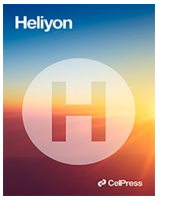
Heliyon 10 (2024) e28389

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Research article

A nomogram model based on the systemic immune-inflammation index to predict the risk of venous thromboembolism in elderly patients after hip fracture: A retrospective cohort study

Xiao Chen [*,1], Yuanhe Fan [1], Hongliang Tu, Jie Chen, Renming Li

Department of Orthopedics, The First People's Hospital of Neijiang, 641000 Neijiang, Sichuan, China

ARTICLE INFO

Keywords:
Venous thromboembolism
Hip fracture
Systemic immune-inflammation index
Inflammatory biomarkers
Nomogram
LASSO regression

ABSTRACT

Background and objectives: Venous thromboembolism (VTE), encompassing deep vein thrombosis (DVT) and secondary pulmonary embolism (PE), represents a significant complication post-hip fracture in the elderly. It is a prevalent cause of VTE-related complications, prolonged hospitalization, and mortality. This study aimed to investigate the potential of the systemic immune-inflammation index (SII) as a predictive marker for VTE in older patients following hip fracture.
Methods: The study was structured as an observational, analytical, retrospective cohort analysis. A total of 346 elderly patients diagnosed with hip fracture were included. We retrospectively collated clinical and laboratory data for these patients. Using the bootstrap method, the patients were divided in a 7:3 ratio into a training cohort (DVT group = 170 patients; no-DVT group = 72 patients) and an internal validation cohort (DVT group = 81 patients; no-DVT group = 23 patients). In the training cohort, relevant indices were initially identified using univariate analysis. Subsequently, least absolute shrinkage and selection operator logistic analysis was employed to determine significant potential independent risk factors ($P < 0.05$). A dynamic online diagnostic nomogram was developed, with its discriminative ability assessed using the area under the receiver operating characteristic curve (AUC). The nomogram's accuracy was further appraised using calibration plots. The clinical utility of the nomogram was evaluated through decision curve analysis (DCA) and corroborated by internal validation within the training set.
Results: SII emerged as the sole independent risk factor identified from the multivariate logistic analysis of the training cohort and was incorporated into the VTE diagnostic nomogram for older patients' post-hip fracture. The nomogram demonstrated AUC values of 0.648 in the training cohort and 0.545 in the internal testing cohort. Calibration curves corroborated the close alignment of the nomogram's predicted outcomes with the ideal curve, indicating consistency between predicted and actual outcomes. The DCA curve suggested that all patients could derive benefit from this model. These findings were also validated in the validation cohort.
Conclusion: The systemic immune-inflammation index is a robust predictor of venous thromboembolism in elderly patients following hip fracture, underscoring its potential as a valuable tool in clinical practice.

* Corresponding author.
E-mail address: 342918992@qq.com (X. Chen).
[1] These authors have contributed equally to this work.

https://doi.org/10.1016/j.heliyon.2024.e28389
Received 16 February 2024; Received in revised form 17 March 2024; Accepted 18 March 2024
Available online 20 March 2024

1. Introduction

Elderly patients are at a heightened risk of hip fractures, attributed to age-related declines in bone density and strength. Such fractures, encompassing femoral neck fractures, intertrochanteric fractures, and subtrochanteric fractures, are prevalent in the elderly and are linked to considerable morbidity and mortality [1]. Beyond the immediate complications of hip fractures, such as pain, immobility, and loss of independence, there are longer-term risks, notably the development of lower extremity deep vein thrombosis (DVT) and pulmonary embolism (PE) [2].

DVT is a grave condition characterised by blood clot formation within the deep veins of the lower extremities. These clots can hinder blood flow and cause local inflammation, resulting in pain and swelling in the affected limb [3]. Furthermore, should a clot dislodge and migrate to the lungs, it can precipitate a potentially fatal PE. The risk of DVT and PE notably escalates post-hip fracture, with incidences reported between 11% and 57% in this patient demographic [4–6]. Considering the significant medical and economic impact of DVT and PE, identifying predictive factors for these conditions in the context of hip fractures is crucial.

Various demographic and clinical factors have been implicated in the development of venous thromboembolism (VTE) following hip fractures. These include age, gender, injury mechanism, and fracture type, the interval between injury and admission, and comorbidities such as cardiovascular disease [7]. Alongside these clinical and demographic indicators, research has explored numerous biochemical markers as potential predictors of VTE in elderly patients with hip fractures. Hematological parameters, including hematocrit, hemoglobin, platelet count, neutrophil count, lymphocyte count, monocyte count, monocyte-to-lymphocyte ratio (MLR), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII), have been associated with VTE risk [8–12].

Despite the expanding corpus of research on this subject, there remains an imperative for a comprehensive predictive model that cohesively integrates demographic, clinical, and laboratory factors. Such a model would be invaluable in accurately determining the risk of DVT and PE in elderly patients with hip fractures. It could assist clinicians in identifying individuals at high risk, thereby enabling targeted interventions, such as prophylactic anticoagulation or mechanical compression devices, to avert these potentially fatal thromboembolic events.

Hence, this clinical prediction study is dedicated to developing a robust model for predicting VTE following hip fractures in older adults. We intend to examine an array of potential predictive factors, encompassing demographic, clinical, and laboratory aspects. The study will employ logistic regression and nomogram techniques to construct a predictive model. Our ultimate objective is to equip clinicians with a tool that can precisely stratify the risk of DVT and PE in this susceptible patient group, thus facilitating prompt interventions and enhancing patient outcomes.

2. Materials and methods

2.1. Study design

This study was conceived as an observational, analytical, retrospective cohort case-control study. It received approval from the Ethics Committee of The First People's Hospital of Neijiang (approval number: 2023-lunshenpi-39) and was waived the informed consents owing to the retrospective nature of this study. We collated clinical data from patients with hip fractures admitted to The First People's Hospital of Neijiang, spanning January 2020 to December 2023. Diagnoses were confirmed using X-ray and CT (computed tomography) coupled with 3D reconstruction examination.

Inclusion criteria.

- Patients diagnosed with hip fractures (including femoral neck fractures, intertrochanteric fractures and subtrochanteric fractures);
- Age 60 years and older;
- The traumatic factors were fall, body twisting, lifting up with weight, car accident, etc.
- Available clinical and laboragtory data for predictive factors;
- Patients signed an informed consent to collect the medical data;

Exclusion criteria.

- Patients with incomplete or missing clinical or laboratory data;
- Patients with a history of lower extremity venous thromboembolism;
- Patients with a history of anticoagulant therapy;
- Patients presenting with multiple fractures, a history of surgery prior to admission (within three months), malignant tumours, pathological fractures (originating from malignant tumours or metabolic bone disease), rheumatic or inflammatory conditions, chronic liver or kidney diseases, unexplained infectious diseases, antiphospholipid antibody syndrome, or a recent history of antibiotic usage were excluded from the study. This exclusion criterion was established to mitigate confounding variables that could potentially skew the results and affect the accuracy of the predictive model for venous thromboembolism following hip fractures in the elderly;
- Patients with cognitive impairment affecting informed consent and data collection;

2.2. Data collection

The following demographic and clinical data were collected: gender, age, body mass index (BMI), history of cardiovascular and cerebrovascular diseases, mechanism of injury, classification of fractures, and the interval between injury and admission. Fasting venous blood samples were obtained immediately upon admission, measuring hematocrit, hemoglobin, platelet count, neutrophil count, lymphocyte count, monocyte count, prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin time (TT), fibrinogen (FIB), D-dimer (D-D), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), total protein (TP), and albumin (ALB).

2.3. Systemic inflammatory makers

The systemic inflammation index was determined from the first blood test result. The ratio was calculated using the equations.

Table 1
Patient demographics and baseline characteristics.

Characteristic	Cohort		p-value
	Training Cohort (n = 242)	Internal Test Cohort (N = 104)	
Gender			0.404
Male	76 (31.4%)	28 (26.9%)	
Female	166 (68.6%)	76 (73.1%)	
Age(years)			0.820
Mean ± SD	81 ± 9	80 ± 8	
Mechanism of injury			0.317
Fall	236 (97.5%)	99 (95.2%)	
Traffic	6 (2.5%)	5 (4.8%)	
Injury-admission interval			0.582
<8h	81 (33.5%)	38 (36.5%)	
≥8h	161 (66.5%)	66 (63.5%)	
Classification of fracture			0.716
Femoral neck fracture	147 (60.7%)	61 (58.7%)	
Intertrochanteric fracture	95 (39.3%)	43 (41.3%)	
Cardiovascular and cerebrovascular diseases			0.411
Without	91 (37.6%)	44 (42.3%)	
With	151 (62.4%)	60 (57.7%)	
SII			0.442
Mean ± SD	1675 ± 1352	1557 ± 1285	
PT (s)			0.174
Mean ± SD	11.50 ± 1.77	11.30 ± 0.91	
APTT (s)			0.023
Mean ± SD	27.1 ± 5.8	28.8 ± 6.1	
TT (s)			0.381
Mean ± SD	16.92 ± 1.32	17.90 ± 11.28	
FIB (g/L)			0.984
Mean ± SD	3.82 ± 1.33	3.82 ± 1.28	
ALT (U/L)			0.800
Mean ± SD	21 ± 14	22 ± 14	
LDH (U/L)			0.061
Mean ± SD	243 ± 73	260 ± 81	
TP (g/L)			0.096
Mean ± SD	65 ± 7	66 ± 6	
ALB (g/L)			0.310
Mean ± SD	37.1 ± 4.4	37.6 ± 4.0	
NLR			0.922
Mean ± SD	9.5 ± 6.2	9.6 ± 6.8	
PLR			0.168
Mean ± SD	230 ± 142	210 ± 114	
MLR			0.651
Mean ± SD	0.77 ± 0.44	0.79 ± 0.39	
D-D (ug/L)			0.437
Mean ± SD	11 ± 8	11 ± 5	
ESR (mm/h)			0.346
Mean ± SD	35 ± 23	33 ± 20	
CRP(mg/L)			0.765
Mean ± SD	40 ± 39	39 ± 33	

Note: SII = systemic immune-inflammation index; NLR = neutrophil-to-lymphocyte ratio; PLR = platelet-to-lymphocyte ratio; MLR = monocyte-to-lymphocyte ratio; PT = prothrombin time; APTT = activated partial thromboplastin time; TT = thrombin time; FIB = fibrinogen; D-D = D-dimer; ESR=Erythrocyte sedimentation rate; CRP=C-reactive protein; ALT = alanine aminotransferase; LDH = lactate dehydrogenase; TP = total protein; ALB = albumin.

- MLR = total number of monocytes/total number of lymphocytes;
- NLR = total number of neutrophils/total number of lymphocytes;
- PLR = total number of platelets/total number of lymphocytes;
- SII = (total number of neutrophils × total number of platelets)/total number of lymphocytes;

2.4. Statistical analysis

The dataset from The First People's Hospital of Neijiang was randomly allocated into training and validation cohorts at a 7:3 ratio. The variables within these cohorts were then compared. Non-normally distributed data were presented as median values with interquartile ranges. In the univariate analysis, the chi-square test or Fisher's exact test was applied to categorical variables, while the Student's t-test or rank-sum test was utilised for continuous variables. In the training cohort, the least absolute shrinkage and selection operator (LASSO) logistic regression analysis was employed for multivariate analysis to identify independent risk factors and to

Table 2
Comparison of variables between DVT group and no-DVT group.

Characteristics	Training Cohort			Internal Test Cohort		
	No-DVT (n = 170)	DVT (n = 72)	p-value	No-DVT (N = 81)	DVT (N = 23)	p-value
Gender			0.429			0.026
Male	56 (33%)	20 (28%)		26 (32%)	2 (9%)	
Female	114 (67%)	52 (72%)		55 (68%)	21 (91%)	
Age(years)			0.043			0.648
Mean ± SD	80 ± 10	82 ± 7		80 ± 9	81 ± 6	
Mechanism of injury			0.366			0.071
Fall	167 (98%)	69 (96%)		79 (98%)	20 (87%)	
Traffic	3 (2%)	3 (4%)		2 (2%)	3 (13%)	
Injury-admission interval			0.743			0.031
<8h	58 (34%)	23 (32%)		34 (42%)	4 (17%)	
≥8h	112 (66%)	49 (68%)		47 (58%)	19 (83%)	
Classification of fracture			0.431			0.475
Femoral neck fracture	106 (62%)	41 (57%)		49 (60%)	12 (52%)	
Intertrochanteric fracture	64 (38%)	31 (43%)		32 (40%)	11 (48%)	
Cardiovascular and cerebrovascular diseases			0.254			0.898
Without	60 (35%)	31 (43%)		34 (42%)	10 (43%)	
With	110 (65%)	41 (57%)		47 (58%)	13 (57%)	
SII			<0.001			0.287
Mean ± SD	1459 ± 1140	2184 ± 1653		1454 ± 999	1919 ± 1981	
PT (s)			0.676			0.669
Mean ± SD	11.52 ± 2.04	11.44 ± 0.85		11.32 ± 0.95	11.24 ± 0.74	
APTT (s)			0.374			0.756
Mean ± SD	27.3 ± 6.1	26.7 ± 4.8		28.9 ± 5.6	28.3 ± 7.7	
TT (s)			0.711			0.395
Mean ± SD	16.90 ± 1.27	16.98 ± 1.43		18.17 ± 12.76	16.93 ± 1.44	
FIB (g/L)			0.426			0.221
Mean ± SD	3.77 ± 1.30	3.93 ± 1.41		3.74 ± 1.26	4.13 ± 1.34	
ALT (U/L)			0.662			0.214
Mean ± SD	21 ± 14	22 ± 15		20 ± 11	26 ± 21	
LDH (U/L)			0.463			0.315
Mean ± SD	240 ± 72	248 ± 76		255 ± 73	279 ± 106	
TP (g/L)			0.006			0.534
Mean ± SD	66 ± 6	63 ± 7		66.1 ± 5.6	65.2 ± 5.6	
ALB (g/L)			0.002			0.126
Mean ± SD	37.7 ± 4.4	35.8 ± 4.2		38.0 ± 3.9	36.5 ± 4.0	
NLR			0.080			0.664
Mean ± SD	9.0 ± 5.9	10.7 ± 6.8		9.8 ± 6.4	9.0 ± 8.1	
PLR			0.021			0.447
Mean ± SD	216 ± 138	264 ± 147		205 ± 102	230 ± 150	
MLR			0.222			0.042
Mean ± SD	0.74 ± 0.45	0.82 ± 0.43		0.82 ± 0.41	0.67 ± 0.28	
D-D (ug/L)			0.943			0.394
Mean ± SD	11 ± 7	11 ± 8		11.0 ± 4.4	9.8 ± 5.7	
ESR (mm/h)			0.918			0.531
Mean ± SD	35 ± 22	36 ± 26		32 ± 20	35 ± 21	
CRP(mg/L)			0.519			0.301
Mean ± SD	41 ± 39	38 ± 42		37 ± 31	46 ± 37	

SII = systemic immune-inflammation index; NLR = neutrophil-to-lymphocyte ratio; PLR = platelet-to-lymphocyte ratio; MLR = monocyte-to-lymphocyte ratio; PT = prothrombin time; APTT = activated partial thromboplastin time; TT = thrombin time; FIB = fibrinogen; D-D = D-dimer; ESR=Erythrocyte sedimentation rate; CRP=C-reactive protein; ALT = alanine aminotransferase; LDH = lactate dehydrogenase; TP = total protein; ALB = albumin.

develop a prediction nomogram for thrombosis. The efficacy of the nomogram was evaluated using the receiver operating characteristic (ROC) curve and calibration curve, with the area under the ROC curve (AUC) ranging from 0.5 (indicating no discrimination) to 1 (indicating perfect discrimination). Decision curve analysis (DCA) was also conducted to ascertain the net benefit threshold of the prediction. Results were deemed significant at a p-value of less than 0.05. All statistical analyses were executed using R software (version 4.2.2) and MSTATA software (www.mstata.com).

3. Results

3.1. Patient characteristics

A total of 346 elderly individuals, diagnosed with hip fractures at The First People's Hospital of Neijiang from January 2020 to December 2023, were included in the study. All participants satisfied the inclusion and exclusion criteria. Subsequently, 70% of the patients were allocated to the training cohort, while the remaining 30% formed the internal validation cohort, using a computerized random selection method. In this study, we analyzed the baseline demographic and clinical characteristics of the participants across the different cohorts (Table 1).

The gender distribution was comparable between the training cohort (N = 242) and the internal validation cohort (N = 104), with no statistically significant difference observed (p = 0.404). Regarding age, there were no notable differences between the two cohorts (p = 0.820), with mean ages of 81 ± 9 years in the training cohort and 80 ± 8 years in the internal validation cohort. Concerning the mechanism of injury, the majority of cases in both cohorts were due to falls (97.5% in the training cohort and 95.2% in the internal validation cohort). A smaller proportion were the result of traffic accidents (2.5% in the training cohort and 4.8% in the internal validation cohort), with no significant difference observed between the cohorts (p = 0.317).

The interval from injury to hospital admission demonstrated no significant disparity between the cohorts (p = 0.582). In terms of fracture types, analysis revealed no notable differences between the cohorts (p = 0.716), with femoral neck fractures being the most common, comprising 60.7% in the training cohort and 58.7% in the internal validation cohort. Furthermore, the prevalence of comorbid cardiovascular and cerebrovascular diseases was similarly distributed between the cohorts (p = 0.411), observed in 37.6% of the training cohort and 42.3% of the internal validation cohort.

Hematological and biochemical parameters, including SII, PT, APTT, TT, FBGC, ALT, LDH, TP, ALB, NLR, PLR, and MLR, exhibited no significant differences between the cohorts. Overall, the demographic and clinical characteristics presented similar distributions between the training cohort and the internal test cohort, indicating a comparable baseline for predictive research.

The Wilcoxon test and chi-square test were employed to compare indices between the DVT and No-DVT groups. Within the training cohort, five significant indicators (P < 0.05, Table 2) were identified, comprising age (P = 0.043), SII (P < 0.001), TP (P = 0.006), albumin (ALB) (P = 0.002), and platelet-to-lymphocyte ratio (PLR) (P = 0.021).

3.2. Predictive model

The candidate predictors – age, SII, TP, ALB, and PLR – were initially included in the original model. This model was then refined to a single potential predictor using LASSO regression analysis conducted in the training cohort. The coefficients of this analysis are presented in Table 3, and a coefficient profile is depicted in Fig. 1A. Additionally, a cross-validated error plot for the LASSO regression model is illustrated in Fig. 1B. As indicated in Fig. 1B, the most regularized and parsimonious model, achieving a cross-validated error within one standard error of the minimum, encompassed one variable.

As demonstrated in Fig. 2, the ROC analysis of the aforementioned variables yielded AUC values exceeding 0.5, with SII achieving an AUC of 0.648. Subsequent multivariate logistic analyses were conducted in different cohorts, with results detailed in Table 4. The final logistic model, incorporating one independent predictor, was transformed into a user-friendly nomogram, as shown in Fig. 3. The model's performance, as depicted in Fig. 4, revealed AUCs of 0.648 (sensitivity = 51.4%, specificity = 74.7%, Youden index = 0.261) in the training cohort and 0.545 (sensitivity = 43.5%, specificity = 67.9%, Youden index = 0.114) in the internal validation cohort, indicating commendable predictive capability. Calibration plots for the nomogram in the respective cohorts are presented in Fig. 5A and B. These plots exhibit a strong concordance between observed and predicted thrombosis. The findings suggest that the original nomogram remains valid for use in the validation sets, with the calibration curve of this model closely aligning with the ideal curve, signifying that the predicted outcomes were consistent with the actual observations.

Table 3
The coefficients of Lasso regression analysis.

Coefficient	variable
−0.96978410388	(Intercept)
0.00000000000	Age_level_
0.00006519538	SII_level_
0.00000000000	TP_level_
0.00000000000	ALB_level_
0.00000000000	PLR_level_

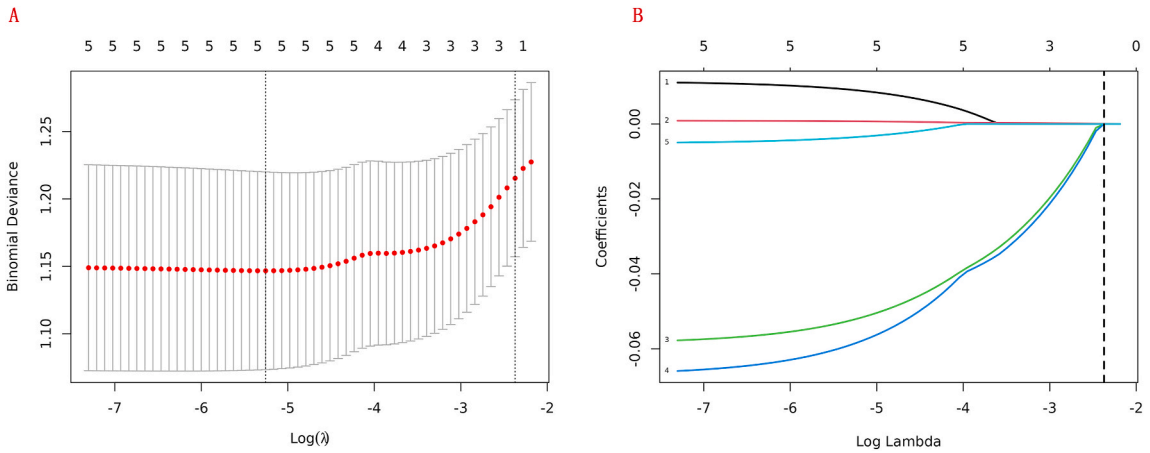


Fig. 1. Lasso regression cross-validation plot (A); lasso regression coefficient path plot (B).

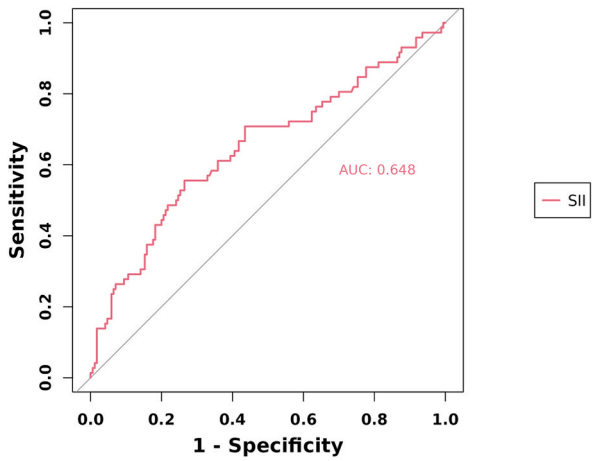


Fig. 2. ROC curve analysis of 3 candidate diagnostic indicators.

Table 4
Results of Multivariate Logistic regression for Training Cohort.

Characteristic	N	Event N	OR[a]	95% CI[1]	p-value
SII	242	72	1.00	1.00, 1.00	<0.001

[a] OR = Odds Ratio, CI = Confidence Interval.

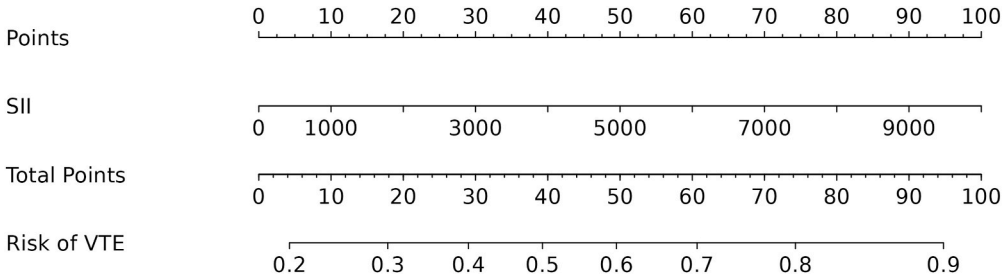


Fig. 3. Nomogram prediction model for elderly patients with hip fractures. (VTE, venous thromboembolism).

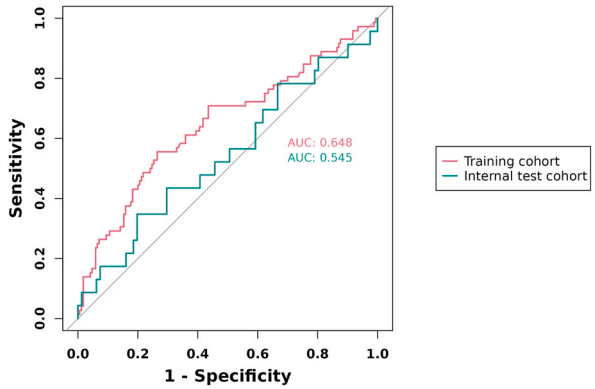


Fig. 4. ROC curves of the nomogram prediction model in the training cohort and internal test cohort.

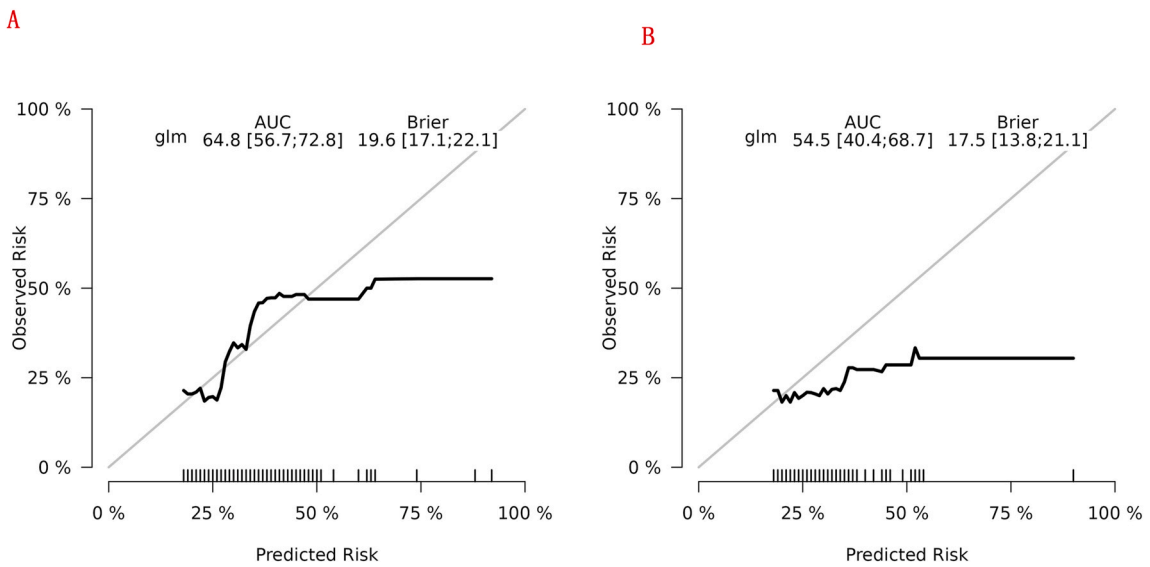


Fig. 5. Calibration curve of the nomogram prediction mode for the training cohort (A) and the internal test cohort (B).

3.3. Decision curve analysis

Fig. 6A and B illustrates the decision curve analysis (DCA) curves pertaining to the nomogram. A high-risk threshold probability indicates the likelihood of significant deviations in the model's predictions when clinicians experience substantial errors in employing the nomogram for diagnostic and decision-making purposes. This study demonstrates that the nomogram provides good net benefits for clinical application, as evidenced by its DCA curve.

4. Discussion

VTE is a common complication in patients undergoing major orthopaedic surgery [2]. The covert onset of VTE contributes to considerable heterogeneity in clinical symptoms and signs among individuals, resulting in a high incidence of missed diagnoses and misdiagnoses. Previous studies have established a close relationship between inflammatory immunity and VTE [13–16]. The inflammatory immune response can activate the coagulation system, diminish the activity of anticoagulant substances in the body, impair the fibrinolytic system function, and lead to thrombosis [17]. The interplay between inflammatory immune responses and VTE is intricate. Inflammation activates transcription factors (including NF-κB) and intracellular enzymes (including cysteine protease family proteases), culminating in the secretion of various inflammatory mediators, such as cytokines, chemokines, and growth factors. These mediators stimulate endothelial cells, WBC, and PLT, inducing the expression of cell adhesion molecules on their surfaces and subsequently triggering coagulation through the stimulation of monocytes to produce TF. The exposure of factor VII to TF serves as the primary initiator of coagulation activation. Complex interactions among endothelial cells, WBC, and PLT lead to endothelial damage and dysfunction, a critical link between inflammation and thrombosis [18–21]. TNF-α, IL-6, IL-8, and MCP-1 may also contribute to the

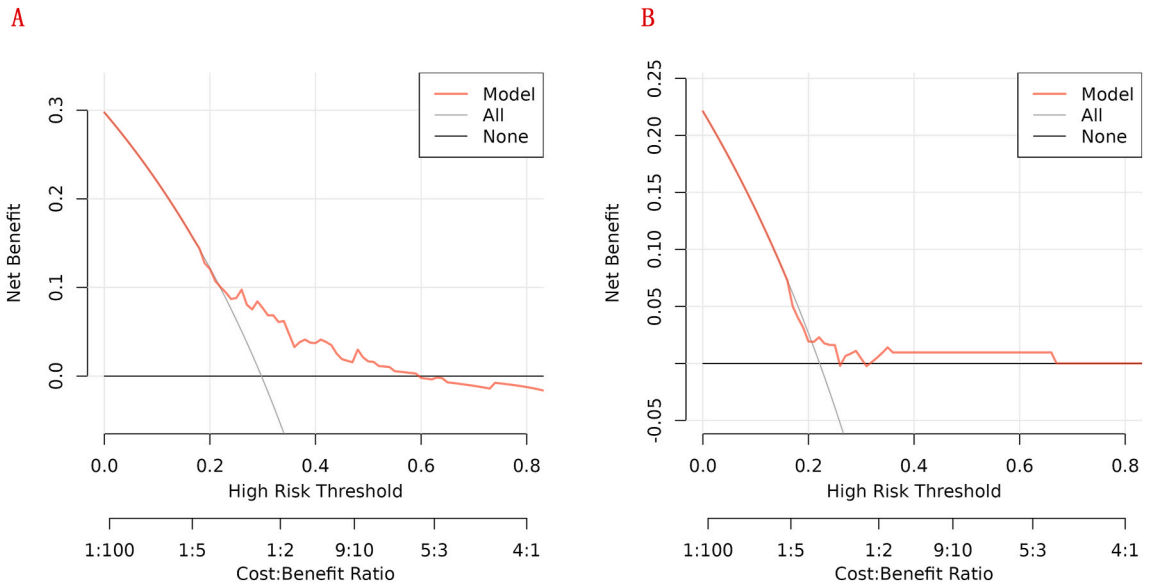


Fig. 6. Decision curve analysis of the nomogram of the training cohort (A) and the internal test cohort (B).

pathogenesis of venous thrombosis [22–26]. Following a fracture, FIB, a typical acute-phase inflammatory protein, is a core component of hemostasis and coagulation, indicative of heightened coagulation and fibrinolytic properties. The thrombin-fibrin axis is regarded as a pivotal pathway mediating the activity of inflammatory cells, with coagulation factors and fibrinolysin downstream of inflammation playing key roles [27,28]. Additionally, PLT activation is a significant factor in the pathophysiological process of inflammation-induced thrombosis [29]. Thus, in the hours post-fracture, the inflammatory immune response triggered by the fracture can often create a pre-thrombotic environment.

The systemic immune-inflammatory index (SII) is an emerging, stable, and readily accessible serological marker of inflammatory immunity [30–32]. In recent years, SII has gained widespread use in reflecting systemic inflammatory immune status, determining prognosis, and stratifying risk. Unlike similar indices such as the NLR, PLR, and MLR, which incorporate only two types of cells (lymphocytes, neutrophils, or monocytes), SII offers the advantage of integrating three cell types (lymphocytes, neutrophils, and platelets). This integration provides a more comprehensive reflection of the balance between inflammation, immunity, and coagulation in the body. Moreover, SII has shown greater efficacy in predicting survival outcomes or prognoses compared to NLR, PLR, and MLR [11,12]. Historically, inflammatory immune response and thrombosis were considered independent pathophysiological processes. However, recent research has revealed partial interconnectivity and mutual influence between these processes in terms of molecular components and signaling pathways, elucidating to some extent the relationship between inflammatory immune response and VTE [10,33,34]. This insight provides a theoretical foundation for investigating the relationship between SII and the risk of VTE following hip fracture in the elderly. Wang et al. [35] employed SII to predict the survival rate of elderly patients with hip fractures in their prospective cohort study, concluding that it possesses significant predictive value and clinical applicability. Another retrospective cohort study identified BMI, NLR, and SII at admission as independent predictors of DVT in patients with intertrochanteric femoral fractures [12]. In our current study, we developed and validated a nomogram for predicting venous thromboembolism after hip fracture in the elderly, based on a cohort of 346 patients. The primary predictor, SII, was incorporated into the nomogram and was statistically significant in the multivariate logistic regression analysis. The model's AUC in the training cohort was 0.648 (0.567–0.728), demonstrating robust predictive capability. This finding corroborates the conclusions of previous studies.

Our study is subject to several limitations that warrant acknowledgement. The cohort was derived solely from patients at The First People's Hospital of Neijiang, which may not accurately represent the broader population. Additionally, there is a possibility of potential unmeasured confounders that were not accounted for in our model. External validation across diverse populations is imperative to ascertain the generalisability of our findings. Future research should focus on the external validation of our nomogram in varied populations and settings. Moreover, the incorporation of novel predictors or biomarkers could potentially enhance the predictive accuracy of the nomogram, meriting further exploration.

5. Conclusions

The predictive model utilising the systemic immune-inflammatory index is highly significant for assessing the risk of venous thromboembolism (VTE) and demonstrates notable efficacy. Owing to its accessibility and cost-effectiveness, it can offer a crucial reference for clinical guidance in the prevention, management, and treatment of VTE following hip fracture in the elderly.

Ethical approval

The study has been evaluated and approved by the ethics community of the First People's Hospital of Neijiang (approval number: 2023-lunshenpi-39).

Funding

This work was supported by the Neijiang Science and Technology Plan Project (grant number Z202309).

Consent to participate

It was waived the informed consents owing to the retrospective nature of this study.

Consent for publication

Not applicable.

Data availability statement

Data will be made available on request.

CRediT authorship contribution statement

Xiao Chen: Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Yuanhe Fan:** Validation, Supervision, Investigation, Data curation, Conceptualization. **Hongliang Tu:** Validation, Supervision, Investigation, Data curation. **Jie Chen:** Visualization, Supervision, Data curation. **Renming Li:** Visualization, Validation, Supervision, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Abbreviations

VTE	venous thromboembolism
DVT	deep vein thrombosis
PE	pulmonary embolism
SII	systemic immune-inflammation index
AUC	area under the receiver operating characteristic curve
ROC:	receiver operating characteristic
DCA	decision curve analysis
MLR	monocyte-to-lymphocyte ratio
NLR	neutrophil-to-lymphocyte ratio
PLR	platelet-to-lymphocyte ratio
BMI	body mass index
PT	prothrombin time
APTT	activated partial thromboplastin time
TT	thrombin time
FIB	fibrinogen
D-D	D-dimer
ESR	erythrocyte sedimentation rate
CRP	C-reactive protein
ALT	alanine aminotransferase
LDH	lactate dehydrogenase
TP	total protein
ALB	albumin

References

[1] J.A. Cauley, D. Chalhoub, A.M. Kassem, H. Fuleihan Gel, Geographic and ethnic disparities in osteoporotic fractures, Nature reviews, Endocrinology 10 (6) (2014) 338–351.
[2] J.A. Heit, Epidemiology of venous thromboembolism, Nat. Rev. Cardiol. 12 (8) (2015) 464–474.
[3] J.B. Brill, J. Badiee, A.L. Zander, J.D. Wallace, P.R. Lewis, M.J. Sise, V. Bansal, S.R. Shackford, The rate of deep vein thrombosis doubles in trauma patients with hypercoagulable thromboelastography, J. Trauma Acute Care Surg. 83 (3) (2017) 413–419.
[4] Y. Tang, K. Wang, Z. Shi, P. Yang, X. Dang, A RCT study of Rivaroxaban, low-molecular-weight heparin, and sequential medication regimens for the prevention of venous thrombosis after internal fixation of hip fracture, Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie 92 (2017) 982–988.
[5] T. Taoka, T. Ohmori, T. Kanazawa, K. Toda, T. Ishihara, Y. Ito, Delayed surgery after hip fracture affects the incidence of venous thromboembolism, J. Orthop. Surg. Res. 18 (1) (2023) 630.
[6] B.F. Zhang, X. Wei, H. Huang, P.F. Wang, P. Liu, S.W. Qu, J.H. Li, H. Wang, Y.X. Cong, Y. Zhuang, K. Zhang, Deep vein thrombosis in bilateral lower extremities after hip fracture: a retrospective study of 463 patients, Clin. Interv. Aging 13 (2018) 681–689.
[7] J.M. Van Gent, R.Y. Calvo, A.L. Zander, E.J. Olson, C.B. Sise, M.J. Sise, S.R. Shackford, Risk factors for deep vein thrombosis and pulmonary embolism after traumatic injury: a competing risks analysis, J. Trauma Acute Care Surg. 83 (6) (2017) 1154–1160.
[8] S. Diao, J. Li, J. Zhao, D. Wang, H. Wang, X. Xu, J. Zhou, Risk factors and new inflammatory indicators of deep vein thrombosis after adult patella fractures, Frontiers in surgery 9 (2022) 1028542.
[9] R.M. Melinte, E.M. Arbănași, Inflammatory biomarkers as prognostic factors of acute deep vein thrombosis following the total knee arthroplasty 58 (10) (2022).
[10] Y. Qin, B. Zhang, S. Zhao, W. Wang, S. Dong, Y. Miao, S. Zhao, L. LiuShenkunTang, Z. Wu, J. Kang, A. Liu, Association between higher systemic immune inflammation index (SII) and deep vein thrombosis (DVT) in patients with aneurysmal subarachnoid hemorrhage (aSAH) after endovascular treatment, Neurosurg. Rev. 46 (1) (2023) 142.
[11] M. Tort, F.C. Sevil, H. Sevil, N. Becit, Evaluation of systemic immune-inflammation index in acute deep vein thrombosis: a propensity-matched, Journal of vascular surgery. Venous and lymphatic disorders 11 (5) (2023) 972–977.e1.
[12] G. Zeng, X. Li, W. Li, Z. Wen, S. Wang, S. Zheng, X. Lin, H. Zhong, J. Zheng, C. Sun, A nomogram model based on the combination of the systemic immune-inflammation index, body mass index, and neutrophil/lymphocyte ratio to predict the risk of preoperative deep venous thrombosis in elderly patients with intertrochanteric femoral fracture: a retrospective cohort study, J. Orthop. Surg. Res. 18 (1) (2023) 561.
[13] B.R. Branchford, S.L. Carpenter, The role of inflammation in venous thromboembolism, Frontiers in pediatrics 6 (2018) 142.
[14] I. Budnik, A. Brill, Immune factors in deep vein thrombosis initiation, Trends Immunol. 39 (8) (2018) 610–623.
[15] F. Galeano-Valle, L. Ordieres-Ortega, C.M. Oblitas, Inflammatory biomarkers in the short-term prognosis of venous thromboembolism: a narrative review 22 (5) (2021).
[16] S. Mukhopadhyay, T.A. Johnson, N. Duru, M.S. Buzza, N.R. Pawar, R. Sarkar, T.M. Antalis, Fibrinolysis and inflammation in venous thrombus resolution, Front. Immunol. 10 (2019) 1348.
[17] C.T. Esmon, Crosstalk between inflammation and thrombosis, Maturitas 61 (1–2) (2008) 122–131.
[18] H.M. Nording, P. Seizer, H.F. Langer, Platelets in inflammation and atherogenesis, Front. Immunol. 6 (2015) 98.
[19] A.T. Nurden, Platelets, inflammation and tissue regeneration, Thrombosis and haemostasis 105 (Suppl 1) (2011) S13–S33.
[20] P. Poredos, M.K. Jezovnik, The role of inflammation in venous thromboembolism and the link between arterial and venous thrombosis, Int. Angiol. : a journal of the International Union of Angiology 26 (4) (2007) 306–311.
[21] T.W. Wakefield, D.D. Myers, P.K. Henke, Mechanisms of venous thrombosis and resolution, Arterioscler. Thromb. Vasc. Biol. 28 (3) (2008) 387–391.
[22] K.G. Lee, H. Lee, J.M. Ha, Y.K. Lee, H.J. Kang, C.G. Park, S.J. Kim, Increased human tumor necrosis factor-α levels induce procoagulant change in porcine endothelial cells in vitro, Xenotransplantation 19 (3) (2012) 186–195.
[23] A. Mahemuti, K. Abudureheman, X. Aihemaiti, X.M. Hu, Y.N. Xia, B.P. Tang, H. Upur, Association of interleukin-6 and C-reactive protein genetic polymorphisms levels with venous thromboembolism, Chinese medical journal 125 (22) (2012) 3997–4002.
[24] M.F. Matos, D.M. Lourenço, C.M. Orikaza, J.A. Bajerl, M.A. Noguti, V.M. Morelli, The role of IL-6, IL-8 and MCP-1 and their promoter polymorphisms IL-6 -174GC, IL-8 -251AT and MCP-1 -2518AG in the risk of venous thromboembolism: a case-control study, Thromb. Res. 128 (3) (2011) 216–220.
[25] U. Yadav, A. Mahemuti, X. Hu, K. Abudureheman, Y. Xia, B. Tang, H. Upur, Single nucleotide polymorphisms in interleukin-6 and their association with venous thromboembolism, Mol. Med. Rep. 11 (6) (2015) 4664–4670.
[26] K.C. Zapponi, B.M. Mazetto, L.F. Bittar, A. Barnabé, F.D. Santiago-Bassora, E.V. De Paula, F.A. Orsi, C.F. Franco-Penteado, N. Conran, J.M. Annichino-Bizzacchi, Increased adhesive properties of neutrophils and inflammatory markers in venous thromboembolism patients with residual vein occlusion and high D-dimer levels, Thromb. Res. 133 (5) (2014) 736–742.
[27] J.P. Luyendyk, J.G. Schoenecker, M.J. Flick, The multifaceted role of fibrinogen in tissue injury and inflammation, Blood 133 (6) (2019) 511–520.
[28] F.M. Szaba, S.T. Smiley, Roles for thrombin and fibrin(ogen) in cytokine/chemokine production and macrophage adhesion in vivo, Blood 99 (3) (2002) 1053–1059.
[29] G. Shi, C.N. Morrell, Platelets as initiators and mediators of inflammation at the vessel wall, Thromb. Res. 127 (5) (2011) 387–390.
[30] J. Han, L. Yang, Z. Lou, Y. Zhu, Association between systemic immune-inflammation index and systemic inflammation response index and outcomes of acute ischemic stroke: a systematic review and meta-analysis, Ann. Indian Acad. Neurol. 26 (5) (2023) 655–662.
[31] T. Huang, Q. Peng, Y. Zhang, Z. Zhu, X. Fan, The Systemic Immune-Inflammation Index (SII) and coronary artery lesions in Kawasaki disease, Clin. Exp. Med. 24 (1) (2024) 4.
[32] B. Liao, Q. Xu, P. Lu, Y. Zhang, The prognostic value of systemic immune-inflammation index in patients with aneurysmal subarachnoid hemorrhage: a systematic review, Neurosurg. Rev. 46 (1) (2023) 219.
[33] X. Chen, Y. Ou, Z. Wang, H. Liu, Y. Liu, M. Liu, Association between systemic immune-inflammation index and risk of lower extremity deep venous thrombosis in hospitalized patients: a 10-year retrospective analysis, Frontiers in cardiovascular medicine 10 (2023) 1211294.
[34] P.G. Zheng, P. Chen, L.J. Wang, N. Zhang, The association of the systemic immune-inflammation index and stent thrombosis in myocardial infarction patients after coronary stent implantation-a retrospectively study, J. Thorac. Dis. 15 (4) (2023) 1726–1733.
[35] Z.C. Wang, W. Jiang, X. Chen, L. Yang, H. Wang, Y.H. Liu, Systemic immune-inflammation index independently predicts poor survival of older adults with hip fracture: a prospective cohort study, BMC Geriatr. 21 (1) (2021) 155.