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ORIGINAL RESEARCH

Predicting Preoperative Deep Vein Thrombosis Using d-Dimer-to-Albumin Ratio Combined with Neutrophil-to-Lymphocyte Ratio in Older Patients with Hip Fracture

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Objective: This study aimed to explore the potential value of the d-dimer to albumin ratio (DAR) combined with the neutrophil-to-lymphocyte ratio (NLR) for predicting preoperative lower extremity deep vein thrombosis (DVT) in older patients with hip fracture.

Methods: Demographic characteristics, comorbidities, medication history, and preoperative laboratory test results were collected from older patients with hip fracture between 2018 and 2023. Binary logistic regression analysis was used to assess the association between the DAR, NLR, and DVT. Receiver operating characteristic (ROC) curve analysis was performed to calculate the potential value of DAR combined with NLR in predicting preoperative DVT.

Results: A total of 1177 patients were included, of whom 23 (2%) developed lower extremity DVT before surgery. Multivariate logistic regression analysis indicated that age (OR = 1.08, 95% CI = 1.01~1.15, $P = 0.015$), DAR (OR = 1.53, 95% CI = 1.21~1.92, $P < 0.001$), and NLR (OR = 1.24, 95% CI = 1.10~1.39, $P < 0.001$) were independently associated with preoperative DVT in older patients with hip fractures. Furthermore, the ROC curve analysis indicated that DAR combined with NLR has a significant predictive value for DVT, with an area under the curve of 78.72% (95% CI = 68.24–89.20%).

Conclusion: The preoperative DAR and NLR were independently associated with preoperative DVT in older patients with hip fractures. DAR combined with NLR can be considered as a predictive indicator of DVT.

Keywords: aged, hip fracture, deep vein thrombosis, d-dimer to albumin ratio, neutrophil to lymphocyte ratio

Introduction

Hip fractures remain a major public health concern, particularly in the older population.[1,2] With the aging global population, the number of hip fractures is expected to reach 6 million by 2050.[3,4] Meanwhile, preoperative lower extremity deep vein thrombosis (DVT) is a significant complication in older patients with hip fracture.[5] The incidence of lower extremity DVT in this population was 2.6–30% due to the different times of admission.[6,7] Therefore, early identification of patients at risk of preoperative DVT is essential for implementing preventive strategies that can reduce morbidity and mortality associated with thromboembolic events.

Previous studies have shown that inflammation, nutrition, and coagulation are involved in the pathogenesis of DVT.[8–10] Recent studies have highlighted the neutrophil-to-lymphocyte ratio (NLR) as a promising biomarker owing to its association with systemic inflammation and potential impact on coagulation pathways.[11,12] Increasing evidence has shown that elevated NLR is associated with prognosis in clinical settings, including stroke, autoimmune inflammatory diseases, venous

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thromboembolism, and post-thrombotic syndrome.[13–17] In addition, the d-dimer to albumin ratio (DAR), which reflects inflammation and nutrition, has been reported to be related to the outcomes of cancer and inflammatory diseases.[18,19]

However, combining the NLR and DAR for predicting preoperative DVT in older patients with hip fractures is yet to be explored. By leveraging the inflammatory markers represented by the NLR and thrombotic risk indicated by the DAR, clinicians may be better equipped to stratify patients based on the likelihood of developing DVT. Thus, our study aimed to investigate the potential value of DAR combined with NLR for predicting preoperative DVT in older patients with hip fracture.

Materials and Methods

Study Design and Participants

This cross-sectional study included patients with hip fracture admitted to our hospital between January 2018 and December 2023. This study was approved by the Ethics Committee of Changhai hospital (CHEC2024-257). The ethics committee waived the requirement for informed consent due to the retrospective collection of de-identified clinical data from patients. In addition, all research procedures were designed and implemented in full compliance with the Declaration of Helsinki principles.

Patients aged ≥ 65 years, with femoral neck, intertrochanteric, or subtrochanteric fractures, and with preoperative ultrasound results of the lower extremity deep vein were included. Exclusion criteria were a history of deep vein thrombosis, multiple fractures, old fractures, and missing NLR or DAR values.

Variables and Outcome

In our study, the baseline information we collected included age, gender, alcohol history, smoking history, and comorbidities (hypertension, diabetes, cardiovascular disease, cerebrovascular disease, and malignant tumors). We also recorded the use of anticoagulants or antiplatelet medications (aspirin 100 mg/day or clopidogrel 75 mg/day) before surgery and the time from injury to hospitalization. Additionally, we collected data on preoperative laboratory tests, including white blood cell count, neutrophil count, lymphocyte count, platelet count, and hemoglobin, albumin, creatinine, and d-dimer levels. NLR was calculated as the neutrophil count (10^9/L)/lymphocyte count (10^9/L) and DAR was derived from d-dimer (mg/L)/albumin (g/dL).

The primary outcome was preoperative DVT, diagnosed as a constant intraluminal filling defect using lower extremity color Doppler ultrasonography.[20] Patients received subcutaneous low molecular weight heparin without contraindications to prevent DVT.

Statistical Analysis

The participants were divided into DVT and non-DVT groups based on preoperative DVT. Student's *t*-test was used to compare continuous variables with normally distributed data, which are presented as the mean ± SD. Continuous variables with non-normal distributions were described as medians (interquartile range) and compared using the Mann–Whitney *U*-test. Categorical variables, described as frequency (%), were analyzed using the chi-square test or Fisher's exact test.

Multivariate logistic regression analysis was conducted to assess the association between NLR, DAR, and DVT. The potential value of NLR combined with DAR was evaluated using a receiver operating characteristic (ROC) curve analysis. Free Statistics software version 1.7.1 (Beijing FreeClinical Medical Technology Co., Ltd, Beijing, China), and R 4.2.2 software (http://www.Rproject.org; The R Foundation, Vienna, Austria) were used to conduct all statistical analyses. Statistical significance was set at $p < 0.05$.

Results

In total, 1,836 patients with ultrasound results of the lower extremity deep vein were identified. After excluding 659 patients (25 had a history of DVT, 303 had multiple fractures, 100 had old fractures, 210 were aged < 65 years, and 21 had missing data on NLR or DAR), 1,177 patients with hip fracture were included in the final data analysis, as shown

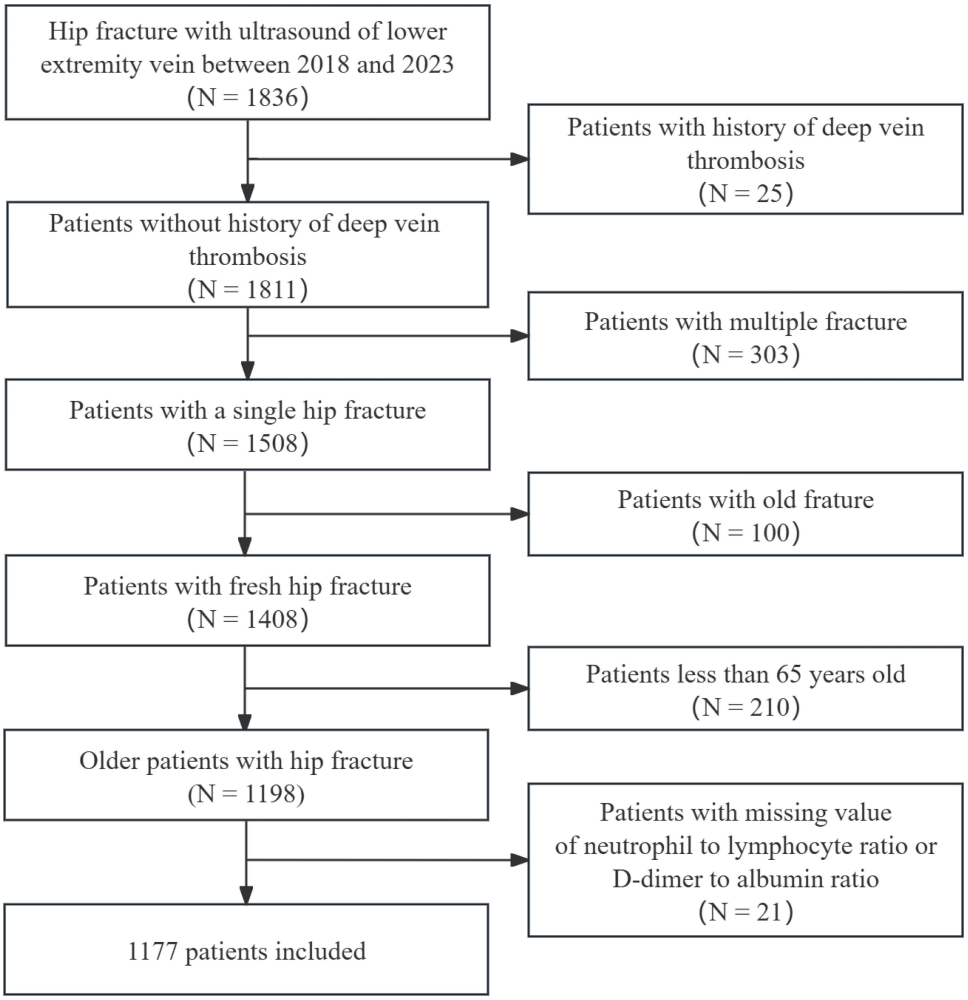

Figure 1 Flowchart of the study population.

in the flow chart (Figure 1). Among them, 23 patients (2%) developed DVT, constituting the DVT group. The remaining patients were assigned to the non-DVT group.

Baseline Characteristics

Compared with the non-DVT group, patients in the DVT group were older and had higher preoperative neutrophil counts, lower lymphocyte counts, higher d-dimer levels, and lower albumin levels (all $P < 0.05$). More importantly, DAR levels in the DVT group were significantly higher than those in the non-DVT group ($P < 0.001$). The NLR was higher in the DVT group than in the non-DVT group ($P = 0.003$). There were no statistically significant differences in the other information between the two groups, as shown in Table 1.

Predictors of Preoperative DVT

Variables with $P < 0.05$ in the Table 1 were included in the multivariate logistic regression analysis. Multivariate logistic regression analysis indicated that age (OR = 1.08, 95% CI = 1.01~1.15, $P = 0.015$), DAR (OR = 1.53, 95% CI = 1.21~1.92, $P < 0.001$), and NLR (OR = 1.24, 95% CI = 1.10~1.39, $P < 0.001$) were independently associated with preoperative lower extremity DVT in older patients with hip fractures (Table 2). In addition, ROC analysis indicated that the area under the curve (AUC) for DAR in predicting preoperative lower extremity DVT in older patients with hip fracture was 72.4% (95% CI = 60.30–85.40%). The AUC for NLR was 67.82% (95% CI = 55.33–80.30%). Moreover,

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Table 1 Characteristics of the Study Participants Between Two Groups

Variable	Non-DVT (n = 1154)	DVT (n = 23)	*P*
Age (year)	79.6 ± 8.2	84.7 ± 5.6	0.003
Male	365 (31.6)	3 (13)	0.057
BMI (kg/m^2)	22.5 ± 3.8	22.6 ± 4.2	0.980
Drinking	16 (1.4)	0 (0)	1
Smoking	43 (3.7)	0 (0)	1
Hypertension	640 (55.5)	17 (73.9)	0.078
Diabetes	333 (28.9)	7 (30.4)	0.869
Cardiovascular disease	302 (26.2)	10 (43.5)	0.063
Cerebrovascular disease	195 (16.9)	4 (17.4)	1
Malignant tumors	33 (2.9)	0 (0)	1
Anticoagulant or antiplatelet drug use	191 (16.6)	6 (26.1)	0.254
Time from injury to hospitalization (h)	18.0 (6.0, 48.0)	17.5 (6.2, 87.0)	0.427
Neutrophil count (10^9/L)	6.1 (4.8, 7.5)	6.7 (6.1, 8.3)	0.044
Lymphocyte count (10^9/L)	1.1 (0.9, 1.4)	0.9 (0.7, 1.2)	0.022
Platelet count (10^9/L)	176.0 (138.0, 217.0)	152.0 (127.5, 202.0)	0.178
White blood cell count (10^9/L)	8.1 (6.7, 9.6)	8.5 (7.5, 10.0)	0.209
Creatinine (μmol/L)	67.0 (57.0, 85.0)	65.0 (59.0, 92.5)	0.883
Hemoglobin (g/L)	114.0 (101.0, 127.0)	105.0 (91.0, 124.5)	0.165
D-dimer (mg/L)	3.7 (1.8, 8.1)	9.9 (2.8, 16.0)	< 0.001
Albumin (g/dL)	3.6 (3.3, 3.9)	3.3 (3.1, 3.8)	0.014
DAR	1.1 (0.5, 2.3)	3.1 (0.8, 6.2)	< 0.001
NLR	5.2 (3.8, 7.2)	7.7 (4.9, 13.0)	0.003

Note: Data are presented as mean ± SD or median (IQR) and frequency (%).
Abbreviations: BMI, Body mass index; DAR, D-dimer to albumin ratio; NLR, neutrophil to lymphocyte ratio; DVT, deep vein thrombosis.

Table 2 Univariable and Multivariable Logistic Regression Analysis to Assess the Association Between DAR, NLR and Lower Extremity Deep Vein Thrombosis

Variable	Unadjusted OR (95% CI)	*P*	Adjusted OR (95% CI)	*P*
Age	1.08 (1.03~1.15)	0.004	1.08 (1.01~1.15)	0.015
DAR	1.74 (1.42~2.14)	<0.001	1.53 (1.21~1.92)	<0.001
NLR	1.31 (1.19~1.45)	<0.001	1.24 (1.10~1.39)	<0.001

Abbreviations: DAR, D-dimer to albumin ratio; NLR, neutrophil to lymphocyte ratio; OR, odds ratio; CI, confidence interval.

DAR combined with NLR had better predictive power for DVT than a single indicator, and the AUC was 78.72% (95% CI = 68.24–89.20%) (Figure 2).

Discussion

Lower extremity DVT is a common complication in older patients with hip fractures that increases the morbidity and mortality associated with thromboembolic events. Therefore, early identification of high-risk DVT patients is particularly important. Our study found that the incidence of preoperative DVT in the older patients with hip fractures was 2%. Multivariate analysis revealed that advanced age, a higher preoperative DAR, and a higher NLR were independently associated with DVT. Furthermore, the AUC for DAR combined with NLR in predicting preoperative DVT was 78.72%.

Previous studies have shown that the incidence of preoperative DVT in older patients with hip fracture ranges from 20 to 30%.[3,21] However, our study found that only 2% of the older patients with hip fracture experienced preoperative DVT events. This discrepancy may be attributed to the fact that over 85% of the patients in our study were hospitalized within 72 hours of their injury. This finding is consistent with a previous study, which indicated that the incidence of preoperative lower extremity DVT was low in patients hospitalized within 72 hours of injury.[6]

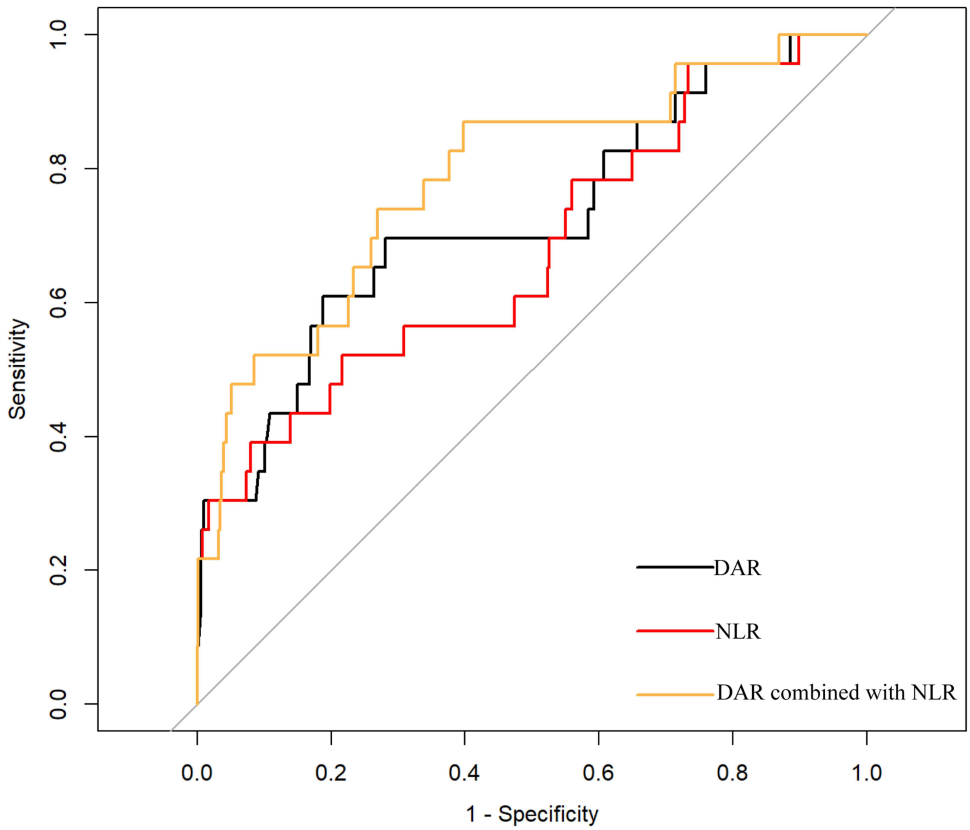

Figure 2 ROC curve of d-dimer to albumin ratio and neutrophil to lymphocyte ratio for prediction of DVT.

Advanced age is a significant risk factor for lower extremity DVT.[22] In older patients, the elasticity and function of blood vessel walls gradually decline, making it easier for blood to coagulate and form clots within the veins. Additionally, neutrophils and lymphocytes play a crucial role in the inflammatory response,[23,24] which can lead to vascular endothelial damage and activate the coagulation system, thereby promoting thrombus formation, particularly after hip fracture. Moreover, increasing evidence indicates that the NLR calculated from neutrophils and lymphocytes is related to prognosis in clinical settings.[25–27] Similarly, our study found that advanced age and a higher preoperative NLR were independently associated with preoperative DVT.

During DVT formation, fibrin is degraded, which leads to d-dimer production.[28] Therefore, elevated d-dimer levels reflect the active coagulation and fibrinolytic processes of DVT. Albumin is a plasma protein primarily synthesized by the liver, reflecting inflammation, nutrition, and coagulation functions,[29,30] which are involved in the occurrence of DVT. Moreover, accumulating studies have shown that high d-dimer and low albumin levels are associated with DVT, which is consistent with our findings.[31,32]

DAR is calculated from D-dimer and albumin levels, reflecting the inflammatory, nutritional, and coagulation status. Recent studies have found that DAR is associated with the prognosis of various diseases, including mortality in patients with cancer, 28-day mortality in patients with sepsis, and readmission rates in patients with chronic obstructive pulmonary disease.[19,33,34] Our study also showed that a higher preoperative DAR is independently associated with preoperative DVT in older patients with hip fractures. Furthermore, our study found that DAR combined with NLR had better predictive power than a single indicator.

This study has some limitations. First, this study could not elucidate the causal relationship between DAR combined with NLR and preoperative DVT due to the nature of cross-sectional research. Second, there may be other variables that affect DVT, which could introduce bias into the results. Furthermore, as this study was conducted at a single center, it is necessary to conduct multi-center longitudinal studies in the future to clarify the relationship and predictive power of DAR combined with NLR for DVT.

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Conclusion

Our investigation showed that advanced age, high DAR, and NLR are associated with preoperative DVT. In addition, DAR combined with NLR has potential value for predicting preoperative DVT in older patients with hip fractures. The efficacy of DAR combined with NLR as a predictive indicator warrants further corroboration in multicenter studies with larger patient cohorts.

Data Sharing Statement

Data supporting the findings of this study can be obtained from the corresponding author upon reasonable request, and the corresponding author/s can be directly contacted for further inquiry.

Ethics Statement

Studies involving human participants were reviewed and approved by the ethics committee of Changhai Hospital. The ethics committee waived the requirement for informed consent due to the retrospective collection of de-identified clinical data from patients. The study project conforms to the ethical guidelines of the Declaration of Helsinki.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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