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Association Between Platelet Indices and Preoperative Deep Vein Thrombosis in Elderly Patients Undergoing Total Joint Arthroplasty: A Retrospective Study

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Abstract

To investigate the association between platelet (PLT) indices and preoperative deep vein thrombosis (DVT) in elderly patients undergoing total joint arthroplasty (TJA). A total of 1391 patients were enrolled. We created receiver operator characteristic (ROC) curve using the ratio of PLT indices 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. Preoperative DVT occurred in 103 cases. Based on the ROC curve, we determined that the cut-off values for PLT, mean platelet volume (MPV), platelet distribution width (PDW), platelet large cell ratio (P-LCR), and plateletcrit (PCT) were 202×10^9/L, 11.4 fL, 13.2 fL, 34.6%, and 0.228%. And the areas under the curve were 0.606, 0.605, 0.617, 0.616, and 0.598. Multivariate binary regression analysis revealed that the risk of preoperative DVT in TJA patients with PLT≥202×10^9/L, MPV≤11.4 fL, PDW≤13.2 fL, P-LCR≤34.6%, and PCT≥0.228% increased by 2.32 ($P < .001$, 95% confidence interval [CI] [1.50-3.60]), 1.86 ($P < .001$, 95% CI [1.22-2.83]), 2.17 ($P < .001$, 95% CI [1.43-3.31]), 2.27 ($P < .001$, 95% CI [1.50-3.45]), and 1.76 times ($P = .013$, 95% CI [1.13-2.76]), respectively. Age, $P < .001$, odds ratio (OR) = 1.08, 95% CI [1.04-1.11]; corticosteroid use, $P = .011$, OR = 3.66, 95% CI [1.34-9.96]. We found that increased PLT count and PCT, decreased MPV, PDW, and P-LCR, old age, and corticosteroid use were independent risk factors for preoperative DVT in elderly TJA patients.

Keywords

total joint arthroplasty, mean platelet volume, platelet distribution width, platelet large cell ratio, plateletcrit, deep vein thrombosis

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Introduction

The number of total joint arthroplasty (TJA), including total hip arthroplasty (THA) and total knee arthroplasty (TKA), performed is expected to increase in the next decade.[1] People undergoing THA and TKA are at high risk for venous thromboembolism (VTE), an umbrella term for deep vein thrombosis (DVT) and pulmonary embolism (PE). Approximately 40% to 60% of the patients undergoing TKA and THA developed DVT, and 4% to 10% of the patients without preventive treatments developed PE.[2,3] Bala A *et al* reported that the incidence of preoperative DVT in patients undergoing TKA is up to 17.9%,[4] and according to Song K *et al* that in patients undergoing THA is as high as 29.4%.[5] If the patient with thrombus underwent surgical trauma, immobilization, and other procedures, DVT may develop, extend, or even detach, causing PE, severe disability, or even death.[6] Therefore, identifying the high-risk factors for preoperative DVT in TJA patients is of great importance to preventing and treating perioperative DVT.

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Human platelets (PLT) are anucleated cells derived from megakaryocytes and they are involved in many pathophysiological processes, including hemostasis and thrombosis, thrombus retraction, vessel constriction and repair, inflammation, host defense, and even tumor growth and metastasis.[7] PLT indices in laboratory examination include mean platelet volume (MPV), platelet distribution width (PDW), platelet large cell ratio (P-LCR), and plateletcrit (PCT). Braekkan *et al* found that increased MPV is associated with increased risk of VTE,[8] while Wang Z *et al* found that low MPV levels are associated with DVT in older patients with hip fracture.[9] Ma J *et al* reported that PDW (<12%) is a risk factor for preoperative DVT in patients with foot fracture.[10] Grotto HZ *et al* found that P-LCR may be used as an indicator of risk factor for thromboembolic ischemic events.[11] Abanoz M *et al* reported that in the receiver operator characteristic (ROC) analysis, the cut-off value for PCT was 0.199 in a retrospective study on preoperative lower extremity VTE.[12]

Most of previous studies are focused on the association between PLT indices and preoperative DVT for acute bone fracture and the impact of PLT indices on postoperative complications. In general, PLT count decreases [13] while MPV increases [14] with age. However, our study found that in elderly TJA patients who were preoperatively diagnosed with osteoarthritis (OA) or rheumatoid arthritis (RA), their PLT counts increased while MPV decreased. Therefore, this study was aimed to investigate the association between PLT indices and preoperative DVT in elderly patients undergoing TJA.

Materials and Methods

Inclusion and Exclusion Criteria

Inclusion criteria: A total of 1540 patients aged 60 years or older who were diagnosed with OA or RA before undergoing TJA in our hospital between January 2017 and December 2021.

Exclusion criteria: (1) a history of VTE (3 cases); (2) use of anticoagulation medications (aspirin, clopidogrel, warfarin, rivaroxaban, dabigatran): atrial fibrillation (4 cases), coronary heart disease (CHD) patients with installed stents and anticoagulant therapy (5 cases); (3) joint infection: knee joint (6 cases); (4) tuberculosis of the joint (10 cases); (5) tumors of the joints (10 cases); (6) thrombophilia genetic disorders (0 cases); (7) no preoperative lower extremity ultrasound records (111 cases); (8) no routine blood test records (0 cases). Finally, a total of 1391 patients were enrolled.

Table 1. Univariate Analysis of Preoperative DVT Risk in Elderly Patients Undergoing TJA.

Variables	DVT	Non-DVT	*P*
Height (cm)	154 ± 6.49	156.55 ± 7.93	.846
Weight (kg)	60 ± 9.26	61.23 ± 10.33	.245
BMI (kg/m^2)	24.56 ± 3.74	25.03 ± 4.68	.326
Age (year)	72.96 ± 6.36	70.24 ± 6.15	.000
PLT (10^9/L)	240.74 ± 10.37	208.23 ± 2.0	.000
PDW (fL)	13.71 ± 2.98	14.84 ± 3.16	.000
MPV (fL)	11.21 ± 1.24	11.63 ± 1.27	.001
P-LCR (%)	34.37 ± 10.4	38.09 ± 10.17	.001
PCT (%)	0.27 ± 0.09	0.24 ± 0.07	.002

Abbreviations: BMI, body mass index; MPV, mean platelet volume; PLT, platelet; PDW, platelet distribution width; P-LCR, platelet larger cell ratio; PCT, plateletcrit; DVT, deep vein thrombosis.
$P < .05$ was statistically significant.

Research Method

We created the ROC curve of PLT count, MPV, PDW, P-LCR, and PCT and divided the patients into 2 groups: one group above and the other below the cut-off value. The risk factors for DVT before TJA were subsequently examined. Based on the deep vein ultrasound results, patients were again divided into 2 groups: DVT group and non-DVT group. High-risked factors for DVT before TJA were subsequently analyzed. Then we used multivariate binary logistic regression analysis to verify. This study has been approved by Medical Research and Ethics Review (No. 184, 2022) and registered in the WHO International Clinical Trials Registration (ChiCRT2100054844).

Data Collection

We collected clinical data through the hospital's electronic medical record system. The basic information of the patients included: admission number, gender, age, height, weight, and BMI (body mass index). Auxiliary examination: Blood type (A, B, AB, O), laboratory examinations, and auxiliary examinations: blood type (type A, B, AB, O), PLT count, MPV, PDW, P-LCR, PCT, preoperative venous ultrasound of lower extremity. Previous medical history: coronary heart disease, diabetes mellitus (DM), hypertension, chronic bronchitis, chronic obstructive pulmonary disease (COPD), OA, RA, cerebral infarction, history of malignant tumors, renal failure, use of corticosteroids, alcohol consumption, smoking, major surgery (major surgery requiring anesthesia [general, orthopedic, neurologic, or gynecologic surgery][15]) within 12 months.

All patients were examined by Philips IE33 GE Vivid 9, C5-1 linear probe with 5-10 Hz pulse Doppler ultrasound in the lower limbs, and were co-diagnosed by 2 experienced sonographers. Positive criteria for DVT include venous incompressibility, defect of intravascular filling, and lack of Doppler signal. In addition, we also collected the sites of DVT formation: distal, proximal thrombus, and mixed thrombus.

Statistical Analysis

We performed statistical analyses using SPSS 26.0, created the ROC curves for PLT count, MPV, PDW, P-LCR, and PCT for determining their cut-off values, and calculated the areas under the curve (AUCs). Based on the cut-off value, patients were divided into 2 groups: one group above the cut-off value and the other below the cut-off value. And risk factors were subsequently analyzed. Chi-square test or Fisher's exact test was adopted for enumeration data. The results were represented in percentage (%) to analyze DVT-related variates. The variates that were statistically significant in the univariate analysis were included in the

Table 2. Summary of Patient Characteristics.

Variables	DVT (103)		Non-DVT (1288)		Total (1391)	
Gender						
Female	77	74.8%	889	69.0%	966	69.4%
Male	26	25.2%	399	31.0%	425	30.6%
Hypertension						
Yes	45	43.7%	473	36.7%	518	37.2%
No	58	56.3%	815	63.3%	873	62.8%
Diabetes						
Yes	16	15.5%	156	12.1%	172	12.4%
No	87	84.5%	1132	87.9%	1219	87.6%
CHD						
Yes	12	11.7%	91	7.1%	103	7.4%
No	91	88.3%	1197	92.9%	1288	92.6%
COPD						
Yes	4	3.9%	25	1.9%	29	2.1%
No	99	96.1%	1263	98.1%	1362	97.9%
Chronic bronchitis						
Yes	4	3.9%	24	1.9%	28	2.0%
No	99	96.1%	1264	98.1%	1363	98.0%
Cerebral infarction						
Yes	5	4.9%	42	3.3%	47	3.4%
No	98	95.1%	1246	96.7%	1344	96.6%
Major surgery in the last 12 months						
Yes	8	7.8%	41	3.2%	49	3.5%
No	95	92.2%	1247	96.8%	1342	96.5%
Cancer						
Yes	2	1.9%	14	1.1%	16	1.2%
No	101	98.1%	1274	98.9%	1375	98.8%
Renal failure						
Yes	2	1.9%	4	0.3%	6	0.4%
No	101	98.1%	1284	99.7%	1385	99.6%
Depression						
Yes	0	0.0%	2	0.2%	2	0.1%
No	103	100.0%	1286	99.8%	1389	99.9%
Corticosteroid						
Yes	6	5.8%	19	1.5%	25	1.8%
No	97	94.2%	1269	98.5%	1366	98.2%
Variables	**DVT (103)**		**Non-DVT (1288)**		**Total (1391)**	
Smoking						
Yes	8	7.8%	124	9.6%	132	9.5%
No	95	92.2%	1164	90.4%	1259	90.5%
Drinking						
Yes	12	11.7%	113	8.8%	125	9.0%
No	91	88.3%	1175	91.2%	1266	91.0%
Blood type						
Blood type A	26	25.2%	430	33.4%	456	32.8%
Blood type B	35	34.0%	309	24.0%	344	24.7%
Blood type AB	34	33.0%	451	35.0%	485	34.9%
Blood type O	8	7.8%	98	7.6%	106	7.6%
Classification of PLT (10^9/L)						
≥202	69	67.0%	635	49.3%	704	50.6%
<202	34	33.0%	653	50.7%	687	49.4%
Classification of PDW (fL)						
≤13.2	58	56.3%	439	34.1%	497	35.7%
>13.2	45	43.7%	849	65.9%	894	64.3%
Classification of MPV (fL)						
≤11.4	66	64.1%	616	47.8%	682	49.0%
>11.4	37	35.9%	672	52.2%	709	51.0%
Classification of P-LCR (%)						
≤34.6	62	60.2%	507	39.4%	569	40.9%
>13.6	41	39.8%	781	60.6%	822	59.1%
Classification of plateletcrit (%)						
≥0.228	70	68.0%	681	52.9%	751	54.0%
<0.228	33	32.0%	607	47.1%	640	46.0%

Abbreviations: CHD, coronary heart disease; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; PLT, platelet; MPV, mean platelet volume; PDW, platelet distribution width; P-LCR, platelet larger cell ratio; PCT, plateletcrit; DVT, deep vein thrombosis.

multivariate analysis to calculate the adjusted odds ratio (OR) and 95% confidence interval (CI) for the evaluation of the correlation between preoperative PLT count, MPV, PDW, P-LCR, PCT, and preoperative DVT in elderly patients undergoing TJA. $P < .05$ was considered statistically significant.

Results

General Information of Elderly Patients Undergoing TJA

The mean age was 70.44 ± 6.21 years, 72.96 ± 6.36 years in DVT group, and 70.24 ± 6.15 years in non-DVT group (Table 1). About 1251 patients were preoperatively diagnosed with OA and 140 patients with RA. Among the 615 TKA cases and 776 THA cases, 425 (30.6%) were male and 966 (69.4%) were female (Table 2). The preoperative comorbidities in patients were hypertension (518 cases), DM (172 cases), and CHD (103 cases) (Table 3).

Characteristics of DVT Formation

Among the 103 cases (7.40%) with DVT before TJA, there were 77 cases (74.76%) with distal thrombus, 12 cases (11.65%) with proximal thrombus, and 15 cases (14.56%) with mixed thrombus. Inferior vena cava filters were used for the proximal and mixed types of thrombus and low molecular weight heparin for the distal thrombus. None of our TJA patients had PE during the perioperative period time.

Analyses on Preoperative PLT and PLT Indices in Elderly Patients Undergoing TJA

MPV (fL) = [(PCT (%)/PLT count ($\times 10^9$/L)] $\times 10^5$. PCT was the ratio of the platelet volume to the whole blood volume. PDW and P-LCR were analyzed from a histogram of platelet size distribution. The distribution width at the level of 20% (the peak of the histogram is 100%) was defined as PDW, and the percentage of platelets with a size of more than 12 fL was defined as P-LCR.[16]

Table 3. Univariate Analysis of Preoperative DVT Risk in Elderly Patients Undergoing TJA.

Influencing factor	Chi-square test value	*P*
Gender	1.48	.266
Diagnosis	0.49	.528
Hypertension	1.98	.169
DM	1.03	.349
CHD	2.92	.113
COPD	1.76	.162
Chronic bronchitis	1.97	.148
Cerebral infarction	0.74	.388
Major surgery in the last 12 months	5.90	.024
Cancer	0.61	.335
Renal failure	5.91	.067
Depression	0.16	1.000
Corticosteroid	10.23	.008
Smoking	0.38	.726
Drinking	0.97	.368
Blood type	5.89	.117
Classification of PLT	11.94	.001
Classification of PDW	20.52	.000
Classification of MPV	10.08	.001
Classification of P-LCR	17.12	.000
Classification of PCT	8.74	.004

Abbreviations: CHD, coronary heart disease; DM, diabetes Mellitus; COPD, chronic obstructive pulmonary disease; PLT, platelet; MPV, mean platelet volume; PDW, platelet distribution width, P-LCR, platelet larger cell ratio; PCT: plateletcrit; DVT, deep vein thrombosis.
$P < .05$ was statistically significant.

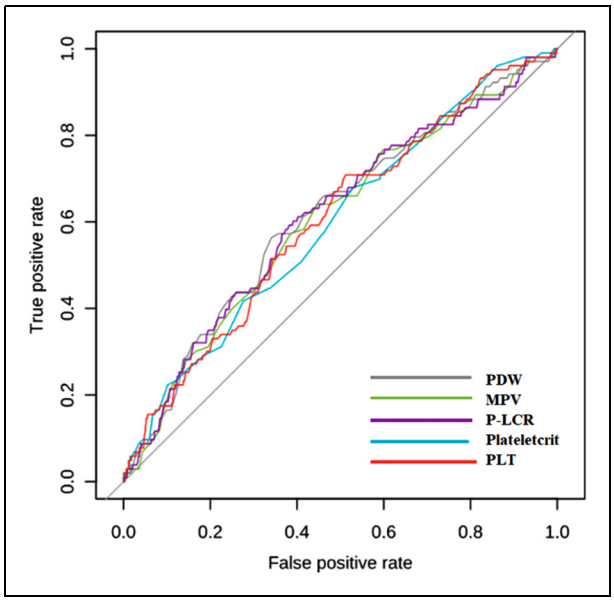

Figure 1. Diagnostic performances of PLT, PDW, P-LCR, and PCT for predicting DVT in elderly patients undergoing TJA.
Abbreviations: PLT, platelet; MPV, mean platelet volume; PDW, platelet distribution width; P-LCR, platelet larger cell ratio; PCT, plateletcrit; DVT, deep vein thrombosis; AUC, area under curve; CI, confidence interval; $P < .05$ was statistically significant.

Table 4. Comparison of Platelet Correlation Values After Platelet Classification.

	PLT $\geq 202 \times 10^9$/L	PLT $< 202 \times 10^9$/L	*P*
PDW (fL)	13.44 ± 2.73	16.1 ± 3.0	< .001
MPV (fL)	11.0 ± 1.03	12.22 ± 1.19	< .001
P-LCR (%)	33.01 ± 8.53	42.73 ± 9.45	< .001
PCT (%)	0.28 ± 0.06	0.19 ± 0.03	< .001

Abbreviations: PLT, platelet; MPV, mean platelet volume; PDW, platelet distribution width; P-LCR, platelet larger cell ratio; PCT: plateletcrit.
$P < .05$ was statistically significant.

Based on the ROC curve, we determined that the cut-off values for PLT count, MPV, PDW, P-LCR, and PCT were 202×10^9/L, 11.4 fL, 13.2 fL, 34.6%, and 0.228%, respectively. The AUCs for PLT, MPV, PDW, P-LCR, and PCT were 0.606 (95% CI [0.547-0.66]), 0.605 (95% CI [0.547-0.663]), 0.617 (95% CI [0.563-0.678]), 0.616 (95% CI [0.552-0.668]), and 0.598 (95% CI [0.535-0.652]), respectively. Other indices are shown in Figure 1. We divided the patients into 2 groups based on the cut-off value of PLT count: the PLT$\geq 202 \times 10^9$/L group and the PLT$< 202 \times 10^9$/L group. As shown in Table 4, the PDW, MPV, P-LCR (%) values in the PLT$\geq 202 \times 10^9$/L group were lower than those in the PLT$< 202 \times 10^9$/L group, except for PCT. And all *P* values were below .001 and were statistically significant.

Analyses on Preoperative PLT and PLT Indices in Elderly Patients Undergoing TJA

Univariate logistic regression analysis revealed that the risk of preoperative DVT in elderly patients undergoing TJA with PLT$\geq 202 \times 10^9$/L, MPV$\leq$11.4 fL, PDW$\leq$13.2 fL, P-LCR$\leq$34.6%, and PCT$\geq$0.228% increased by 2.09 ($P < .001$, 95% CI [1.50-3.19]), 1.95 ($P < .001$, 95% CI [1.28-2.95]), 2.49 ($P < .001$, 95% CI [1.66-3.74]), 2.33 ($P < .001$, 95% CI [1.50-3.51]), and 1.89 times ($P = .001$, 95% CI [1.23-2.90]), respectively. We also found that age, preoperative corticosteroid use, major surgery within 12 months, and renal failure were risk factors for preoperative DVT in elderly TJA patients (Figure 2).

Considering the multicollinearity of PLT count, MPV, PDW, P-LCR, and PCT, we conducted a binary logistic regression analysis on these variables separately with age, corticosteroid use, major surgery in the last 12 months, and renal failure (Figure 3). Multivariate binary regression analysis revealed that the risk of preoperative DVT in TJA patients with PLT$\geq 202 \times 10^9$/L, MPV$\leq$11.4 fL, PDW$\leq$13.2 fL, P-LCR$\leq$34.6%, and PCT$\geq$0.228% increased by 2.32 ($P < .001$, 95% CI [1.50-3.60]), 1.86 ($P < .001$, 95% CI [1.22-2.83]), 2.17 ($P < .001$, 95% CI [1.43-3.31]), 2.27 ($P < .001$, 95% CI [1.50-3.45]), and 1.76 times ($P = .013$, 95% CI [1.13-2.76]), respectively. Age, $P < .001$, OR = 1.08, 95% CI [1.04-1.11]; the risk of preoperative DVT in patients with corticosteroid use increased by approximately 3.658 times ($P = .011$, 95% CI [1.34-9.96]).

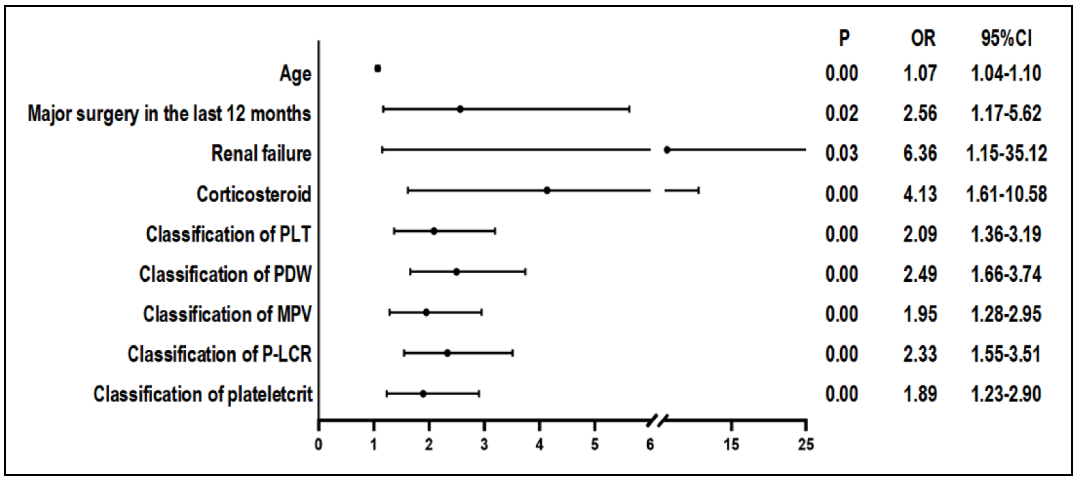

Figure 2. Univariate logistic regression analysis of preoperative risk factors for DVT in elderly patients undergoing TJA.
Abbreviations: PLT, platelet; MPV, mean platelet volume; PDW, platelet distribution width; P-LCR, platelet larger cell ratio; PCT, plateletcrit; DVT, deep vein thrombosis; CI, confidence interval; $P < .05$ was statistically significant.

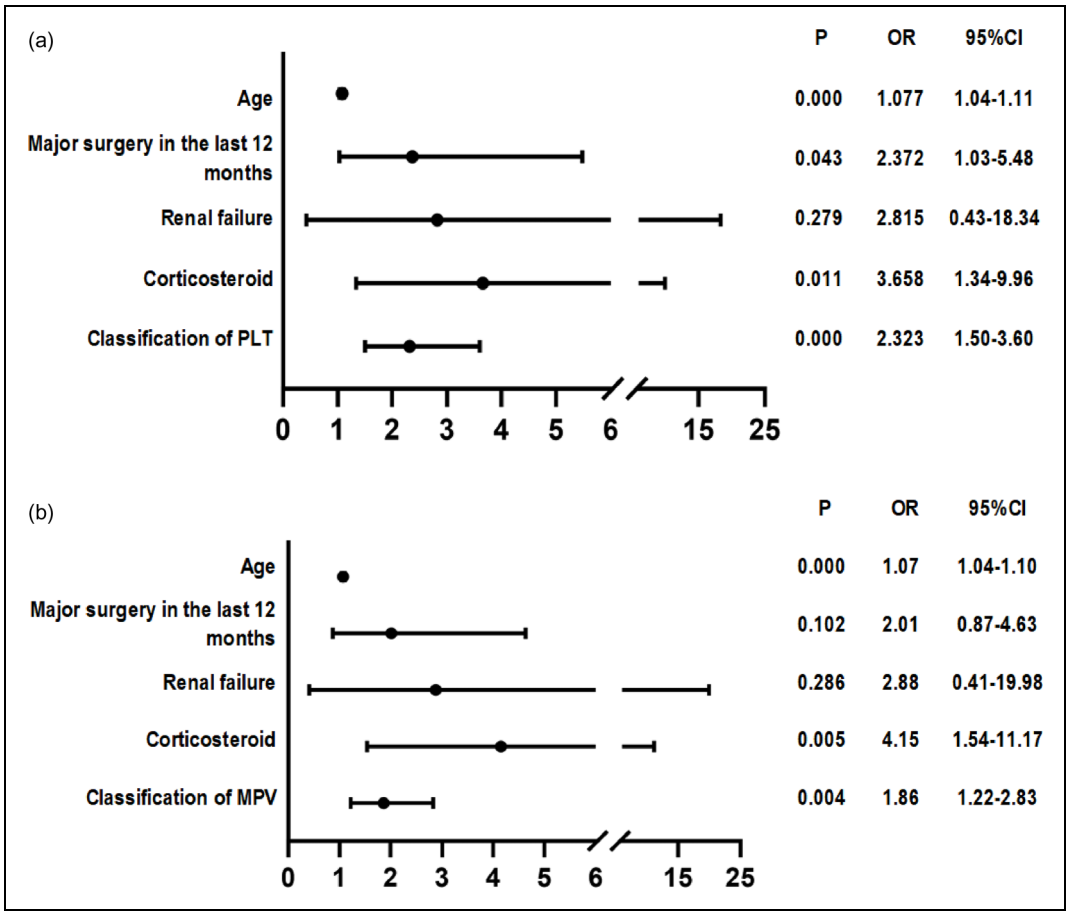

Figure 3. Multivariate logistic regression analysis of preoperative risk factors for DVT in elderly patients undergoing TJA. (**a)** Multivariate logistic regression analysis of PLT and DVT preoperative in elderly patients undergoing TJA. (**b**) Multivariate logistic regression analysis of MPV and DVT preoperative in elderly patients undergoing TJA. (**c**) Multivariate logistic regression analysis of PCT, PDW, and DVT preoperative in elderly patients undergoing TJA. (**d**) Multivariate logistic regression analysis of P-LCR and DVT preoperative in elderly patients undergoing TJA.
Abbreviations: PLT, platelet; MPV, mean platelet volume; PDW, platelet distribution width; P-LCR, platelet larger cell ratio; PCT, plateletcrit; DVT, deep vein thrombosis; CI, confidence interval; $P < .05$ was statistically significant. (continued)

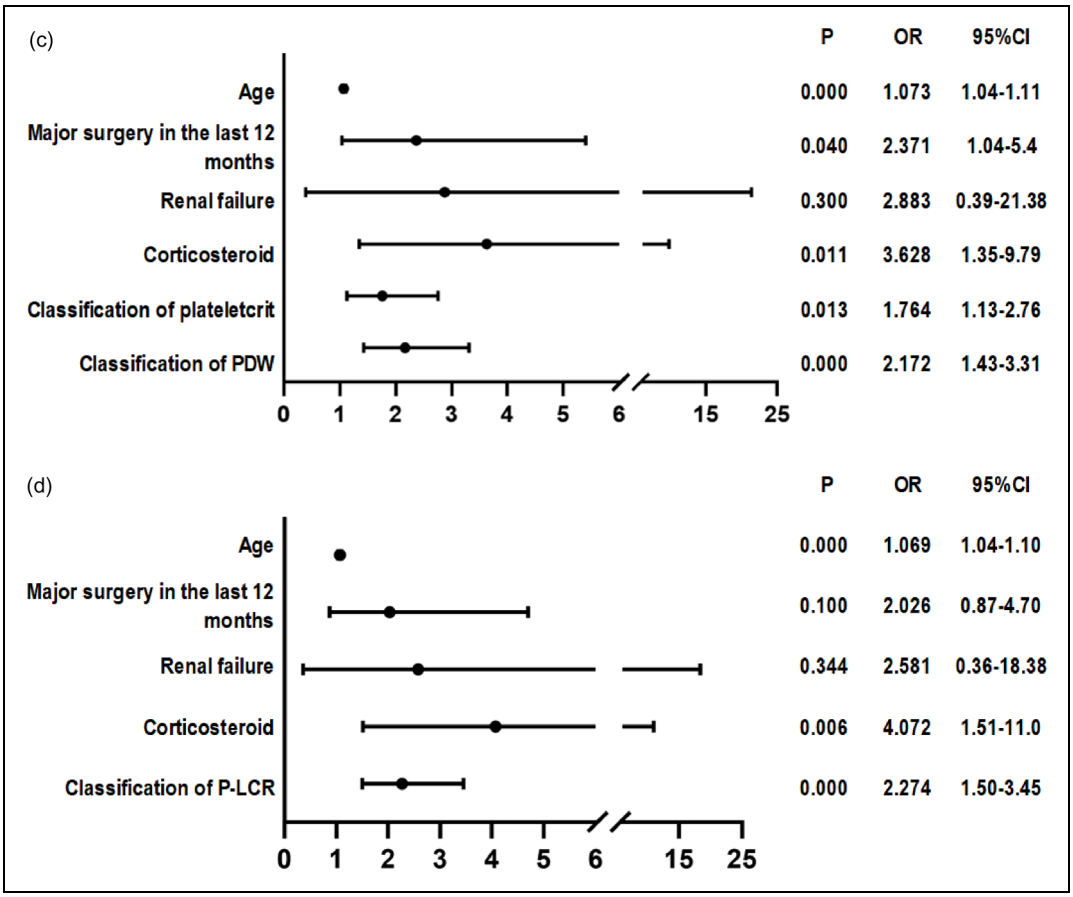

Figure 3. Continued.

Discussion

A study by Wang Z *et al* found that a low MPV level is associated with DVT in older patients with hip fracture. The cut-off point according to the ROC curve for MPV was 13.3 fL, and multivariate logistic regression analysis showed that MPV level below 13.3 fL was significantly associated with an increased risk of DVT (OR = 4.857), and with every 1.0 fL decrease in MPV, the risk increased by 27.7%.[9] Although the subject of their study, like the present one, were older patients, it focused on those with hip fracture and it had a small sample size (352 cases), and only investigated the association between MPV and DVT. Ma J *et al* reported that the risk of preoperative DVT increased by 3.06 times in PDW<12% patients with foot fracture.[10] However, these studies focus on bone fracture and investigate acute DVT and PLT indices. The present study is the first one that investigates the association between PLT, MPV, PDW, P-LCR, and preoperative DVT in elderly patients (with OA or RA) undergoing TJA.

Both OA and RA are Chronic Inflammation

Inflammation plays a key role in the pathogenesis of OA. Furthermore, OA pathogenesis involves not only breakdown of cartilage, but also remodeling of the underlying bone, formation of the ectopic bone, hypertrophy of the joint capsule, and inflammation of the synovial lining. Moreover, the inflammation in OA is distinct from that in RA and other autoimmune diseases: it is chronic, comparatively low-grade, and mediated primarily by the innate immune system.[17,18] Many cytokines and chemokines are detected in OA synovial fluid, such as Interleukin-1 (IL-1), Interleukin-6 (IL-6), Interleukin-7 (IL-7), Interleukin-8 (IL-8), and Tumor Necrosis Factor-alpha (TNF-alpha).[19]

RA is a systemic inflammatory disease, mainly affecting joints.[20] RA manifests as chronic inflammation of the synovial lining of the joint, resulting in pain, swelling, and ultimately destruction of cartilage and bone.[21] IL-17, IL-6, and TNF are the most important cytokines and chemokines in the inflammatory pathogenesis of RA.[22] During early inflammatory process of RA, IL-17 plays an important role in coordinating immune cells. IL-17 is also detected in the synovium of the joint.[22] In OA patient, IL-17 coordinates local inflammation, induces proinflammatory cytokines to prolong the inflammation process, and contributes to the development of cartilage, synovitis, and bone destruction.[22]

PLT and PLT Indices

Increased PLT. Platelets are anucleated cells that are produced by bone marrow megakaryocytes and are related to

inflammation and thrombosis.[23] In healthy population, PLT counts decrease with age.[13] According to Vázquez-Santiago *et al*, values of PLT≥312×10^9/L and PCT≥0.33% were associated with an increased risk of VTE in females.[24] Zakai *et al* reported that an elevated PLT count ≥350×10^9/L was an independent risk for VTE with an OR of 2.5.[25] Our study found that the risk of preoperative DVT had a 2.32-fold increase with PLT≥202×10^9/L and that the elevated PLT count was an independent risk factor for preoperative DVT in elder patients undergoing TJA. A study by Kwon *et al* showed significantly higher PLT and white blood cell counts in patients with symptomatic OA. And the study also found a linear relationship between OA and PLT count.[26] Xiong *et al* found that the elevated PLT count was a risk factor for preoperative DVT in patients with knee arthritis before TKA.[6] Thrombocytosis is a frequent finding in active RA.[27] Several hormonal and immune agents influence the maturation of thrombopoietic cells and release of PLTs into the circulation. Of these, thrombopoietin, granulocyte-macrophage colony-stimulating factor, IL-1, TNF-alpha, and IL-6 are important.[28] The action of IL-6 is associated with enhanced Tpo generation in the liver and its direct effect on megakaryocytes through the membranous receptor IL-6.[29] This means that PLT count may increase markedly in an inflammatory condition.[29]

PLT Indices. MPV is the most commonly used measure of PLT size and is regarded as a potential marker of PLT activity.[16] In physiological conditions, MPV is inversely proportional to the PLT count, which is associated with hemostasis maintenance and preservation of constant PLT mass.[30] In a large population study, mean MPV increases with aging.[13] MPV reflects both proinflammatory and prothrombotic conditions, where thrombopoietin and numerous inflammatory cytokines (eg, IL-1, IL-6, and TNF-alpha) regulate thrombopoiesis.[31] Most of previous studies have reported that high MPV levels increase the risk of VTE. However, our study found that low MPV was an independent risk factor for preoperative DVT in elderly patients undergoing TJA, the risk of DVT increased 1.86 times when MPV was no higher than 11.4 fL. Decreased MPV has been noted in tuberculosis during disease exacerbation, ulcerative colitis, systemic lupus erythematosus in adult, and different neoplastic diseases.[29] Lower MPV levels indicate active and/or chronic inflammatory state in the body.[32] The decrease of MPV under inflammatory conditions may be due to the following reasons: (1) The frequently described inverse relationship between PLT count and MPV in physiological and some pathological conditions reflects the tendency to maintain hemostasis by preserving a constant PLT mass [30]; (2) This inverse relationship is often seen in inflammatory disorders, where enhanced thrombopoiesis increases the quantity of circulating PLTs, and large amount of highly reactive large-sized PLTs migrate to inflammatory sites, where they are intensely consumed [30]; (3) The course of an inflammatory condition is also associated with increased percentage of large PLTs, probably due to intracellular synthesis of procoagulatory and proinflammatory factors, degranulation of granules, and initiation of the PLT pool stored in the spleen[33]; (4) Increased degradation of large PLTs under inflammation may lead to a decrease in MPV, possibly because larger PLTs are more responsive to stimulation, and a significant number of larger PLTs are more likely to be selectively degraded.[34] It was found by Riedl J *et al* that MPV was lower at the time of acute VTE compared to the values that had been measured at the time of cancer diagnosis. These data would support the hypothesis that smaller PLTs might exhibit a stronger prothrombotic tendency in cancer patients than larger PLTs.[35]

PDW measures the variability in PLT size and is another marker of PLT activation.[16] Öztürk ZA *et al* found that PDW is significantly lower in the active phase of ulcerative colitis and Crohn's disease than in the remission phase, which suggests that the reduction of PDW may be related to the progression or activation of a disease, rather than the disease itself.[36] According to a small-sample study on cerebral venous sinus thrombosis, in ROC analysis, a cut-off value of 16.5 for PDW could predict the severity of cerebral venous sinus thrombosis.[37] Ma J *et al* found that a decreased PDW level (<12%) was significantly associated with the occurrence of DVT (OR = 3.06).[10] The decreased PDW value suggests a higher homogeneity of platelet volume and highly active status of PLTs, which might indicate blood hypercoagulability and contribute to the subsequent DVT.[10]

The P-LCR is an indicator of circulating PLTs that are larger than 12 fL, and has been used to monitor the activity of PLTs.[16] Most studies have found that the bigger PLT is a risk factor for thrombosis, because in steady-state operation, these bigger PLTs release more thromboxane B2 than regular PLTs. PLTs with bigger sizes are more hemostatically active and hence have a higher chance of forming a thrombus.[38] However, our study found that the cut-off value for P-LCR was 34.6% and that P-LCR≤34.6% was an independent risk factor for DVT before TJA in older patients and the risk of preoperative DVT was 2.27 times higher. Small PLTs are produced under inflammatory conditions possibly because that overproduction of pro-inflammatory cytokines and acute-phase reactants can suppress PLT size by interfering with megakaryopoiesis with subsequent release of small size PLTs from the bone marrow.[31] Giles C. found that under the same hemostatic conditions, only a small number of large PLTs is needed to obtain the same overall effect that a higher number of small PLTs might obtain.[39] In this present study, as the DVT group had more PLTs, the compensatory release of circulating small PLTs increased. Therefore, as there were more small PLTs than large PLTs, it was easier to provoke thrombosis.

PCT = platelet count × MPV/10,000.[16] The PCT has been proven to act as a biomarker for determining active Crohn's disease with a cut-off value of 0.28%.[40] Xiong *et al* found that the elevated PCT count was a risk factor for preoperative DVT before TKA.[6] Abanoz M *et al* reported that in the ROC analysis, the cut-off value for PCT was 0.199 in a retrospective study on preoperative lower extremity DVT.[12] In the present study, according to the ROC analysis, the cut-off value for PCT was 0.228 (AUC = 0.598, $P < .001$, 50% sensitivity, and

70% specificity). However, the risk of preoperative DVT in older patients before TJA increased 1.764 times. Moreover, PCT≥0.228 was an independent risk factor for preoperative DVT in elderly patients undergoing TJA.

Association Between PLT, PLT Indices, and DVT

Our patients had long course of disease, from years to decades, because patients with OA or RA are in long-term, chronic inflammatory condition. Besides, their mean age was above 70 years. Theoretically, their PLT counts should be decreased, but PLT counts in our patients were increased. A possible mechanism responsible for thrombocytosis in inflammation is: in patients with ongoing inflammation, the increasing concentration of pro-inflammatory cytokines, mainly IL-6, can lead to platelet release.[29] IL-6 causes an increase in the ploidy of megakaryocytic nuclei and an increase in cytoplasm volume, which in consequence leads to the production of a large number of PLTs.[41] During coagulation, the count may decrease due to PLT wear, whereas the activation of megakaryocytes by pro-inflammatory cytokines may lead to a considerable increase in the production and release of thrombocytes.[29] The elevated PLT count can promote an inflammatory response[42] and activate fibrin production and lead to hypercoagulability.[43]

Therefore, overall, as OA and RA are chronic inflammatory conditions, inflammation leads to the increase of PLT count and the changes in PLT indices. Such changes, together with inflammation, further cause preoperative DVT more likely to occur in elder patients undergoing TJA. Moreover, we also found that aging and corticosteroid use were independent risk factors for preoperative DVT in patients undergoing TJA. Aging causes abnormalities in coagulation system. Older people have elevated levels of factor VII, factor V antigen, fibrinogen, and D-Dimmer in the plasma and are in constant prothrombotic condition.[44] Corticosteroid has been found to increase the levels of factor VII, VIII, XI, and fibrinogen, which may contribute to increasing the risk of VTE in patients with chronic corticosteroid use.[45] This study found a 3.66-fold increase in the risk of VTE in patients with corticosteroid use.

In this study, the correlation with DVT in older patients undergoing TJA was explored by using materials such as preoperative medical history, preoperative laboratory examinations, and preoperative auxiliary examinations. However, this study has certain limitations. As a retrospective study, some data are incomplete. The AUCs for PLT, MPV, PDW, and P-LCR were 0.606, 0.605, 0.617, 0.616, and 0.598, respectively. Future studies with bigger sample size and more data might be needed to further verify the association between PLT, PLT indices, and preoperative DVT in TJA patients.

Conclusion

This study found that increased PLT count and PCT, decreased MPV, PDW, and P-LCR, old age, corticosteroid were independent risk factors for preoperative DVT in elderly TJA patients. The elderly patients with PLT≥202×10^9/L, MPV≤11.4 fL, PDW≤13.2 fL, P-LCR≤34.6%, and PCT≥0.228% should be screened for preoperative DVT before TJA.

Abbreviations

AUC	area under curve
BMI	body mass index
CHD	coronary heart disease
COPD	chronic obstructive pulmonary disease
CI	confidence interval
DM	diabetes mellitus
DVT	deep vein thrombosis
HB	hemoglobin
IL-1	Interleukin-1
IL-6	Interleukin-6
IL-7	Interleukin-7
IL-8	Interleukin-8
IL-17	Interleukin-17
MPV	mean platelet volume
OA	osteoarthritis
OR	odds ratio
PLT	platelet
PCT	platelet crit
PDW	platelet distribution width
PE	pulmonary embolism
LCR	platelet large cell ratio
RA	rheumatoid arthritis
ROC	receiver operating characteristic
TF	tissue factor
THA	total hip arthroplasty
TJA	total joint arthroplasty
TKA	total knee arthroplasty
TNF	tumor necrosis factor
PLT	platelets
VTE	venous thromboembolism.

Author Contributions

Xiaojuan Xiong, Ting Li, Shuang Yu, and Bo Cheng contributed to the conception and design of the study. Xiaojuan Xiong, Ting Li, and Shuang Yu contributed to the acquisition and analysis of data. Xiaojuan Xiong wrote the manuscript. Bo Cheng revised the manuscript. All authors read and approved the final manuscript.

Consent to Participate

As this was a retrospective study, and data were analyzed anonymously, informed consent was therefore waived by the committee.

Data Sharing Statement

The data used during the current study are available from the corresponding author on reasonable request.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval

This study has been approved by Medical Research and Ethics Review (No. 184, 2022).

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