# **RESEARCH ARTICLE**



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



Guowei Zeng<sup>1,2†</sup>, Xu Li<sup>1†</sup>, Wencai Li<sup>3†</sup>, Zhijia Wen<sup>1,2</sup>, Shenjie Wang<sup>1,2</sup>, Shaowei Zheng<sup>1</sup>, Xia Lin<sup>1,2</sup>, Haobo Zhong<sup>1,2\*</sup>, Jianping Zheng<sup>1\*</sup> and Chunhan Sun<sup>1,2\*</sup>

## Abstract

**Objectives** Deep vein thrombosis (DVT) has been considered as a frequent and serious consequence of intertrochanteric femoral fractures in the elderly. Several negative repercussions of DVT can be considerably mitigated by its timely recognition and treatment. The current work was aimed at exploring the factors independently predicting DVT among cases suffering from intertrochanteric femoral fractures and validate their predictive usefulness in diagnosing DVT.

**Methods** Between April 2017 and July 2022, clinical information from 209 cases showing preoperative DVT for femoral intertrochanteric fractures were retrospectively evaluated. In patients with femoral intertrochanteric fractures, logistic regression analysis with a backward stepwise method was adopted for detecting independent predictors for the diagnosis of preoperative DVT. Using multivariate logistic regression, a nomogram prediction model was developed and verified with the testing group.

<sup>†</sup>Guowei Zeng, Xu Li and Wencai Li equal contribution to the present study.

\*Correspondence: Haobo Zhong 402161066@qq.com Jianping Zheng hz-vip@163.com Chunhan Sun sunchunhan@126.com Full list of author information is available at the end of the article



© The Author(s) 2023. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

**Results** According to multivariate logistic regression model, body mass index (BMI) (OR 0.79, 95% CI 0.63–0.99, P=0.042), neutrophil/lymphocyte ratio (NLR) (OR 7.29, 95% CI 1.53, 34.64, P=0.0012), and systemic immune-inflammation index (SII) (OR 6.61, 95% CI 2.35, 18.59, P=0.001) were independent predictors for DVT before surgery among cases developing intertrochanteric femoral fracture. AUC values were 0.862 and 0.767 for training and testing groups, separately, while their mean errors in the calibration curve were 0.027 and 0.038 separately. Decision curve analysis (DCA) curve revealed a high value of clinical application for both groups.

**Conclusion** Upon admission, BMI, NLR, and SII are independent predictors of DVT before surgery among cases developing intertrochanteric femoral fractures. Additionally, the nomogram based on the BMI, NLR, and SII can assist clinicians in determining if preventive and symptomatic therapies are required to improve DVT prognosis and reduce its associated mortality.

**Keywords** Deep venous thrombosis (DVT), Immune inflammatory factors, Intertrochanter femoral fracture, Nomogram, SII, NLR, BMI

## Introduction

Intertrochanteric femoral fracture is a type of hip fracture that accounts for 63% of all hip fractures. It is the most commonly seen fracture in the elderly, accounting for 10–15% of all fractures in the elderly population [1, 2]. DVT is a primary factor causing global disability and mortality [3, 4], which is a common consequence of an intertrochanteric femoral fracture. Intertrochanteric fractures particularly predispose to DVT owing to its certain unique characteristics, such as the presence of heavy bleeding, the existence of a hypercoagulable state, overall stress reaction, inflammatory response, and forced immobility due to pain [5].

Because of its non-invasive nature and good reproducibility, ultrasound Doppler is most commonly used for diagnosing lower limb DVT [6]. Color Doppler ultrasonography, on the other hand, struggles to produce good image quality in conditions such as a fixed posture, acute limb edema, and extreme discomfort. In clinical practice, color Doppler ultrasonography is not employed frequently for the regular assessment of lower limb fractures or cannot be done on time, resulting in treating patients with thrombosis out of time. In addition, thrombosis is evaluated clinically by several coagulation indicators, like fibrinogen (FIB) levels, D-dimer levels, prothrombin time (PT), thrombin time (TT), activated partial thromboplastin time (APTT), and platelet count (PLT). Among them, D-dimer, FIB, and PLT are commonly used in the clinical evaluation of thrombosis. Plasma D-dimer concentrations are final products generated by plasminase-dependent cross-linked fibrin breakdown, and its large serum levels indicate hypercoagulability and hyperfibrinolysis. Therefore, D-dimer levels are suggestive of DVT with a high sensitivity of more than 95%. However, their specificity is low, at just 20–40% [7–9]. As a result, D-dimer's efficacy among the old cases suffering from fractures remains debatable [10]. Furthermore, FIB stimulates blood clotting towards the end of the coagulation process, and an increase in PLT count implies hypercoagulability [11]. These indicators can also be elevated in non-fractured individuals, in which case a single signal has limited specificity and a significant false positive rate (FPR) for diagnosing DVT [12].

Apart from those three major factors in the pathophysiology of thrombus formation, namely, stasis or blood flow changes, blood hypercoagulation, and vascular wall injury, inflammatory molecules, and immune cells are now considered to be major contributors to thrombosis. Budnik and Brill detailed immune factors' effects on DVT pathogenesis in their review [3]. Colling et al. detailed the mechanisms by which the immune and coagulation processes interact with and regulate each other [13]. Branchford et al. suggested that systemic inflammatory responses are related to an elevated risk of DVT. The ensuing platelet activation enhances the prethrombotic state and leads to the development of DVT [14]. Restricted blood flow or stasis induces rapid leukocyte recruitment, which leads to the formation of DVT [15]. Neutrophils, monocyte, lymphocytes, and platelets also make a vital impact on the development of DVT [16–18]. Based on these single indicators, corresponding indices including monocyte/lymphocyte ratio (MLR), platelet/lymphocyte ratio (PLR), neutrophil/lymphocyte ratio (NLR), and (platelet × neutrophil)/lymphocyte (systemic immune-inflammation index, SII) are established. Moreover, these indicators have been confirmed to better show the immune inflammatory state of the body [19– 22]. These new combination indexes of peripheral bloodderived markers are progressively utilized in orthopedic surgery and its related complications [23-30].

Therefore, the present study aimed to find independent risk factors for thrombosis in intertrochanteric femoral fractures by integrating the risk factors of thrombosis and novel immune inflammatory indices. On this basis, a prediction model was built to assess the DVT event among

Page 3 of 12

cases suffering from intertrochanteric femoral fractures simply and effectively.

#### Methods

## Patient and public involvement

This study is a retrospective one, with the research questions and assessments being predetermined and not determined by the patient's priorities, experience, and preferences. Ethics Committee of First People's Hospital of Huizhou reviewed this work and determined that it would not harm the patient or present any potential risk factors. Therefore, no patient involvement or informed consent was required. Moreover, the findings of the study will be reported to the participants and used in clinical trials to observe any potential clinical benefits. The interventions of this study are examinations which are already available to the patient during their hospitalization and do not require any additional cost to the patient.

## Patient selection

In this retrospective study, patients whose intertrochanteric femoral fractures were diagnosed in the orthopedic department of Huizhou First Hospital during April 2017-July 2022 were included. Patients conforming to criteria below were included: (1) cases hospitalized within 5 days (120 h) of disease inception with a definitive radiographic fracture diagnosis, and (2) those aged over > 60 years (a total of 716 patients). Cases conforming to criteria below were eliminated: (1) patients having insufficient information including medical records and preoperative vascular color doppler ultrasonography results (a total of 247 patients); (2) those aged under 60 years (a total of 113 patients); (3) patients with the following conditions: multiple fractures diagnosed at this admission, pathological fracture diagnosed at this admission, previous and recent anticoagulant use, inflammatory diseases, unclear diagnosis of infection at admission, and anti-infective drug use (a total of 147 patients). Ultimately, a sum of 209 patients was incorporated into our research.

The current work was performed following the Helsinki Declaration and was approved by Huizhou First Hospital's ethical committee (2,022,138). Based on the retrospective character of the investigation, no written informed consent was required. With the aim of protecting patients' privacy, the identifying information of those who took part in this study was rendered anonymous.

## **Data extraction**

This work gathered basic clinical information from each case, containing their age, sex, fracture site, time of injury to the hospital (damage time, Dtime), diastolic blood pressure (DBP), systolic blood pressure (SBP), temperature (the first measurement on admission), breaths per minute (BPM, the first measurement on admission), pulse (the first measurement on admission), and a medical history of hypertension, diabetes, smoking, and alcoholism. We determined hypertension with the past hypertension history and SBP/DBP of 140/90 mmHg on admission, whereas diabetic with having the past diabetes history, random blood glucose of 11.1 mmol/L on admission and fasting blood glucose (FBG) of 7 mmol/L. Patients' routine blood, hemostatic function, and other serological test results acquired at emergency department or in one day after admission were collected. The normal range for hemoglobin count was between (115- $150) \times 10^{9}$ /L and  $(130-175) \times 10^{9}$ /L for women and men, respectively, for RBC count,  $(4.3-5.8) \times 10^9$ /L, for WBC count,  $(2-7) \times 10^{9}$ /L, for NC count,  $(2-7) \times 10^{9}$ /L, for LYM count,  $(0.8-3.5) \times 10^9$ /L, for MNC count, (0.1-0.6)×10<sup>9</sup>/L, for PLT count, (100–300)×10<sup>9</sup>/L, for FIB, (1.8–3.5) g/L, for TT, (14–21) s, for PT–INR, (0.85–1.20), for APTT, (22.5-34.0) s, for D-dimer, (0-0.5) mg/L, and PT, (9.8-13.2) s. Values outside the above-mentioned normal ranges were considered to be abnormal. The correlation inflammatory-immune index was evaluated by collecting PLT, NC, LYM, and MNC data during routine blood investigations performed at the emergency department or right after admission. The formulae used were:

NLR=NC/LYM; PLR=PLT/LYM; MLR=MNC/LYM; and SII=PLT×NC/LYM.

## Outcome event

The event of DVT in the elderly with intertrochanteric femoral fracture was considered the outcome event in this study. The positive result was characterized as DVT, whereas the negative outcome was defined as No DVT. "Thrombus" was used as a label to record whether patients with intertrochanteric femoral fractures developed a DVT, which was recorded according to preoprerative color Doppler ultrasonography. The following were the diagnostic criteria for DVT in color Doppler ultrasonography: 1. Abnormal echoes. 2. The vein beneath the ultrasound probe at the fracture site should not have been compressed shut. 3. The venous thrombus section should have shown no clear indication of blood flow. 4. A reduction in the should have occurred afflicted limb's blood flow and vascular width. A skilled sonographer used color doppler ultrasonography to evaluate blood vessels in the lower extremities and provided a diagnostic report to identify DVT. The bilateral common femoral vein, superficial/deep femoral vein, popliteal vein, anterior/posterior tibial vein, as well as peroneal vein were all tested according to the aim of the present study. Because of the limited clinical relevance of superficial or myenteric veins, the present work did not include superficial vein thrombi.

## Statistical analysis

Before data analysis, we applied R studio version 4.0.3 (The R Foundation for Statistical Computing, Vienna, Austria) to randomly sample the patients into a 7:3 ratio of training group (n=147) and testing group (n=62). SPSS 26 (SPSS Inc., Chicago, IL, USA) was adopted in assessing data for normalcy. Normally-distributed continuous variables were represented by mean and standard deviation and compared by t-test, while abnormally-distributed ones were represented by median and quartile and compared by rank sum test. Numeration variables were represented by percentage n (%) for comparisons among groups by chi-square test or Fisher's test when over 1/5 of cells in contingency table had the predicted frequency of less than 5. To determine the comparability of both groups and to guarantee our prediction model viability, we compared the baseline data of the both groups.

We further classified training group into DVT (n=28) or No DVT group (n=119) based on the outcome events. Rank sum test, t-test, Fisher's test and chi-square test were adopted to compare data between two groups. Two sets of violin plots of deference data were created with R studio (version 4.0.3), which included BMI, WBC, NC, LYM, NLR, PLR, and SII. We drew ROC curves for assessing predictive power of the deference data for DVT. Furthermore, based on these cutoff values, high and low groups within each variable were established. In order to determine the variables connected to the outcome event, univariate logistic regression was initially performed, and odds ratios (ORs) together with associated 95% confidence intervals (CIs) were determined. Significant variables (P < 0.05) from the univariate analysis were incorporated into multivariate regression, using a backward stepwise strategy to find independent predictors of DVT. P<0.05 indicated statistical significance for the two-sided tests. A nomogram prediction model was built utilizing age and significant variables found in the multivariate regression and displayed using R studio (version 4.0.3). The predictive model nomogram effectiveness was evaluated by ROC curve and area under the curve (AUC). The calibration curve and mean absolute error were employed with the purpose of assessing the nomogram's goodness of fit. The clinical effects of the nomogram were evaluated based on decision curve analysis (DCA) using the high-risk threshold.

The grouping criteria and model construction process are shown in Fig. 1.

## Results

## **Baseline characteristics**

The 209 included cases were randomized as training or testing group, in a ratio of 7:3. Thirty-eight men (25.85%) and 109 women (74.15%) comprised the test group with a



Fig. 1 Flow chart. The process of population screening criteria and prediction model establishment in this study

(P > 0.05), supporting the model training and verification

mean age and BMI of 83 (77, 87) years and 22.43 (21.62, 2 23.37) kg/m<sup>2</sup>, respectively. Sixteen men (25.81%) and 46 5 women (74.19%) with a mean BMI of 22.67 kg/m<sup>2</sup> and ti age 83.5 (74.5, 87) years, respectively, made up the testing group. All of the variables including sex, age, BMI, 0 alcoholism, smoking, hypertension, diabetes, fracture ti site, thrombus, DBP, SBP, Dtime, temperature, BPM, 0 and pulse were not significantly different of both groups c

on both groups (Additional file 1: Table S1). Based on the results of preoperative vascular color doppler ultrasonography, the training group was subdivided into No DVT (n=119) and DVT (n=28). The No DVT group included 31 men (26.05%) and 88 women (73.95%), their average age was 83 (77, 87) years, while their BMI was 22.43 (21.62, 23.37) kg/m<sup>2</sup>. The DVT group included 7 men (25%) and 21 women (75%), with a mean age of 85 (82, 87.25) years and a BMI of 21.84 (20.7, 22.41) kg/m<sup>2</sup>. BMI was significantly different of both groups (P < 0.05), but no differences in baseline characteristics (P > 0.05)such as sex, age, alcoholism, smoking, hypertension, diabetes, fracture site, DBP, SBP, Dtime, temperature, BPM, and pulse. Following admission, a series of routine blood tests (HGB, RBC, WBC, NC, LYM, MNC, and PLT) and tests for coagulation (FIB, TT, PT-INR, APTT, D-D dimer, and PT) were carried out to complete the study data collection. There existed significant differences in WBC, NC, and LYM levels in DVT compared with No DVT groups (P<0.05), while MNC, PLT, FIB, TT, PT-INR, APTT, D-D dimer, and PT levels did not show significant difference (P>0.05). We acquired the correlation inflammatory-immune indices including MLR, NLR, PLR, and SII based on routine blood test indexes; typically, PLR was notably different in DVT compared with No DVT groups (P=0.008). Furthermore, the NLR and SII levels in DVT group obviously increased compared with No DVT group (P < 0.001). (Additional file 2: Table S2). A violin plot was created from the statistically significant data (Fig. 1).

# Factors correlated with DVT among old cases experiencing intertrochanter femoral fracture

WBC, NC, NLR, PLR, and SII values of DVT group (median values:  $8.75 \times 10^9$ /L,  $7.43 \times 10^9$ /L, 7.05 L/L, 212.69 L/L, and  $1558.09 \times 10^9$ /L, respectively) were notably higher than those in the No DVT group (median values:  $8.13 \times 10^9$ /L,  $6.17 \times 10^9$ /L, 5.46 L/L, 161.18 L/L, and  $1013.07 \times 10^9$ /L, respectively). The value of BMI and LYM in the DVT group (median: 21.84 kg/m<sup>2</sup>,  $0.96 \times 10^9$ /L) obviously decreased compared with No DVT group (median: 22.64 kg/m<sup>2</sup>,  $1.12 \times 10^9$ /L) (P < 0.05, Additional file 2: Table S2, Fig. 2). Based on ROC curves, the optimal thresholds of BMI, WBC, NC, LYM, PLR, and SII were

22.45444 kg/m<sup>2</sup>,  $8.46 \times 10^{9}$ /L,  $6.79 \times 10^{9}$ /L,  $1.285 \times 10^{9}$ /L, 5.323077 L/L, 205.2885 L/L, and 1528.033 L/L, respectively, with a sensitivity of 0.786, 0.714, 0.643, 0.929, 0.929, 0.571, and 0.536, respectively, and specificity of 0.563, 0.538, 0.664, 0.37, 0.462, 0.756, and 0.899, respectively. The AUCs of those data were 0.686, 0.633, 0.684, 0.639, 0.743, 0.662, and 0.734, respectively, which were considered to be a certain predictive value in diagnosing DVT (Additional file 3: Table 3, Fig. 3).

We split the 147 patients into high and low groups on the basis of the ROC cutoff value to better comprehend the relationship between the aforementioned differential variables and DVT. As shown in the univariate analyses, low BMI and high WBC, NC, LYM, NLR, PLR, and SII were linked to DVT. Upon multivariate regression, low BMI, high NLR, and high SII were discovered to be factors independently predicting DVT among cases developing an intertrochanteric femoral fracture (Additional file 4: Table S4, Fig. 4).

## Predictive nomogram development

Next, with the aim of predicting the DVT development among cases developing an intertrochanteric femoral fracture, we created the nomogram model using age, BMI, NLR, and SII using a binary logistic regression equation (Fig. 5). Other indicators, such as NLR and SII, were binary variables, whereas age and BMI were continuous variables. Zero denoted a low NLR, while 1 denoted a high NLR. Similarly, zero denoted a low SII, while 1 stood for a high SII. The calibration curve, nomogram, DCA curve and ROC curve mapped. Our nomogram contained a score for each component, and the aggregate of the values indicated the risk of DVT. The training group's AUC was 0.862 (Fig. 6A), whereas the testing group's AUC was 0.767 (Fig. 6B). The calibration curves were plotted to calibrate our nomogram, that of training group (Fig. 7A) indicated the mean model error of 0.027 for predicting vs. actually producing bad result, while that of testing group (Fig. 7B) was 0.038, indicating that the predictions were conformed to the data. The training group's DCA curve revealed that when the highrisk threshold was 0.02-0.78, our prediction model could offer superior clinical benefits (Fig. 8A). Testing group's DCA curve revealed that the prediction model could offer higher clinical benefits when the high-risk threshold was between 0.06 and 0.57 (Fig. 8B).

## Discussion

Intertrochanteric femoral fracture has been a commonly seen fracture that requires hospitalization among the old cases [31]. As global life expectancy and the proportion of older individuals increases, hip fracture risk among the old people, particularly intertrochanteric fractures, will



Fig. 2 Violin plot of significant variables obtained after univariate logistic regression analysis

continue to elevate [32]. Survival and prognosis analysis has been the focus of research in recent years. Patients with intertrochanteric fractures often require surgical treatment, and the preoperative and postoperative complications are the major reason for high disability and mortality rates in these patients [33]. DVT is regarded as a frequently seen complication secondary to intertrochanteric fractures [34]. However, the low specificity of a single clinical index and the late completion time of color Doppler ultrasonography often delays the clinical diagnosis of DVT [7–9]. This defers the treatment of DVT, leading to a series of complications, delayed surgery, and even death [3, 12, 35]. In the present study, after multivariate logistic regression analysis, BMI, NLR, and SII were found to be independent predictive factors in the diagnosis of DVT in intertrochanteric femoral fractures. The above prediction indexes are easy to obtain and calculate. For doctors, it can greatly improve the efficiency of diagnosis and treatment of DVT. For patients, it is of great help to reduce the rate of disability and



Fig. 3 ROC of significant variables obtained after univariate logistic regression analysis

mortality and improve the prognosis. A nomogram prediction model was also constructed based on these three factors, and its validity and practicability in clinical were analyzed. This model can assist in the rapid, accurate, and effective prediction of DVT in patients suffering from intertrochanteric femoral fractures.

Currently, BMI's effect on DVT pathogenesis is unknown. As per one school of thought, cases showing the high BMI probably show relatively more adipose tissues, which may increase inflammatory factor production and enhance tissue factor generation, in turn activating exogenous coagulation pathways as well as promoting thrombus formation [36]. Matsumoto et al. attempted to analyze age, BMI, and D-dimer in thrombotic cases compared with non-thrombotic cases and showed that BMI was not significantly different between them [37]. Pahlkotter et al. analyzed the ACS-NSQIP database and discovered that the occurrence of DVT in obese patients was 1.7 times that in normal BMI patients, and that in cases having BMI <18.5 kg/m<sup>2</sup> was 1.4 folds









that in normal BMI patients [38]. This indicates that patients with abnormal BMI, whether obese or thin, have an elevated DVT incidence relative to cases showing normal BMI. As observed from the research on cases receiving total hip replacement, Yu et al. found BMI>28 kg/  $m^2$  as the factor predicting DVT incidence [39]. In our study, BMI, as an independent protective factor, was less correlated with DVT than were NLR and SII (OR 0.79; 95% CI 0.63–0.99; P, 0.042), which is contrary to the findings of previous studies, possibly due to the narrow range of BMI values in our study (testing group, 22.43 kg/m<sup>2</sup> (21.62, 23.37); training group, 22.67 kg/m<sup>2</sup> (21.52, 23.92)). Most patients were roughly within the normal range. This likely led to BMI being a protective factor in the prediction of intertrochanteric fracture thromboses in our model. An increase in BMI within a certain range may represent an increase in muscle strength. The improved blood flow associated with greater muscle strength can reduce the risk of DVT [5]. Nevertheless, our findings need to be confirmed by increasing the sample size or increasing the range of BMI in the population.

Previously, our understanding of DVT was confined to the Virchow triad, but there is now increasing evidence that the immune-inflammatory system also makes a vital impact on the process of thrombosis [40]. Budnik and Brill systematically described the mechanisms of immune factors in thrombosis, such as the depletion of neutrophils that inhibits venous thrombus formation [3]. The process of immune inflammation is described in Branchford's paper. The release of various inflammatory factors under the combined action of neutrophils, T-lymphocytes and circulating monocytes has an important effect on thrombogenesis [14]. Many immune and inflammatory reactions can be detected during DVT occurrence and disappearance [41]. NLR, which includes neutrophils and lymphocytes, collectively represents the immune inflammatory system, and it is also widely used [25, 30, 42]. In this study, NLR was discovered to independently predict thrombosis among cases undergoing intertrochanteric femoral fracture, and had a good predictive value (AUC, 0.743; 95% CI 0.646, 0.84; P<0.001). As easily available clinical data, NLR can enable faster diagnoses and accurate treatments in clinical medicine.

SII is a popular immunoinflammatory index in recent years. It includes the combination of neutrophils, lymphocytes and PLTs, which allows for better prediction in the field of orthopedics. According to our results, SII represented the strong factor predicting DVT among cases experiencing intertrochanteric femoral fractures. When the SII threshold was 1528.033 in the ROC curve, the AUC was 0.734 (95%: 0.616, 0.852; P<0.001), which markedly increased compared with BMI (AUC, 0.686; 95 CI% 0.576, 0.796; P<0.002). Wang et al. used SII for predicting the survival rate of old cases experiencing hip fractures in their prospective cohort study, and concluded that it had a good predictive value and strong clinical practicability [43]. In a multi-arm prospective cohort study, researchers used SII to predict fracture among postmenopausal cases. In this study, age, longer menopause duration, higher NLR, and higher SII were detected to be independent risk factors, among which the predictive effect of SII was more prominent than that of other factors [44]. SII also plays a predictive role in the diagnosis of thrombosis after knee replacement [45]. Therefore, the prediction model constructed in this study, with the combined effect of SII, can help determine the diagnosis and appropriate treatments more quickly and accurately.

However, certain limitations should be noted in this work: (1) This was an unicentric retrospective study which had limited sample size as well as several confounding variables. Clinically significant risk variables,



Fig. 6 ROC of the prediction in the testing group and the training group



Fig. 7 Calibration curve of the training group and the testing group





such as time from trauma to admission and age, were not thoroughly examined. A multicenter regression study and thorough examination of data results for risk variables could be conducted in future studies. This will improve the predictive value and accuracy of the model. (2) The preoperative preliminary diagnosis of DVT was caused by a delay in ultrasonography time. When the time to refine the results was extended, the DVT developed in certain individuals differed from the results required for our study. Future studies can incorporate the time of diagnosis, the time of reporting, and the time difference between the two results. (3) This work was not validated by external data and the model's correctness and usefulness were not clarified. When multi-center retrospective studies are conducted in the future, external verification can be carried out with data from other hospitals to



confirm the authenticity of the model. (4) A large number of cases were ruled out of this work and the prediction model scope was small. It is suggested to increase the sample size as much as possible on the basis of strictly following the inclusion and exclusion criteria in future multi-center studies. (5) This study only studied the risk of DVT before surgery. The further discussion on the risk of DVT after surgery can be carried out in the future.

## Conclusion

The BMI, NLR, and SII at admission are independent predictors of DVT in patients with intertrochanteric femoral fractures. These indices can be acquired conveniently and quickly. In addition, the nomogram on the basis of BMI, NLR, and SII can assist clinicians in evaluating the need for DVT. In clinical practice, faster and better treatment decisions can be made visually.

#### Abbreviations

DVT	Deep vein thrombosis
BMI	Body mass index
FIB	Fibrinogen
PT	Prothrombin time
TT	Thrombin time
PT-INR	Prothrombin time-international normalized ratio
APTT	Activated partial thromboplastin time
PLT	Platelet count
MNC	Mononuclear cell
NC	Neutrophilic cell
LYM	Lymphocyte
WBC	White blood cell
RBC	RED blood cell
HCT	Red blood cell specific volume

MCV	Mean corpuscular volume
MCH	Mean corpuscular hemoglobin
MCHC	Mean corpuscular hemoglobin concentration
HGB	Hemoglobin
PDW	Platelet distributionwidth
FBG	Fasting blood glucose
DBP	Diastolic blood pressure
SBP	Systolic blood pressure
Dtime	Damage time
MLR	Monocyte/lymphocyte ratio
PLR	Platelet/lymphocyte ratio
SII	Systemic immune-inflammation index
NLR	Neutrophil/lymphocyte ratio, platelet x neutrophilic cell/
	lymphocyte
DCA	Decision curve analysis
AUC	Area under the curve
ROC	Receiver operating characteristic curve
ORs	Odds ratios
Cls	Confidence intervals

## **Supplementary Information**

The online version contains supplementary material available at https://doi.org/10.1186/s13018-023-03966-4.

Additional file 1. Table S1: Baseline characteristics of all studied patients. Additional file 2. Table S2: Comparison of clinical and laboratory data

between the No DVT group and DVT group in the Testing Group. Additional file 3. Table S3: AUC and Cutoff value of ROC curve in the

significant variables.

Additional file 4. Table S4: Outcomes of the binary logistic regression analysis.

## Acknowledgements

We appreciate Bullet Edits Limited for the linguistic editing and proofreading of the manuscript. We are delighted to be part of this research project, and congratulate all the participants! We are grateful for the support of our patients and appreciate the contributions they have made. We look forward to your continued involvement in our research.

#### Author contributions

GZ and CS were responsible for study design and conception. GZ, JZ, and WL organized the database. GZ, XL, and HZW carried out statistical analyses. GZ was in charge of manuscript drafting. GZ, ZW, SW, and SZ wrote sections of the manuscript. GZ and XL participate in table and image drawing. The authors participated in the manuscript revision, and read, and agreed with the eventual version for submission.

#### Funding

This work was supported by the Foundation of Guangdong Basic and Applied Basic Research Foundation (Grant Nos. 2022A1515140046 and 2022A1515140151) and Huizhou Priority Clinical Speciality Cultivation Project (Orthopedics and Sports Medicine) and Scientific Research Projects of Guangdong Provincial Bureau of Traditional Chinese Medicine (Grant Nos. 20221400) and Research and Huizhou Science and Technology Project (Grant Nos. 2022CZ010146 and 2022CZ010423).

#### Availability of data and materials

All data supporting the present work are contained in this study, which can be obtained from corresponding authors on request.

#### Declarations

#### Ethics approval and consent to participate

The study was conducted following Helsinki Declaration and gained approval from Huizhou First Hospital's ethical committee (2022138). Based on the retrospective character of the investigation, ethics Committee waived the need of informed consent.

#### **Consent for publication**

To protect patients' privacy, identifying information of those who took part in this study was rendered anonymous.

#### **Competing interests**

The authors declare that they have no competing interests.

#### Author details

<sup>1</sup>Present Address: Department of the Orthopedics, Huizhou First Hospital, Guangdong Medical University, Huizhou 516000, Guangdong, China. <sup>2</sup>Present Address: Guangdong Medical University, Zhanjiang 524000, Guangdong, China. <sup>3</sup>Present Address: Department of Neurosurgery, Huizhou Central People's Hospital, Huizhou, China.

#### Received: 24 April 2023 Accepted: 29 June 2023 Published online: 03 August 2023

#### References

- Bouyer B, Leroy F, Rudant J, Weill A, Coste J. Burden of fractures in France: incidence and severity by age, gender, and site in 2016. Int Orthop. 2020;44(5):947–55. https://doi.org/10.1007/s00264-020-04492-2.
- Schultz KA, Westcott BA, Barber KR, Sandrock TA. Elevated 1-year mortality rate in males sustaining low-energy proximal femur fractures and subgroup analysis utilizing age-adjusted Charlson comorbidity index. Geriatr Orthop Surg Rehabil. 2020;11:2151459319898644. https://doi.org/ 10.1177/2151459319898644.
- Budnik I, Brill A. Immune factors in deep vein thrombosis initiation. Trends Immunol. 2018;39(8):610–23. https://doi.org/10.1016/j.it.2018.04.010.
- Lapidus LJ, Rosfors S, Ponzer S, et al. Prolonged thromboprophylaxis with dalteparin after surgical treatment of achilles tendon rupture: a randomized, placebo-controlled study. J Orthop Trauma. 2007;21(1):52–7. https://doi.org/10.1097/01.bot.0000250741.65003.14.
- Bovill EG, van der Vliet A. Venous valvular stasis-associated hypoxia and thrombosis: what is the link? Annu Rev Physiol. 2011;73:527–45. https:// doi.org/10.1146/annurev-physiol-012110-142305.

- Chinese Orthopaedic Association. Prevention of venous thromboembolism after major orthopaedic surgery. Orthop Surg. 2010;2(2):81–5. https://doi.org/10.1111/j.1757-7861.2010.00068.x.
- Dempfle CE, Korte W, Schwab M, Zerback R, Huisman MV. Sensitivity and specificity of a quantitative point of care D-dimer assay using heparinized whole blood, in patients with clinically suspected deep vein thrombosis. Thromb Haemost. 2006;96(1):79–83. https://doi.org/10.1160/ th05-12-0826.
- Bongard O, Wicky J, Peter R, et al. D-dimer plasma measurement in patients undergoing major hip surgery: use in the prediction and diagnosis of postoperative proximal vein thrombosis. Thromb Res. 1994;74(5):487–93. https://doi.org/10.1016/0049-3848(94)90269-0.
- Han C, Zhao Y, Cheng W, et al. The performance of age-adjusted D-dimer cut-off in Chinese outpatients with suspected venous thromboembolism. Thromb Res. 2015;136(4):739–43. https://doi.org/10.1016/j.thromres. 2015.07.024.
- Rumley A, Emberson JR, Wannamethee SG, Lennon L, Whincup PH, Lowe GD. Effects of older age on fibrin D-dimer, C-reactive protein, and other hemostatic and inflammatory variables in men aged 60–79 years. J Thromb Haemost. 2006;4(5):982–7. https://doi.org/10.1111/j.1538-7836. 2006.01889.x.
- Yang T, Wei G, Zhu C, Pan A. Incidence and risk factor analysis of deep venous thrombosis in patients with severe traumatic brain injury. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue. 2019;31(2):182–6. https://doi.org/10. 3760/cma.j.issn.2095-4352.2019.02.012.
- Ruskin KJ. Deep vein thrombosis and venous thromboembolism in trauma. Curr Opin Anaesthesiol. 2018;31(2):215–8. https://doi.org/10. 1097/aco.00000000000567.
- 13. Colling ME, Tourdot BE, Kanthi Y. Inflammation, infection and venous thromboembolism. Circ Res. 2021;128(12):2017–36. https://doi.org/10. 1161/circresaha.121.318225.
- Branchford BR, Carpenter SL. The Role of inflammation in venous thromboembolism. Front Pediatr. 2018;6:142. https://doi.org/10.3389/fped. 2018.00142.
- Wang H, Wang Q, Wang J, et al. Proprotein convertase subtilisin/ kexin type 9 (PCSK9) deficiency is protective against venous thrombosis in mice. Sci Rep. 2017;7(1):14360. https://doi.org/10.1038/ s41598-017-14307-x.
- Stewart GJ. Neutrophils and deep venous thrombosis. Haemostasis. 1993;23(Suppl 1):127–40. https://doi.org/10.1159/000216922.
- von Brühl ML, Stark K, Steinhart A, et al. Monocytes, neutrophils, and platelets cooperate to initiate and propagate venous thrombosis in mice in vivo. J Exp Med. 2012;209(4):819–35. https://doi.org/10.1084/jem. 20112322.
- Dewyer NA, El-Sayed OM, Luke CE, et al. Divergent effects of Tlr9 deletion in experimental late venous thrombosis resolution and vein wall injury. Thromb Haemost. 2015;114(5):1028–37. https://doi.org/10.1160/ th14-12-1031.
- Forrest EH, Storey N, Sinha R, et al. Baseline neutrophil-to-lymphocyte ratio predicts response to corticosteroids and is associated with infection and renal dysfunction in alcoholic hepatitis. Aliment Pharmacol Ther. 2019;50(4):442–53. https://doi.org/10.1111/apt.15335.
- Wang BL, Tian L, Gao XH, et al. Dynamic change of the systemic immune inflammation index predicts the prognosis of patients with hepatocellular carcinoma after curative resection. Clin Chem Lab Med. 2016;54(12):1963–9. https://doi.org/10.1515/cclm-2015-1191.
- Chan AW, Chan SL, Wong GL, et al. Prognostic nutritional index (PNI) predicts tumor recurrence of very early/early stage hepatocellular carcinoma after surgical resection. Ann Surg Oncol. 2015;22(13):4138–48. https://doi. org/10.1245/s10434-015-4516-1.
- Wei M, Guo H, Liu S, et al. Combined immune score predicts the prognosis of newly diagnosed multiple myeloma patients in the bortezomibbased therapy era. Medicine (Baltimore). 2021;100(41):e27521. https://doi. org/10.1097/md.00000000027521.
- Chen T, Cao X, Liu C, Wang J. Dynamic modeling and analysis of fivedegree-of-freedom active suspension systems. Appl Sci. 2020;10(5):1776.
- Xu H, Xie JW, Liu L, Wang D, Huang ZY, Zhou ZK. Combination of CRP with NLR is a sensitive tool for screening fixation-related infection in patients undergoing conversion total hip arthroplasty after failed internal fixation for femoral neck fracture. Bone Joint J. 2021;103-b(9):1534–40. https://doi. org/10.1302/0301-620x.103b.Bjj-2021-0105.R1.

- Song BW, Kim AR, Moon DH, et al. Associations of neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio and monocyte-to-lymphocyte ratio with osteoporosis and incident vertebral fracture in postmenopausal women with rheumatoid arthritis: a single-center retrospective cohort study. Medicina (Kaunas). 2022. https://doi.org/10.3390/medicina58 070852.
- Chen P, Liu Y, Lin X, et al. Diagnostic value of the blood neutrophil-to-lymphocyte ratio and monocyte-to-lymphocyte ratio in tibia fracture-related infection. Dis Mark. 2022;2022:6119583. https://doi.org/10.1155/2022/ 6119583.
- Wang Z, Wang Y, Wang Y, Chen W, Zhang Y. Correction to: Are postoperative NLR and PLR associated with the magnitude of surgery-related trauma in young and middle-aged patients with bicondylar tibial plateau fractures? A retrospective study. BMC Musculoskelet Disord. 2022;23(1):62. https://doi.org/10.1186/s12891-022-04996-5.
- Araki Y, Yamamoto N, Hayashi K, et al. Pretreatment neutrophil count and platelet-lymphocyte ratio as predictors of metastasis in patients with osteosarcoma. Anticancer Res. 2022;42(2):1081–9. https://doi.org/10. 21873/anticanres.15570.
- Diao S, Li J, Zhao J, et al. Risk factors and new inflammatory indicators of deep vein thrombosis after adult patella fractures. Front Surg. 2022;9:1028542. https://doi.org/10.3389/fsurg.2022.1028542.
- Wang Z, Wang Y, Wang Y, Chen W, Zhang Y. Are postoperative NLR and PLR associated with the magnitude of surgery-related trauma in young and middle-aged patients with bicondylar tibial plateau fractures? A retrospective study. BMC Musculoskelet Disord. 2021;22(1):816. https:// doi.org/10.1186/s12891-021-04695-7.
- Sandmann G, Biberthaler P. Pertrochanteric femoral fractures in the elderly. Unfallchirurg. 2015;118(5):447–60. https://doi.org/10.1007/ s00113-015-0007-x.
- Dhanwal D, Dennison E, Harvey N, Cooper C. Epidemiology of hip fracture: worldwide geographic variation. Indian J Orthop. 2011;45(1):15–22. https://doi.org/10.4103/0019-5413.73656.
- Khow K, Shibu P, Yu S, Chehade M, Visvanathan R. Epidemiology and postoperative outcomes of atypical femoral fractures in older adults: a systematic review. J Nutr Health Aging. 2017;21(1):83–91. https://doi.org/ 10.1007/s12603-015-0652-3.
- Fu Y, Liu P, Xu X, et al. Deep vein thrombosis in the lower extremities after femoral neck fracture: a retrospective observational study. J Orthop Surg (Hong Kong). 2020;28(1):2309499019901172. https://doi.org/10.1177/ 2309499019901172.
- Zhang L, He M, Jia W, et al. Analysis of high-risk factors for preoperative DVT in elderly patients with simple hip fractures and construction of a nomogram prediction model. BMC Musculoskelet Disord. 2022;23(1):441. https://doi.org/10.1186/s12891-022-05377-8.
- Hunt BJ. The effect of BMI on haemostasis: implications for thrombosis in women's health. Thromb Res. 2017;151(Suppl 1):S53–5. https://doi.org/ 10.1016/s0049-3848(17)30068-3.
- Matsumoto M, Kurasako T, Niguma T, Yaida Y, Iwasaki E, Ishii N. Preoperative screening of deep venous thrombosis: cutoff value of D-dimer, age and BMI for further examination of DVT by echo-color-Doppler. Masui. 2014;63(12):1350–4.
- Pahlkotter MK, Mohidul S, Moen MR, et al. BMI and VTE risk in emergency general surgery, does size matter?: an ACS-NSQIP database analysis. Am Surg. 2020;86(12):1660–5. https://doi.org/10.1177/0003134820940272.
- Yu X, Wu Y, Ning R. The deep vein thrombosis of lower limb after total hip arthroplasty: what should we care. BMC Musculoskelet Disord. 2021;22(1):547. https://doi.org/10.1186/s12891-021-04417-z.
- Wakefield TW, Myers DD, Henke PK. Mechanisms of venous thrombosis and resolution. Arterioscler Thromb Vasc Biol. 2008;28(3):387–91. https:// doi.org/10.1161/atvbaha.108.162289.
- Meissner MH, Wakefield TW, Ascher E, et al. Acute venous disease: venous thrombosis and venous trauma. J Vasc Surg. 2007;46 Suppl:25s–53s. https://doi.org/10.1016/j.jvs.2007.08.037.
- Ming L, Jiang Z, Ma J, Wang Q, Wu F, Ping J. Platelet-to-lymphocyte ratio, neutrophil-to-lymphocyte ratio, and platelet indices in patients with acute deep vein thrombosis. Vasa. 2018;47(2):143–7. https://doi.org/10. 1024/0301-1526/a000683.
- 43. Wang ZC, Jiang W, Chen X, Yang L, Wang H, Liu YH. Systemic immuneinflammation index independently predicts poor survival of older adults

with hip fracture: a prospective cohort study. BMC Geriatr. 2021;21(1):155. https://doi.org/10.1186/s12877-021-02102-3.

- 44. Fang H, Zhang H, Wang Z, Zhou Z, Li Y, Lu L. Systemic immune-inflammation index acts as a novel diagnostic biomarker for postmenopausal osteoporosis and could predict the risk of osteoporotic fracture. J Clin Lab Anal. 2020;34(1):e23016. https://doi.org/10.1002/jcla.23016.
- Melinte RM, Arbănaşi EM, Blesneac A, et al. Inflammatory biomarkers as prognostic factors of acute deep vein thrombosis following the total knee arthroplasty. Medicina (Kaunas). 2022. https://doi.org/10.3390/ medicina58101502.

## **Publisher's Note**

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.