0.238
BMI (kg/m²)	21.05 ± 3.42	21.22 ± 3.33	0.716
Caprini score			0.550
5,n (%)	3 (2.4%)	0 (0%)	
6,n (%)	12 (9.8%)	6 (6.9%)	
7,n (%)	26 (21%)	14 (16%)	
8,n (%)	51 (41%)	42 (48%)	
9,n (%)	17 (14%)	16 (18%)	
10,n (%)	11 (8.9%)	8 (9.2%)	
11,n (%)	3 (2.4%)	1 (1.1%)	
D-dimer(μg/mL FEU), median (Q1, Q3)	6.56 (2.85, 18.46)	4.73 (2.21, 8.90)	0.002
FDP(μg/mL), median (Q1, Q3)	14.90 (6.90, 40.30)	10.70 (6.40, 21.80)	0.002
Fibrinogen (g/L)	3.62 ± 0.93	3.51 ± 0.96	0.398
Platelet count (×10⁹/L)	194.95 ± 64.07	210.43 ± 78.17	0.130
RDW-SD (fL)	43.22 ± 4.42	43.45 ± 4.13	0.694
MPV (fL)	10.70 ± 1.29	10.45 ± 1.14	0.136
ESR (mm/h)	25.02 ± 20.13	26.37 ± 20.35	0.636
Smoking, n (%)	10 (8.1%)	13 (15%)	0.183

Note: Values are mean +/- SD, median (Q1, Q3), or n (%). Continuous variables were compared with Welch's t-test; non-normally distributed variables (D-dimer, FDP) and Caprini score with the Mann-Whitney U test; categorical variables with Pearson's chi-squared test. FEU, fibrinogen equivalent units; IQR, interquartile Univariable Firth-penalised logistic regression.

Univariable Firth-penalised logistic regression

In univariable analysis, D-dimer (OR = 0.960, 95% CI 0.929–0.988, P = 0.003) and FDP (OR = 0.982, 95% CI 0.969–0.994, P = 0.002) were significantly associated with DVT. Age, BMI, Caprini score, fibrinogen, PLT, RDW, MPV, ESR, and smoking were not statistically significant (all P > 0.05) (Table 2).

Table 2
Univariable Firth-penalised logistic regression for DVT-related factors

Variable	OR (95% CI)	P-value
Age	1.013 (0.991, 1.036)	0.262
BMI	1.015 (0.936, 1.101)	0.715
Caprini score	1.151 (0.911, 1.463)	0.240
D-dimer	0.960 (0.929, 0.988)	0.003
FDP	0.982 (0.969, 0.994)	0.002
Fibrinogen	0.882 (0.655, 1.179)	0.400
Platelet count	1.003 (0.999, 1.007)	0.119
RDW	1.013 (0.950, 1.079)	0.691
MPV	0.846 (0.668, 1.060)	0.147
ESR	1.003 (0.990, 1.017)	0.628
Smoking	1.959 (0.833, 4.721)	0.123

Multicollinearity between D-dimer and FDP

D-dimer and FDP were strongly positively correlated (Spearman rho = 0.990, P < 0.001), with a variance inflation factor of 17.46, indicating strong collinearity (Fig. 2). When both markers were entered simultaneously in one model, the overall likelihood-ratio test was significant (P = 0.0158) but neither marker reached significance (Table 3). The consequence of this collinearity is instability of the joint coefficient estimates and reduced precision (wider confidence intervals), rather than biased estimation; the two biomarkers were therefore fitted in separate multivariable models.

Table 3
Exploratory multivariable model including D-dimer and FDP simultaneously

Variable	Coefficient	OR (95% CI)	P-value
D-dimer	0.013	1.014 (0.891–1.133)	0.818
FDP	-0.022	0.978 (0.929–1.031)	0.394
Platelet count	0.002	1.002 (0.998–1.007)	0.378
MPV	-0.136	0.872 (0.669–1.135)	0.300
Smoking (Yes)	0.521	1.685 (0.713–4.212)	0.248

Note: Exploratory model simultaneously incorporating both D-dimer and FDP. Strong collinearity (rho = 0.990; VIF = 17.46) attenuated the statistical significance of both markers; the consequence is instability and reduced precision of the joint estimates, not biased .

Multivariable Firth-penalised logistic regression

In Model A (adjusted for sex, age, BMI, and smoking; n = 210, 87 events), both lower D-dimer (OR = 0.961, 95% CI 0.929–0.989, P = 0.004) and lower FDP (OR = 0.983, 95% CI 0.969–0.995, P = 0.003) were independently and inversely associated with early DVT. In Model B (adjusted for Caprini score; n = 210, 87 events), the inverse associations persisted for D-dimer (OR = 0.960, 95% CI 0.928–0.988, P = 0.003) and FDP (OR = 0.982, 95% CI 0.969–0.994, P = 0.002). In Model A, smoking was associated with higher odds of DVT (OR = 2.800, 95% CI 1.013–8.226, P = 0.047), a borderline result that is reported transparently and discussed below; the Caprini score was not significantly associated with early DVT in Model B (P = 0.257) (Table 4, Fig. 3).

Table 4
Multivariable Firth-penalised logistic regression results (primary analysis)

Variable	Model A OR (95% CI)	Model A P	Model B OR (95% CI)	Model B P
Sex (male vs female)	0.806 (0.395–1.604)	0.541	-	-
Age	1.018 (0.994–1.044)	0.143	-	-
BMI	1.027 (0.945–1.117)	0.522	-	-
Smoking	2.800 (1.013–8.226)	0.047	-	-
Caprini score	-	-	1.151 (0.903–1.476)	0.257
D-dimer	0.961 (0.929–0.989)	0.004	0.960 (0.928–0.988)	0.003
FDP	0.983 (0.969–0.995)	0.003	0.982 (0.969–0.994)	0.002

Note: Two a priori primary models are shown. Model A adjusted for sex, age, BMI, and smoking status; Model B adjusted for the Caprini score only. D-dimer and FDP were fitted in separate models to mitigate collinearity. Sample size was identical across models (n = 210; 87 events). These are the verified primary estimates referred to throughout the manuscript and in the abstract.

Non-linear association between D-dimer/FDP and DVT

Quadratic terms were non-significant for D-dimer (P = 0.094 in Model A, P = 0.102 in Model B) and for FDP (P = 0.070 in Model A, P = 0.085 in Model B; Table 5). Thus, no statistically significant departure

from the specified linear form was detected within the observed range. On this basis, linear-form estimates were used for the primary presentation. In the supplementary RCS analyses (Figures S1-S4), no significant non-linearity was detected for D-dimer (P-for-non-linearity = 0.464, 0.515) or FDP (P-for-non-linearity = 0.803, 0.845), again indicating insufficient evidence of departure from the specified linear form.

Table 5
Quadratic-term Firth-penalised logistic regression (non-linearity test)

Biomarker	Model	Quadratic term	P for quadratic term	Conclusion
D-dimer	Model A	I(Dd^2)	0.093	No significant departure from linear form detected
D-dimer	Model B	I(Dd^2)	0.102	No significant departure from linear form detected
FDP	Model A	I(FDP^2)	0.070	No significant departure from linear form detected
FDP	Model B	I(FDP^2)	0.085	No significant departure from linear form detected

Discriminative performance (ROC analysis)

AUCs were 0.603 (95% CI 0.527–0.680) for D-dimer and 0.605 (95% CI 0.529–0.682) for FDP, only marginally above 0.5. At the Youden-derived cut-off of 12.67 μg/mL FEU, D-dimer yielded sensitivity 0.874 (95% CI 0.736–0.943) and specificity 0.333 (95% CI 0.130–0.463); at the FDP cut-off of 22.50 μg/mL, sensitivity was 0.759 (95% CI 0.540–0.885) and specificity 0.415 (95% CI 0.309–0.528). The DeLong test showed no significant difference between the two AUCs (Z = 0.360, P = 0.719) (Fig. 4). The wide confidence intervals for sensitivity and specificity reflect the modest event count and do not incorporate uncertainty from threshold selection. These cut-offs are exploratory and are not proposed as clinical decision thresholds.

Sensitivity analyses

Sensitivity analyses were consistent with the primary result (Table 6). In log-transformed models (adjustment: Model A; n = 210), both log(D-dimer) (OR = 0.614, 95% CI 0.435–0.849, P = 0.003) and log(FDP) (OR = 0.633, 95% CI 0.459–0.858, P = 0.003) remained inversely associated with early DVT. After excluding 1st/99th percentile extremes (adjustment: Model A; n = 210), D-dimer (OR = 0.943, 95% CI 0.905–0.977, P = 0.001) and FDP (OR = 0.978, 95% CI 0.963–0.992, P = 0.001) remained inversely associated. Additional adjustment for PLT, MPV, RDW, ESR, and fibrinogen gave consistent estimates for D-dimer (OR = 0.958, 95% CI 0.925–0.986, P = 0.002) and FDP (OR = 0.981, 95% CI 0.967–0.993, P = 0.002). Both the log-transformed and outlier-excluded analyses indicate that the inverse association was not driven by skewed distributions or extreme values.

Table 6
Sensitivity analyses assessing robustness of the biomarker-DVT associations

Analysis	Variable	OR (95% CI)	P-value
Primary model	D-dimer	0.961 (0.899–0.981)	0.009
Primary model	FDP	0.983 (0.959–0.992)	0.003
Log-transformed model (log(x + 1))	log(D-dimer)	0.614 (0.435–0.849)	0.003
Log-transformed model (log(x + 1))	log(FDP)	0.633 (0.459–0.858)	0.003
Excluding 1% extreme values (1st-99th percentile)	D-dimer	0.943 (0.905–0.977)	0.001
Excluding 1% extreme values (1st-99th percentile)	FDP	0.978 (0.963–0.992)	0.001

Note: The primary estimates are those of Model A (Table 4). The sensitivity analyses are reported separately with their own estimates; an earlier version incorrectly labelled a differing estimate as the 'primary model'.

Discussion

Principal findings

In this retrospective cohort of 210 patients admitted within 24 h of intertrochanteric fracture, lower D-dimer and FDP concentrations measured within 24 h of injury were associated with ultrasound-detected DVT within the following 5 days. In the primary model (Model A), D-dimer and FDP were independently associated with early DVT with ORs below 1, and no statistically significant departure from a linear form was detected. Discrimination was limited (AUC approximately 0.60), and sensitivity analyses were consistent with the primary estimate. The inverse direction of the association contrasts with findings in non-trauma medical populations [19, 31] and is the principal observation of this study.

Interpretation of the Caprini score

All participants in this cohort had Caprini scores of 5–11 and therefore fell within a single (highest) risk stratum, and the score did not separate patients who developed DVT from those who did not. We restrict our claims to what was evaluated here: within this high-risk fracture cohort, the categorical Caprini strata provided no separation. This observation is consistent with, but does not by itself establish, the existence of a ceiling effect for the numerical score, and our data do not demonstrate that the continuous score lacks discriminatory value. Further evaluation-for example, reporting the continuous score's discrimination with uncertainty and calibration in an adequately sized cohort-would be required before such a claim could be made. With that limitation, our findings suggest that the score alone may be insufficient for early DVT risk identification in this population, which motivates the continued evaluation of admission-phase laboratory markers [32, 33].

Interpretation of the D-dimer and FDP association

D-dimer and FDP are interrelated markers of thrombus formation and fibrinolysis and were nearly identical in this cohort (rho = 0.990; VIF 17.46). They were therefore fitted in separate models; because they are not independent, the consistency of the two models should not be interpreted as independent replication of the same finding [34]. Although the mechanism is not established here, one possibility is that patients with a muted fibrinolytic response after trauma have relatively low D-dimer and FDP concentrations despite ongoing microthrombus accumulation, whereas those with a more robust fibrinolytic response show higher marker concentrations and lower early thrombotic risk. This explanation remains explicitly hypothetical: no direct or serial assessment of fibrinolysis was performed, and it requires prospective validation. Most patients in this cohort had trauma-related biomarker elevation with few values in the normal reference range, so conventional outpatient D-dimer cut-offs for VTE exclusion are not directly applicable in the acute post-fracture phase [20, 35].

Interpretation of the high DVT detection rate

The absolute detection rate of 41.4% (87/210) is higher than the rates usually quoted for symptomatic VTE, and this requires explicit interpretation. Three points are important. First, the denominator describes an actively screened cohort, not a clinically diagnosed one: every participant underwent a protocol-mandated lower-limb venous Doppler ultrasound on day 5 regardless of symptoms, so the endpoint is an ultrasound-detected DVT rate rather than a symptomatic VTE incidence. Surveillance protocols identify events that symptom-driven testing would not, and the difference is largely accounted for by asymptomatic and distal, small-vessel thrombi. Second, the endpoint deliberately included isolated calf-muscular vein thrombosis (isolated muscular vein thrombosis), which is frequently asymptomatic, is often not sought outside surveillance protocols, and is of uncertain clinical significance. Third, the observed rate is within the range reported by other ultrasound-screening studies in hip-fracture populations, where admission or peri-operative DVT detection has ranged from approximately 10% to 44% depending on the imaging protocol, the timing of screening, and whether distal/muscular thrombi were counted [5, 6, 9]. We therefore interpret the 41.4% as a protocol-driven detection rate in a high-risk trauma population rather than as evidence of an implausibly high symptomatic event rate, and we caution that this rate should not be transferred directly to series using symptom-driven diagnosis.

Non-linearity, discrimination, and clinical utility

The quadratic and spline tests did not reject the specified linear form, which indicates insufficient evidence of departure from linearity rather than proof that the relationship is linear [36]. This observation is limited by sample size and by the restricted 5-day window; non-linear patterns could emerge later, and D-dimer should always be interpreted with reference to time since injury [37]. The AUCs (0.603 for D-dimer, 0.605 for FDP) indicate limited standalone discrimination; the study did not demonstrate that either marker, alone or combined, improves discrimination over the Caprini score, nor that biomarker-guided prophylaxis improves outcomes. Accordingly, we regard these markers as candidate components of future, externally validated multivariable prediction models rather than as standalone tools [38, 39].

The borderline association of smoking in Model A (P = 0.047) is reported without adjustment for multiple comparisons and should be interpreted cautiously. PLT, MPV, and the other laboratory indices were not independently associated with DVT within this very early 5-day window.

Strengths

The study focused on biomarkers measured within 24 h of injury for predicting ultra-early DVT within 5 days, a window less often examined than late post-operative VTE; used a scheduled baseline and day-5 imaging protocol; applied Firth-penalised regression to address separation and sparse-event estimation; addressed strong collinearity between D-dimer and FDP; and tested both linear and quadratic/spline forms.

Limitations

(1) This was a single-centre retrospective cohort of 210 patients; the sample size limits the power to detect modest or non-linear associations, and external generalizability requires multicentre validation. (2) Requiring complete data, surgery within 48 h, and day-5 imaging selected a particular subgroup; patients who died, were transferred, or were discharged before the day-5 examination were excluded if imaging was not completed, which may introduce selection bias, and included and excluded patients were compared only on the available characteristics. (3) Only a single 24-h post-injury sampling time point was available, so serial biomarker dynamics could not be evaluated, and 'within 24 h' is a window rather than a standardised interval. (4) The endpoint was ultrasound-detected DVT; detection of small calf-muscular thrombi is operator-dependent and subject to under-diagnosis, and no pulmonary embolism was identified, so the study does not address PE. (5) Although patients receiving pre-admission anticoagulant or antiplatelet therapy were excluded, unmeasured confounding cannot be fully excluded. (6) No external validation cohort was available, so the derived cut-offs and any model performance are unvalidated. (7) The analysis was exploratory; no adjustment for multiple comparisons was applied, and the findings require prospective confirmation.

In summary, the pathophysiology of early DVT after intertrochanteric fracture is complex. In this exploratory cohort, lower D-dimer and FDP measured within 24 h of injury were associated with ultrasound-detected DVT within 5 days, a direction that differs from non-trauma populations, although their standalone discrimination was limited. Future work should evaluate whether these markers provide incremental value within externally validated prediction models that combine the Caprini score with admission-phase laboratory data.

Conclusion

In conclusion, this single-centre retrospective study found that lower ultra-early post-injury D-dimer and FDP concentrations were independently associated with ultrasound-detected DVT within five days after intertrochanteric fracture. The inverse associations were consistent across sensitivity analyses. No statistically significant departure from a linear form was detected. Because discrimination was limited

(AUC approximately 0.60) and because the study did not demonstrate incremental value beyond the Caprini score or improved outcomes with biomarker-guided prophylaxis, these findings are exploratory: D-dimer and FDP should not be used alone for early DVT screening or as clinical decision thresholds, but may serve as candidate supplementary indicators in future, externally validated risk-stratification models for patients with intertrochanteric fractures.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Xingtai Ninth Hospital (Ethics No.:2025-017) and conducted in accordance with the Declaration of Helsinki 1964. Given its retrospective design, the requirement for informed consent was waived.

Consent for publication

Not applicable.

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests.

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Figures

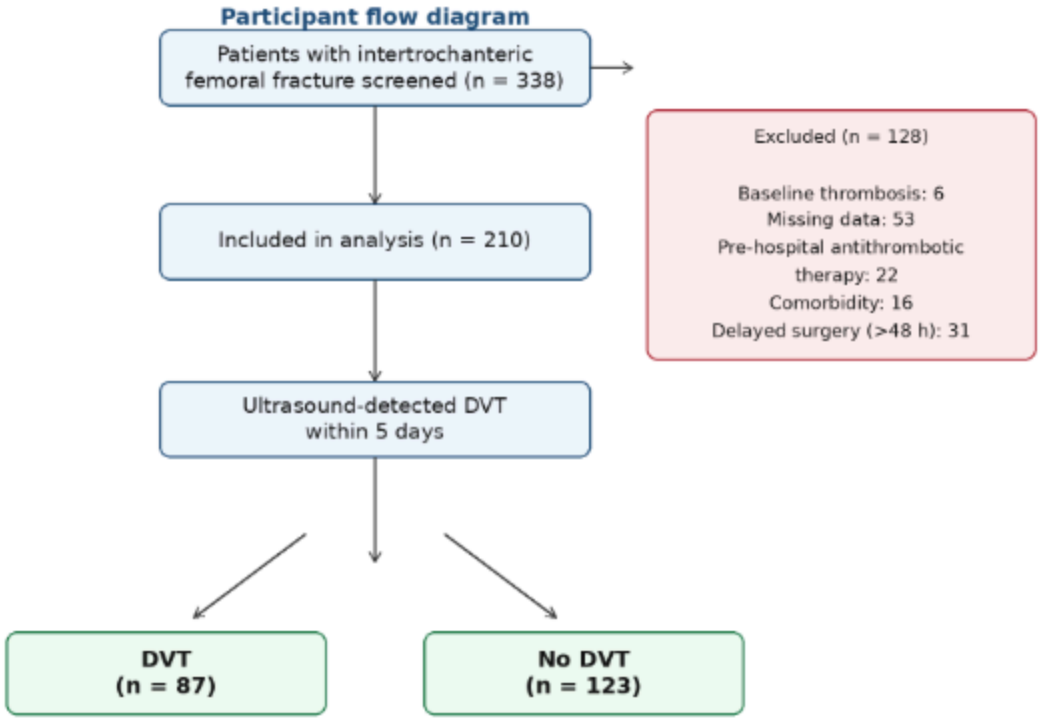


Figure 1

Participant flow diagram. Of 338 screened patients, 128 were excluded (baseline thrombosis, n=6; missing data, n=53; pre-hospital antithrombotic therapy, n=22; comorbidity, n=16; delayed surgery >48 h,

n=31), leaving 210 patients in the analysis (ultrasound-detected DVT, n=87; no DVT, n=123).

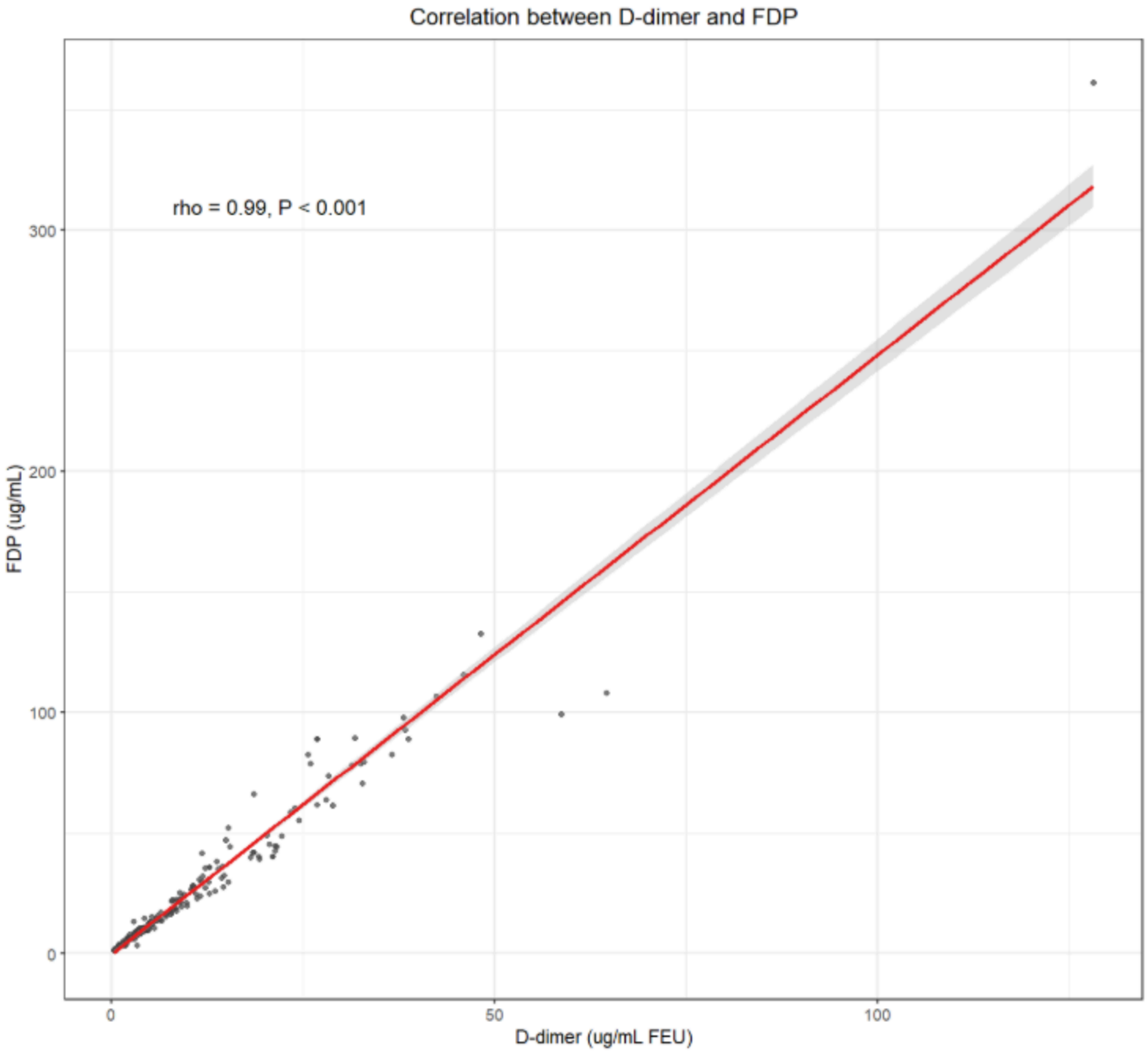


Figure 2

Correlation between D-dimer and FDP (Spearman rho=0.990, P<0.001).

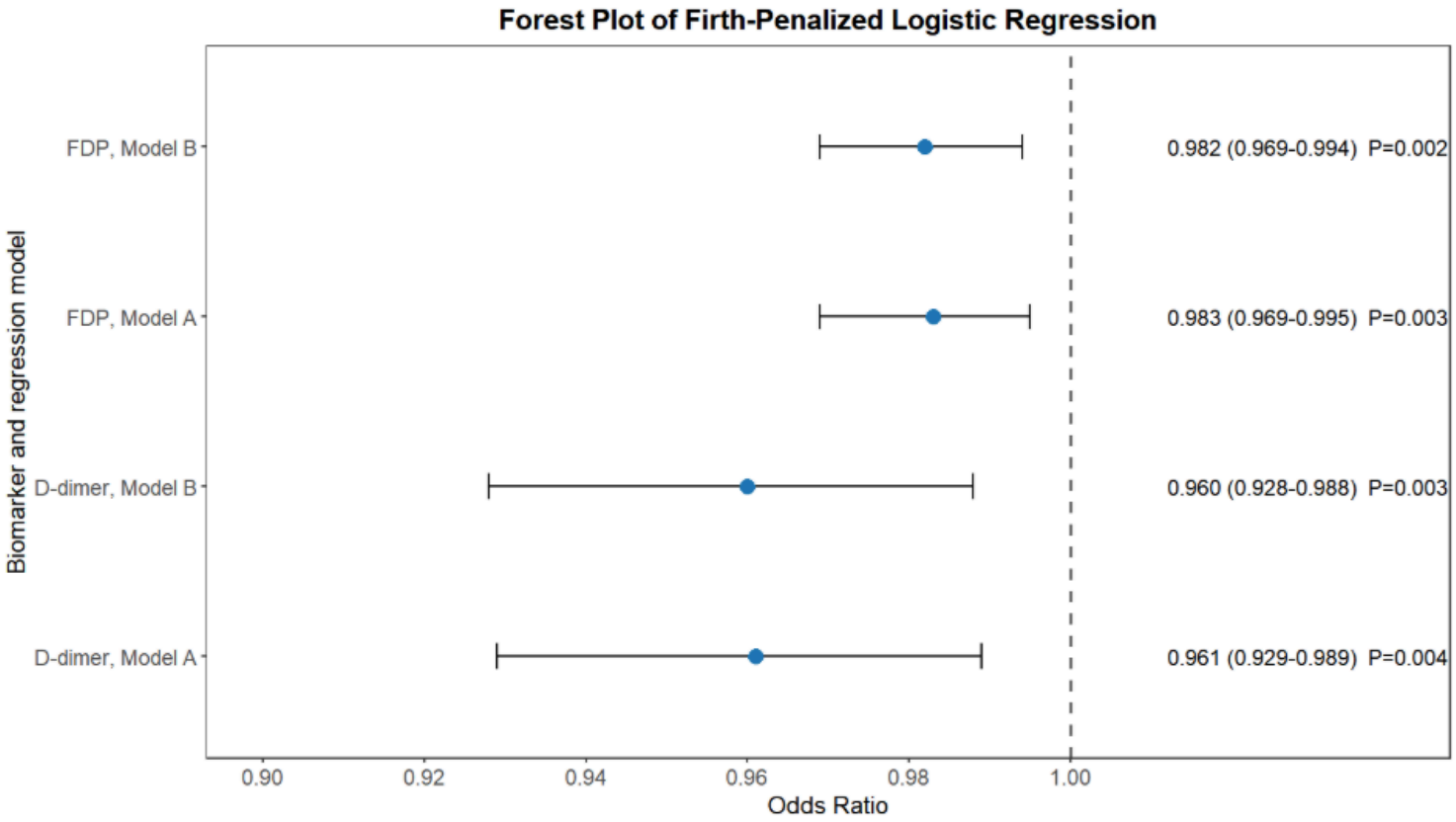


Figure 3

Forest plot of Firth-penalised logistic regression: associations of 24-h post-injury D-dimer and FDP with 5-day early DVT. Model A adjusted for sex, age, BMI, and smoking; Model B adjusted for the Caprini score. Horizontal bars are 95% CIs; the dashed line is OR=1.

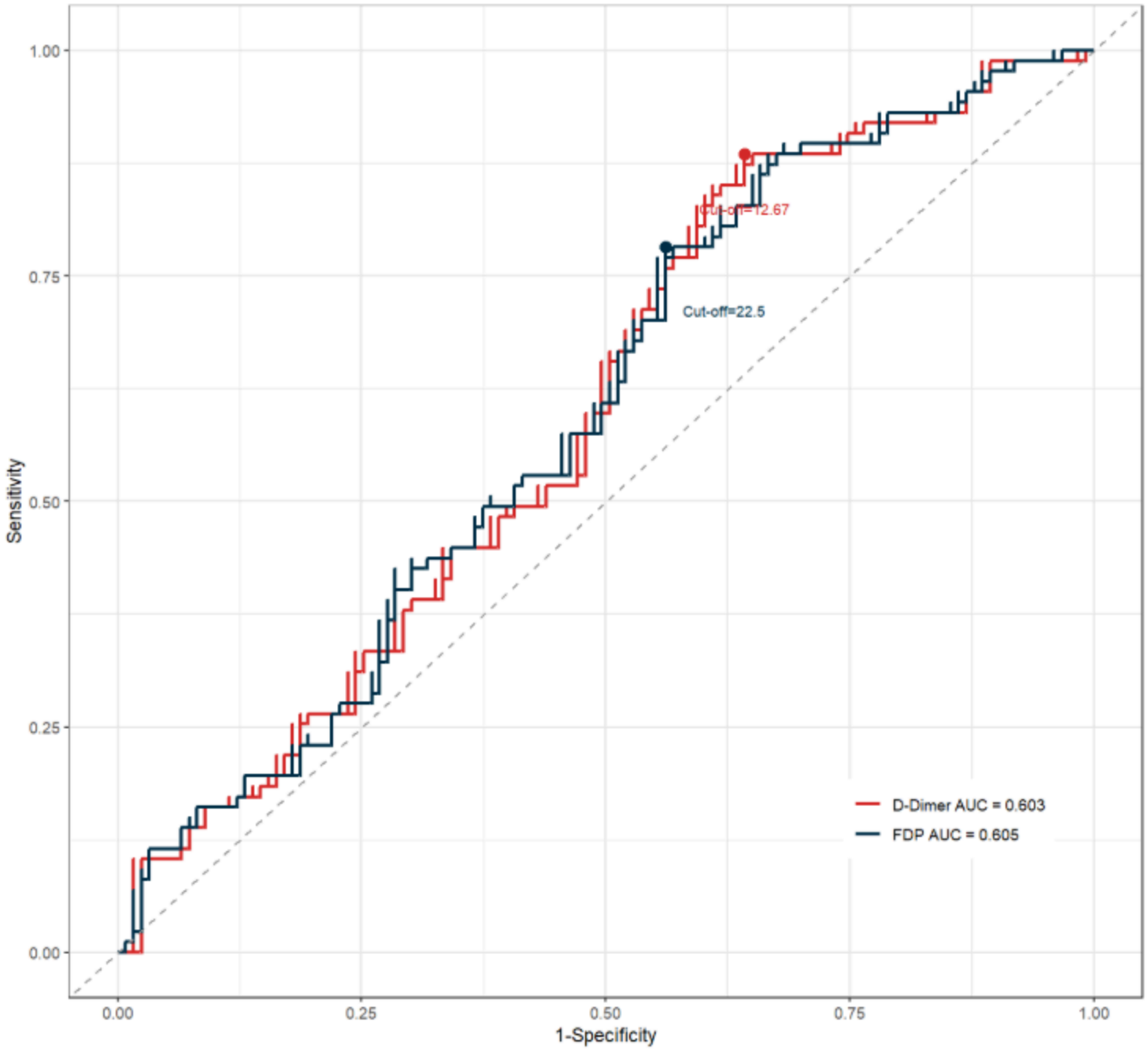


Figure 4

ROC curves for D-dimer and FDP predicting early DVT (AUC 0.603 and 0.605, respectively).