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Association between inflammatory indices and preoperative deep vein thrombosis in patients undergoing total joint arthroplasty: a retrospective study

Xiaojuan Xiong[1†], Peng Hu[2†], Ting Li[1], Shuang Yu[1] and Qingxiang Mao[1*]

Abstract

Background To investigate the association between inflammatory indices-systemic immune-inflammation index (SII), monocyte-lymphocyte ratio (MLR), neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR) and preoperative deep vein thrombosis (DVT) in patients undergoing total joint arthroplasty (TJA).

Methods We created the receiver operator characteristic (ROC) curve using the ratios of SII, MLR, NLR, PLR to DVT before TJA, divided the enrolled patients into groups based on the cut-off value, and then analyzed risk factors for DVT before TJA in the multivariate binary logistic regression analysis.

Results A total of 2125 patients were enrolled and preoperative DVT occurred in 110 cases (5.18%). Based on the ROC curve, we determined that the cut-off values for SII, MLR, NLR, and PLR were $470*10^9$ /L, 0.306, 2.08, and 127; and the areas under the curve (AUC) were 0.623, 0.601, 0.611, and 0.62. Multivariate binary regression analysis revealed that the risk of preoperative DVT in TJA patients with SII ≥ $470*10^9$/L, MLR ≥ 0.306, PLR ≥ 127, and NLR ≥ 2.08 increased by 2.26 ($P < 0.001$, 95% confidence interval (CI) [1.52–3.37]), 1.92 ($P = 0.002$, 95% CI [1.28–2.9]), 2.1 ($P < 0.001$, 95% CI [1.4–3.16]), and 1.94 ($P = 0.002$, 95% CI [1.29–2.92]) times, respectively. Age, $P < 0.001$, odds ratio (OR) = 1.08, 95%CI [1.05–1.10]; corticosteroid use, $P = 0.002$, OR 3.8, 95% CI [1.94–9.22]).

Conclusion We found that higher SII, MLR, NLR, and PLR levels, age, and corticosteroid use were independent risk factors for preoperative DVT in patients undergoing TJA.

Clinical trial registration ChiCTR2100054844; Registration Date: 2021.12.28.

Keywords Systemic immune-inflammation index, Monocyte–lymphocyte ratio, Neutrophil-lymphocyte ratio, Platelet-lymphocyte ratio, Total joint arthroplasty, Deep vein thrombosis

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Background

Total joint arthroplasty (TJA), which consists of total hip arthroplasty (THA) and total knee arthroplasty (TKA), can significantly relieve pain and improve function in patients with severe hip or knee osteoarthritis (OA) [1]. Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), is the third most common form of cardiovascular disease [2]. Preoperative DVT is an important risk factor for VTE, and it can contribute to significant mortality. Early detection of preoperative DVT is crucial for preventing postoperative VTE [3]. In some patients, DVT may progress to PE, with approximately one-third of DVT patients experiencing PE [4]. PE is a leading cause of sudden death, particularly when large pulmonary arteries are completely obstructed by thrombus, with a mortality rate as high as 34% [5]. Therefore, recognizing and managing preoperative DVT is critical for reducing the incidence of postoperative VTE and preventing fatal complications. Xiong et al. [6] and Song K et al. [7] reported that the incidence of DVT before TKA and THA was as high as 6.85% and 29.4%, respectively. If TJA patients have DVT before surgery, after surgical trauma, limb immobilization and other factors, DVT may be further expanded, and PE or even death will occur in severe cases. Therefore, in order to reduce the morbidity and mortality of perioperative VTE, surgeons should pay attention to the formation of DVT in TJA patients before surgery.

DVT formation is a complex process that involves the interaction of various blood cells, such as leukocytes and platelets (PLTs) [8]. Leukocyte subtypes include monocyte, lymphocyte, and neutrophil. The immune inflammatory status can be reflected by many peripheral blood-derived indices, including the systemic immune inflammatory index (SII, SII = PLT* neutrophil/ lymphocyte), monocyte/lymphocyte ratio (MLR), PLT/lymphocyte ratio (PLR) and neutrophil/lymphocyte ratio (NLR) [9, 10]. In the past decade, SII, LMR, PLR, and NLR, have been demonstrated to be closely related with systemic inflammation/immune response status, and have predictive value for the prognosis of various infectious, neoplastic, and autoimmune diseases [10, 11]. Yao C et al. reported the independent association of elevated PLR with postoperative DVT in TJA [12]. Zhu X et al. found that the low level of preoperative and postoperative MLR was significantly associated with DVT after primary TJA [13]. Peng et al. reported a higher SII level in patients with VTE compared to those without VTE and that SII was an independent predictor of VTE after hip fracture of elderly patients [14].

Current research has primarily focused on specific inflammatory factors such as TNF-α, IL-6, IL-8, and C-reactive protein (CRP) in relation to DVT formation [14]. Compared to other inflammatory cytokines, SII, MLR, NLR, PLR are advantageous in several aspects: they can be obtained from complete blood count tests, are easy to calculate, inexpensive, and can be repeated. Therefore, we aimed to investigate the association between SII, MLR, NLR, PLR, and preoperative DVT in patients with OA or rheumatoid arthritis (RA) undergoing TJA.

Materials and methods

Inclusion and exclusion criteria

Inclusion criteria: A total of 2716 TJA patients in our hospital from January 1, 2017 to December 31, 2021 were analyzed.

Exclusion criteria: (1) infection or tuberculosis of the joint; (2) tumors of the joints; (3) a history of VTE; (4) use of anticoagulant drugs; (5) fractures; (6) no record of preoperative lower extremity ultrasound; (7) >18 years old.

Data collection

Clinical data were collected through the hospital's electronic medical record system. The patients' general information included: height, weight, body mass index (BMI), gender, and age. Medical history included hypertension, coronary heart disease (CHD), chronic bronchitis, diabetes, cerebral infarction, chronic obstructive pulmonary disease (COPD), RA, OA, renal failure, smoking, use of corticoids, alcohol consumption, history of malignant tumor, and history of major surgery within 12 months.

The auxiliary examination included blood type (A, B, AB, O), PLT count, neutrophil count, monocyte count, lymphocyte count, and preoperative venous ultrasound. The lower limbs of all patients were assessed using Philips IE303 and GE Vivid 9 ultrasound systems, equipped with a C5-2 linear probe and 5–10 MHz pulsed Doppler. Preoperative lower limb Doppler venous assessment is routinely performed on all TJA patients in our hospital. Diagnoses were made collaboratively by two experienced sonographers, with positive criteria for DVT including venous compression, intravascular filling defects, and absence of Doppler signals. In addition, we also collected the sites of DVT formation: distal, mixed thrombus, and proximal.

Statistical analysis

IBM SPSS Statistics 26.0 (2019, Armonk, NY: IBM Corp) was used for statistical analysis. We used the ratio of SII, MLR, NLR, and PLR to preoperative DVT to create ROC curves, and then we selected the cut-off value for each index based on the point that maximized the Youden index (sensitivity + specificity − 1). This method allowed us to identify the optimal cut-off value that best discriminates between the presence and absence of preoperative DVT. The area under the curve (AUC) was then

calculated to assess the diagnostic performance of each index. $P < 0.05$ was considered statistically significant.

Based on the cut-off value, the patients were divided into two groups. Categorical data were analyzed by Chi-Square test or Fisher's Exact test. The results were expressed as percentage (%) to analyze DVT-related variables. Based on the results of deep vein ultrasound results, patients were divided into the DVT group and the non-DVT group. Variables that demonstrated statistical significance in the univariate analysis were then included in the multivariate binary logistic regression. Finally, we calculated the adjusted odds ratio (OR) and 95% confidence interval (95% CI) to evaluate the associations between SII, MLR, NLR, PLR, and preoperative DVT in TJA patients.

Results

Patient selection

The exclusion criteria included joint infection or tuberculosis (19 cases), joint tumors (25 cases), history of venous thromboembolism (VTE) (7 cases), use of anticoagulant medications (15 cases), history of fractures (342 cases), and absence of preoperative lower extremity ultrasound records (182 cases). A total of 2,125 patients were enrolled in the study, among which 110 (5.18%) were diagnosed with preoperative DVT.

Patient characteristics

The average age was (63.3 ± 12) years old among the 2125 TJA patients, (71.49 ± 8.83) years old in DVT group and (62.86 ± 12.0) years old in non-DVT group (Table 1). Among the TJA patients, 1957 were OA and 168 were RA. And among 1002 cases of TKA and 1123 cases of THA, 37.3% were male and 62.7% were female (Table 1). The highest incidence of preoperative comorbidities in TJA patients was hypertension, followed by DM and CHD (Table 1).

Characteristics of DVT formation

A total of 110 TJA patients had DVT, including 80 cases of distal thrombosis and 30 cases of proximal and mixed thrombosis, before surgery, with an incidence of 5.18%. All patients with TJA were implanted with an inferior vena cava IVC filter immediately after detection of proximal and mixed thrombi before surgery, and distal thrombi were treated with low molecular weight heparin. Thus, none of our patients developed PE during the perioperative period.

Analysis of preoperative SII, MLR, NLR, and PLR

PLT (10^9/L), neutrophil (10^9/L), and lymphocyte (10^9/L) levels in the DVT group were 239.17 ± 104.82, 3.97 ± 1.93, and 1.57 ± 0.64, respectively, compared to 213.4 ± 72.49, 3.49 ± 1.44, and 1.78 ± 1.02 in the Non-DVT group ($P = 0.026$, $P = 0.011$, and $P = 0.036$, respectively) (Table 1). Based on the ROC curve, we found that the cut-off values for SII, MLR, NLR, and PLR were $470*10^9$ /L, 0.306, 2.08, and 127, respectively. The AUCs for SII, MLR, NLR, PLR were 0.623 ($P < 0.001$, 95% CI [0.567–0.679]), 0.601 ($P < 0.001$, 95% CI [0.544–0.659]), 0.611 ($P < 0.001$, 95% CI [0.552–0.67]), and 0.62 ($P < 0.001$,95% CI [0.564–0.677]), respectively (Fig. 1).

Analysis of risk factors of preoperative DVT

Considering the multicollinearity of SII, MLR, NLR, and PLR, we conducted a binary logistic regression analysis on these variables separately with gender, age, diabetes, hypertension, CHD, corticosteroid, and major surgery in the last 12 months (Fig. 2). Multivariate binary regression analysis revealed that the risk of preoperative DVT in TJA patients with SII ≥ $470*10^9$ /L, MLR ≥ 0.306, PLR ≥ 127, and NLR ≥ 2.08 increased by 2.26 ($P < 0.001$, 95% CI [1.52–3.37]), 1.92 ($P = 0.002$, 95% CI [1.28–2.9]), 2.1 ($P < 0.001$, 95% CI [1.4–3.16]), and 1.94 times ($P = 0.002$, 95% CI [1.29–2.92]), respectively. Age, $P < 0.001$, OR = 1.08, 95% CI [1.05–1.10]; the risk of preoperative DVT in patients with preoperative corticosteroid use increased by approximately 3.8 times ($P = 0.002$, 95% CI [1.94–9.22]).

Discussion

Zhang L et al. identified SII as an independent risk factor for hip fracture complicated with DVT in elderly patients, as well as a novel risk factor for preoperative DVT [15]. Their study, similar to the present one, investigated the association between SII and preoperative DVT. However, the participants in the present study were OA or RA patients undergoing TJA, whose thrombosis formation is mostly chronic. Yao et al. found the independent association between postoperative PLR and the occurrence of DVT in 733 patients after TJA [12]. Xiong et al. found that a higher NLR level was a risk factor for preoperative DVT before TKA [6]. But this study had a small sample size and only studied NLR. Unlike previous studies, it is the first to identify those higher levels of SII, MLR, NLR, and PLR are associated with preoperative DVT in OA and RA patients undergoing TJA.

Association of SII, MLR, NLR, and PLR, with DVT

SII

SII, a comprehensive indicator based on peripheral blood neutrophil, PLT and lymphocyte counts, has been reported to be better able to reflect the balance of immune status and host inflammatory [10]. Zhang L et al. observed that SII was an independent risk factor for hip fracture complicated with DVT in elderly patients [15]. Peng et al. observed that SII was elevated in VTE patients and was an independent predictor of VTE

Table 1 Univariate analysis of preoperative DVT risk in patients undergoing TJA

	DVT	Non-DVT	*P*
Height (cm)	156.58 ± 6.44	158.08 ± 8.33	0.021
Weight (kg)	59.9 ± 9.38	61.73 ± 10.42	0.072
BMI (kg/m2)	24.45 ± 3.74	24.73 ± 4.3	0.510
Age (year)	71.49 ± 8.83	62.86 ± 12.0	< 0.001
PLT (10*9/L)	239.17 ± 104.82	213.4 ± 72.49	0.026
Neutrophils (10*9/L)	3.97 ± 1.93	3.49 ± 1.44	0.011
Lymphocyte (10*9/L)	1.57 ± 0.64	1.78 ± 1.02	0.036
Monocyte (10*9/L)	0.49 ± 0.18	0.47 ± 0.18	0.305
MLR	0.36 ± 0.23	0.30 ± 0.15	0.002
SII (10*9/L)	781.97 ± 84.68	487.07 ± 9.39	0.001
NLR	3.18 ± 2.93	2.24 ± 1.62	0.001
PLR	177.17 ± 11.4	134.35 ± 1.49	< 0.001
Gender			0.008
Female 1332 (62.7%)	82 (74.5%)	1250 (62.0%)	
Male 793 (37.3%)	28 (25.5%)	765 (38.0%)	
Hypertension			< 0.001
Yes 611 (28.8%)	48 (43.6%)	563 (27.9%)	
No 1514 (71.2%)	62 (56.4%)	1452 (72.1%)	
Diabetes			0.046
Yes 206 (9.7%)	17 (15.5%)	189 (9.4%)	
No 1919 (90.3%)	93 (84.5%)	1826 (90.6%)	
CHD			0.060
Yes 112 (5.3%)	13 (11.8%)	99 (4.9%)	
No 2013 (94.7%)	97 (88.2%)	1916 (95.1%)	
COPD			0.059
Yes 29 (1.4%)	4 (3.6%)	25 (1.2%)	
No 2096 (98.6%)	106 (96.4%)	1990 (98.8%)	
Chronic Bronchitis			0.066
Yes 30 (1.4%)	4 (3.6%)	26 (1.3%)	
No 2095 (98.6%)	106 (96.4%)	1989 (98.7%)	
Cerebral infarction			0.099
Yes 48 (2.3%)	5 (4.5%)	43 (2.1%)	
No 2077 (97.7%)	105 (95.5%)	1972 (97.9%)	
Major surgery in the last 12 months			0.051
Yes 73 (3.4%)	8 (7.3%)	65 (3.2%)	
No 2052 (96.6%)	102 (92.7%)	1950 (96.8%)	
Cancer			0.223
Yes 18 (0.8%)	2 (1.8%)	16 (0.8%)	
No 2107 (99.2%)	108 (98.2%)	1999 (99.2%)	
Renal failure			0.061
Yes 8 (0.4%)	2 (1.8%)	6 (0.3%)	
No 2117 (99.6%)	108 (98.2%)	2009 (99.7%)	
Depression			0.640
Yes 4 (0.2%)	0	4 (0.2%)	
No 2121 (99.8%)	110 (100.0%)	2011 (99.8%)	
Corticosteroid			0.030
Yes 59 (2.8%)	7 (6.4%)	52 (2.6%)	
No 2066 (97.2%)	103 (93.6%)	1963 (97.4%)	
Smoking			0.760
Yes 327 (15.4%)	10 (9.1%)	317 (15.7%)	
No 2098 (98.7%)	100 (90.9%)	1998 (99.2%)	
Drinking			0.584
Yes 317 (14.9%)	14 (12.7%)	303 (15.0%)	

Table 1 (continued)

	DVT	Non-DVT	*P*
No 1808 (85.1%)	96 (87.3%)	1712 (85.0%)	
Blood type			0.134
Type A 694 (32.7%)	27 (24.5%)	667 (33.1%)	
Type B 553 (26.0%)	38 (34.5%)	515 (25.6%)	
Type AB 718 (33.8%)	37 (33.6%)	681 (33.8%)	
Type O 160 (7.5%)	8 (7.3%)	152 (7.5%)	
Classification of MLR			< 0.001
≥ 0.306 756 (35.6%)	59 (53.6%)	697 (34.6%)	
< 0.306 1369 (64.4%)	51 (46.4%)	1318 (65.4%)	
Classification of SII (10*9/L)			< 0.001
≥ 470 765 (36.0%)	61 (55.5%)	704 (34.9%)	
< 470 1360 (64.0%)	49 (44.5%)	1311 (65.1%)	
Classification of NLR			< 0.001
≥ 2.08 902 (42.4%)	67 (60.9%)	835 (41.4%)	
< 2.08 1223 (57.6%)	43 (39.1%)	1180 (58.6%)	
Classification of PLR			< 0.001
≥ 127 958 (45.1%)	70 (63.6%)	888 (44.1%)	
< 127 1167 (54.9%)	40 (36.4%)	1127 (55.9%)	

CHD: Coronary heart disease; COPD: chronic obstructive pulmonary disease; DVT: deep vein thrombosis; BMI: Body Mass Index; SII: systemic immune-inflammation index; MLR: monocyte lymphocyte ratio; NLR: platelet lymphocyte ratio; PLR: platelet lymphocyte ratio; PLT: platelet; $P < 0.05$ was statistically significant

following hip fracture in elderly patients. According to the ROC analysis, the cut-off value was 847.78, sensitivity was 53.8%, specificity was 92.3%, and AUC was 0.795 ($P < 0.001$, 95% CI [0.71–0.88]) [14]. In comparison, the present study revealed a cut-off value of $470*10^9$/L and an AUC of 0.623 ($P < 0.001$, 95% CI [0.567–0.679]) and identified SII ≥ $470*10^9$ /L as an independent risk factor for preoperative DVT in patients undergoing TJA. The risk of preoperative DVT in patients with SII ≥ $470*10^9$/L was increased by 2.26 times ($P < 0.001$, 95% CI [1.52–3.37]). The patients with a higher preoperative SII usually have decreased PLTs, neutrophilia, or lymphopenia, suggesting an elevated inflammatory status and weak immune response [10].

MLR

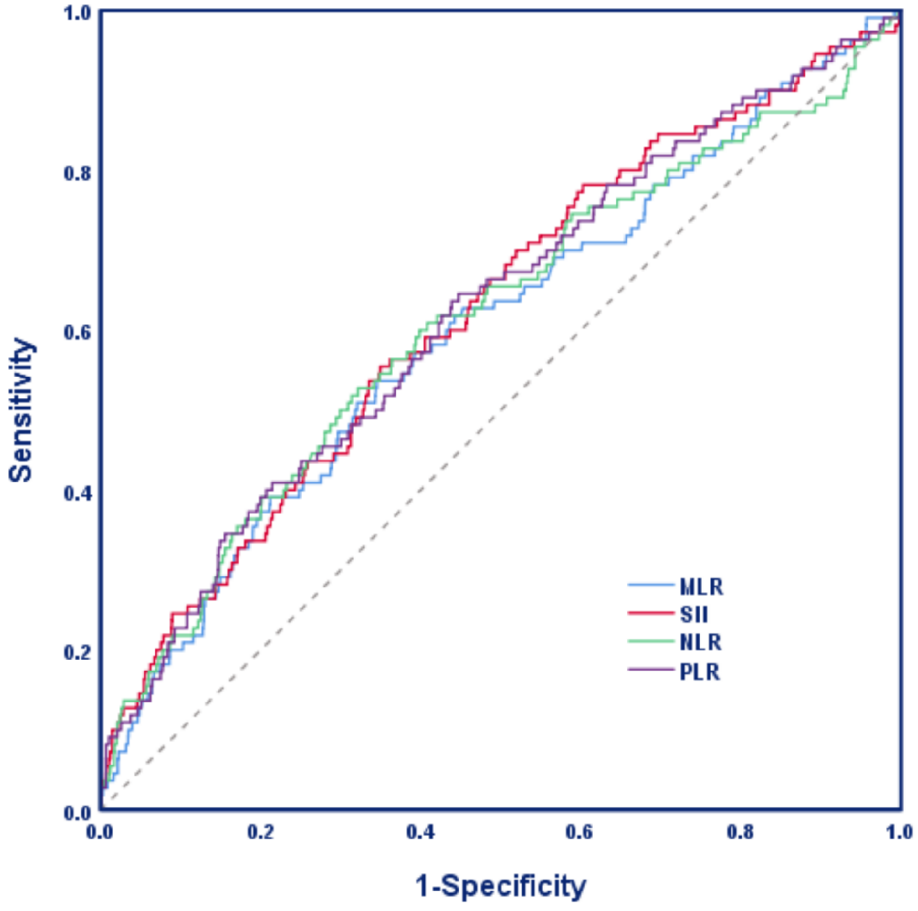
MLR has been proposed as a surrogate marker of the occurrence of endothelial inflammation and dysfunction in different populations and it also has predictive value for prognosis [16]. Zhu X et al. found that low preoperative and postoperative MLR level was significantly associated with DVT after primary TJA [13]. The present study is the first to analyze the association between SII and MLR with preoperative DVT in patients undergoing TJA. Our study found that MLR ≥ 0.306 was an independent risk factor for preoperative DVT in patients undergoing TJA and the risk of preoperative DVT in patients with MLR ≥ 0.306 increased by 1.92 times.

PLR

PLR, an indicator of innate and adaptive immunity, can be calculated from complete blood count [17]. Akboga YE et al. identified PLR and NLR as independent predictive factors for CVST and proposed that PLR > 115 and NLR > 2.1 were cut-off values [18]. Kuplay et al. found that NLR correlated with thrombus location. Mean NLR was higher in patients with proximal DVT than those with distal DVT [19]. In comparison, the present study revealed a cut-off value of 127 and AUC of 0.62 ($P < 0.001$, 95% CI [0.564–0.677]), and identified PLR ≥ 127 as an independent risk factor for preoperative DVT in patients undergoing TJA. When PLR ≥ 127, TJA patients had a 2.1 times higher risk for preoperative DVT *(*$P < 0.001$, 95% CI [1.4–3.16]).

NLR

NLR is also a marker of systemic inflammation, representing both adaptive and innate immunity [20]. Yao C et al. showed that high preoperative and postoperative NLR levels and low postoperative PLR level were significantly associated with DVT following TJA [12]. Seo et al. observed that VTE occurred in 102 cases at 1 week postoperatively in 264 patients after TKA and identified preoperative NLR ≥ 1.90 as the only independent predictor of postoperative VTE [21]. A high preoperative NLR (1.90) was an independent predictor of VTE after TKA, which suggests that chronic low-grade systemic inflammatory response could lead to hyper-coagulation and increase the risk of VTE [21]. Barker et al. identified a positive relationship between increased NLR level (day 1 and day 2, pre- and postoperative) and the risk of VTE after TKA [20]. Yao C et al. reported that a higher NLR was independently associated with postoperative DVT in TJA [12]. The present study found the cut-off value



Maker	Cut off value	P-value	sensitivity	specificity	AUC	95% CI
MLR	0.306	<0.001	70%	50%	0.601	0.544-0.659
SII	470	<0.001	70%	60%	0.623	0.567-0.679
NLR	2.08	<0.001	60%	60%	0.611	0.552-0.67
PLR	127	<0.001	60%	60%	0.62	0.564-0.677

Fig. 1 Diagnostic performances of MLR, SII, NLR, and PLR for predicting DVT in patients undergoing TJA
DVT: Deep vein thrombosis; AUC: Area Under Curve; CI: confidence interval; SII: systemic immune-inflammation index; MLR: monocyte lymphocyte ratio; NLR: platelet lymphocyte ratio; PLR: platelet lymphocyte ratio; $P < 0.05$ was statistically significant

for NLR of 2.08 and an AUC of 0.611 ($P < 0.001$, 95% CI [0.552–0.67]), and NLR ≥ 2.08 was an independent risk factor for DVT formation before TJA and the risk of DVT increased by 1.94 times ($P = 0.002$, 95% CI [1.29–2.92]).

Neutrophil, lymphocyte, monocyte, PLT

Neutrophils are the most abundant blood leukocyte in humans. Together with monocytes, they are the major initiators of the innate immune response. PLTs form heterotypic aggregates with neutrophils as a function of platelet toll-like receptors activation in the circulation [22]. Kushnir et al. found that an elevated neutrophil count was associated with higher risk of VTE and that neutrophilia may be a marker of vulnerability to VTE [23]. Patients with a neutrophil count ≥ $9*10^9$/L had a 2.0 times increased risk of VTE [23]. In our study, the neutrophil count was significantly higher in the DVT group of TJA patients compared to the non- DVT group ($P < 0.05$). An elevated neutrophil count represents a systemic inflammatory process, while the decrease of lymphocyte indicates ongoing disease-related stress [24]. Apart from its well-known inflammatory functions, the neutrophil can promote thrombus formation. It has been proven to be an essential source of TF in the early phase of thrombus formation [25].

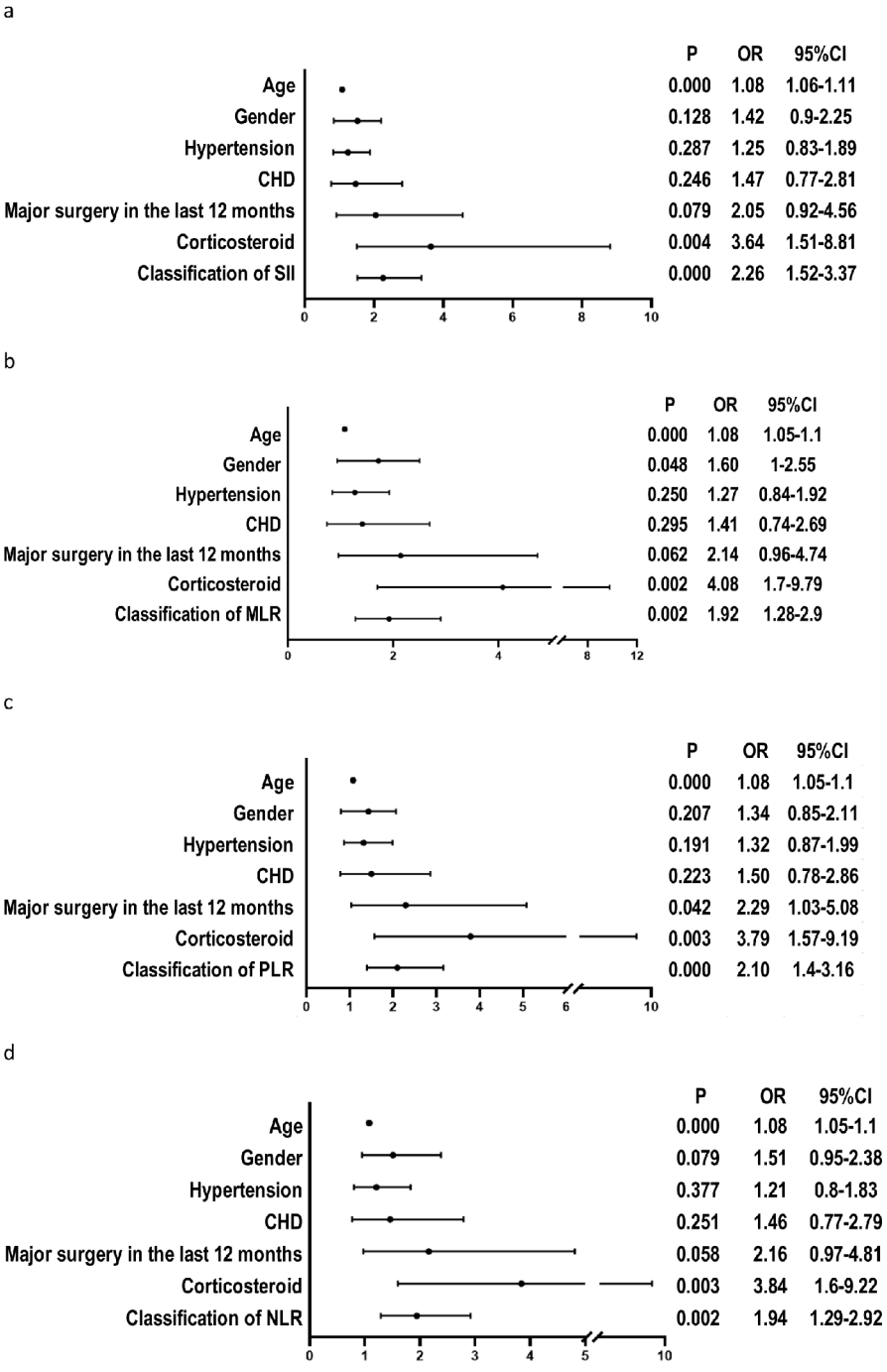


Fig. 2 Multivariate logistic regression analysis of preoperative risk factors for DVT in patients undergoing TJA. **a** Multivariate binary logistic regression analysis of SII and DVT preoperative in patients undergoing TJA. **b** Multivariate binary logistic regression analysis of MLR and DVT preoperative in patients undergoing TJA. **c** Multivariate binary logistic regression analysis of PLR and DVT preoperative in patients undergoing TJA. **d** Multivariate binary logistic regression analysis of NLR and DVT preoperative in patients undergoing TJA

DVT: Deep vein thrombosis; AUC: Area Under Curve; CHD: Coronary heart disease; CI: confidence interval; SII: systemic immune-inflammation index; MLR: monocyte lymphocyte ratio; NLR: platelet lymphocyte ratio; PLR: platelet lymphocyte ratio; $P < 0.05$ was statistically significant

Lymphocytes, as an important subtype of the leucocyte family, are also involved in inflammation [26]. In the present study, the lymphocyte count in DVT group was lower but the PLT count was higher than those in the non-DVT group. Therefore, our PLR count was increased. Horne BD et al. demonstrated the low lymphocyte count was associated with increased cardiovascular disease [26]. An elevated PLR reflects inflammatory status, atherosclerosis, and PLT activation [27]. Unlike higher PLTs promoting the thrombocyte activation, lymphocytes control and suppress the aggravated inflammatory process [17].

Loukov D et al. found that monocytes and neutrophils were the first circulating cells to actively accumulate at the vascular surface during DVT development [28]. Monocytes are not only the main producers of inflammatory cytokines including interleukin-1β and tumor necrosis factor α (TNF-α) [29], but also a major source of tissue factor (TF), a key initiator of DVT formation [30]. According to recent research by Amadio et al., monocytes could directly trigger DVT through PTGI2/ANXA2/TF pathway [31].

Human PLTs are involved in pathophysiological processes, such as hemostasis and thrombosis, thrombus retraction, inflammation, vessel repair and constriction, tumor growth and metastasis, and host defense [32]. In the present study, the PLT count in the DVT group was higher than that in the non-DVT group. Elevated PLT counts can produce more CD40L and enhance an inflammatory response [33].

Association between inflammation and DVT

There are primarily two mechanisms involved in the formation of DVT in our patients with OA or RA undergoing TJA. First, the neutrophil extracellular trap (NET) mechanism, in which neutrophils, lymphocytes, monocytes, and PLTs contribute to DVT formation [38]. Chronic inflammation in both OA and RA leads to an imbalance in immune cells, with an increase in neutrophils, monocytes, and PLTs, and a decrease in lymphocytes, which promotes the formation of NETs. Second, inflammatory cytokines released in response to OA or RA further contribute to blood hypercoagulability, increasing the risk of thrombus formation. These two mechanisms interact, further increasing the likelihood of DVT before TJA in OA or RA patients. Among various inflammatory markers, those related to this inflammatory state, particularly those affecting immune cell distribution and cytokine release, are more clinically accessible and potentially more useful for predicting preoperative DVT. Therefore, we recommend the clinical application of these markers to improve risk stratification for DVT in these patients.

In addition, we found that corticosteroid use increases the incidence of preoperative DVT in TJA patients. The main mechanism may be that corticosteroids disrupt the balance between procoagulant and antithrombotic factors, increasing prothrombin levels and the concentrations of factors VII, VIII, XI, and fibrinogen, which contribute to a higher VTE risk in patients with chronic use [34–36].

The present study investigated the association between inflammatory indices and DVT in patients undergoing TJA by using materials including preoperative medical history, preoperative laboratory examinations, and preoperative auxiliary examinations. But it has certain limitations. For example, as a retrospective study, some data are insufficient. The AUCs for MLR, SII, NLR, and PLR were 0.601, 0.623, 0.611, and 0.62, respectively. Future studies with bigger sample size and more data might be needed to further verify the association between MLR, SII, NLR, PLR and preoperative DVT in TJA patients. Besides, the potential confounding effect of chronic inflammatory conditions in patients using steroids. Since many of the steroid users in our cohort had underlying chronic inflammatory diseases, such as rheumatoid arthritis and osteoarthritis, which are known to increase the risk of DVT, it is possible that the underlying pathology, rather than steroid use itself, contributed to the observed association with preoperative DVT. While we adjusted for key confounders, future studies should further investigate the independent effects of steroid use by stratifying patients based on the presence and severity of these chronic conditions to better isolate the role of steroids in DVT risk.

Conclusion

We found that higher SII, MLR, NLR, and PLR levels, age, and corticosteroid use were independent risk factors for preoperative DVT in patients undergoing TJA. It is recommended that the patients with SII, MLR, NLR, PLR higher than $470*10^9$/L, 2.08, 0.306, 127, respectively, be screened for DVT before TJA.

Abbreviations

AUC	Area Under Curve
BMI	Body Mass Index
CHD	Coronary heart disease
COPD	Chronic obstructive pulmonary disease
CI	Confidence interval
CVST	Cerebral venous sinus thrombosis
DM	Diabetes Mellitus
DVT	Deep vein thrombosis
IL-6	Interleukin-6
MLR	Monocyte lymphocyte ratio
NET	Neutrophil extracellular trap
NLR	Platelet lymphocyte ratio
OA	Osteoarthritis
OR	Odds ratio
PLT	Platelet
PLR	Platelet lymphocyte ratio
PE	Pulmonary embolism
RA	Rheumatoid Arthritis
ROC	Receiver operating characteristic

SII Systemic immune-inflammation index
TF Tissue factor
THA Total hip arthroplasty
TJA Total Joint Arthroplasty
TKA Total knee arthroplasty
TNF Tumor Necrosis Factor
PLT Platelets
VTE Venous Thromboembolism

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Author contributions
Xiaojuan Xiong, Ting Li, Shuang Yu, Peng Hu, and Qingxiang Mao contributed to the conception and design of the study. Xiaojuan Xiong, Ting Li, Peng Hu and Shuang Yu: contributed to the acquisition and analysis of data. Xiaojuan Xiong wrote the manuscript. Peng Hu and Qingxiang Mao revised the manuscript. All authors read and approved the final manuscript.

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Data availability
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This retrospective observational study, approved by the Army Medical Center of PLA (ratification number: 2021(288)), was conducted in accordance with the Declaration of Helsinki, with informed consent waived by the ethics committee.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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