



Prediction and Risk Factors of Lower Extremity Deep Vein Thrombosis after Total Joint Arthroplasty

Zhenhua Wang,¹ Zhiwei Liu¹ and Zhaoxing Tian¹

¹Emergency Department, Beijing JiShuiTan Hospital, Beijing, China

This study was to retrospectively analyze the incidence of deep vein thrombosis (DVT) in patients undergoing total joint arthroplasty (TJA) and analyze the risk factors for DVT. 113 patients with TJA were divided into the DVT group ($n = 11$) and the non-DVT group ($n = 102$) according to the postoperative ultrasound diagnosis, and the incidence of DVT after TJA was calculated. Logistic regression was used to analyze the correlation between DVT and patients' age, medical history, surgical factors, blood indexes to identify the risk factors of DVT after TJA. Receiver operator characteristic (ROC) curve was constructed to evaluate the diagnostic accuracy of risk factors for DVT. According to the results of ultrasound examination, DVT occurred in 11 of 113 patients after TJA, and the incidence rate of DVT was 9.73%. Univariate analysis showed that the levels of age, diabetes mellitus, operation time, intraoperative blood loss, intraoperative blood transfusion, antithrombin-III (AT-III), plasma protein C (PC), soluble platelet endothelial cell adhesion molecules-1 (SPECAM-1) and tissue-type plasminogen activator (t-PA) in the DVT group were significantly different from those in the non-DVT group ($P < 0.05$). Multivariate analysis showed that combined diabetes, decreased PC and t-PA were risk factors for DVT ($P < 0.05$). ROC analysis showed that PC combined with t-PA had the highest diagnostic accuracy for DVT. Patients with diabetes mellitus are at high risk for DVT after TJA, the increase of D-dimer, the decrease of PC and t-PA after 24 h of TJA is the the risk factors for DVT occurrence.

Keywords: deep vein thrombosis; diagnosis; prediction; risk factors; total joint arthroplasty

Tohoku J. Exp. Med., 2025 March, 265 (3), 113-121.

doi: 10.1620/tjem.2024.J099

Introduction

Artificial joint prosthesis technology is one of the greatest research achievements in the medical field in the 20th century. With the continuous breakthrough in the field of bioengineering and material science, artificial joint replacement has solved the pain of more and more patients with advanced joint diseases and improved their quality of life (Ferraro et al. 2021). Total joint arthroplasty (TJA) includes total knee arthroplasty (TKA) and total hip arthroplasty (THA) (Scales et al. 2010; Ginnetti et al. 2022). As the aging of the population becomes more and more serious, the number of TJA operations is increasing every year (Wang et al. 2022). Although TJA may not be satisfactory to all patients after surgery, it is still considered as one of the best methods to improve the quality of life of patients with joint disease. However, this operation also has many complications, such as poor wound healing, prosthesis loos-

ening, infection, and deep vein thrombosis (DVT) of lower extremity (Wu et al. 2020).

DVT is a thrombus formed in the deep veins of the lower extremities under the combined action of internal and external factors, which can be divided into proximal, distal, and mixed types according to the location of occurrence (Navarrete et al. 2023). Under normal physiological conditions, the body always keeps a dynamic balance between coagulation and fibrinolysis. If this balance is broken, the tendency of blood clots in the vessels is strengthened, which will lead to abnormal aggregation of fibrin, abnormal increase of fibrin degradation products, and activation of various thrombin enzymes (Navarrete et al. 2023; Waheed et al. 2025). It is reported that the incidence of DVT in patients after THA is 40%-58% without anticoagulation therapy (Rachidi et al. 2013). Nicol et al. (2009) reported that no measures have been taken to prevent thrombosis after spinal surgery, and the incidence of DVT was gener-

Received June 16, 2024; revised and accepted September 2, 2024; J-STAGE Advance online publication September 12, 2024

Correspondence: Zhaoxing Tian, Emergency Department, Beijing JiShuiTan Hospital, No. 68, Huinan North Road, Changping District, Beijing 102200, China.

e-mail: drtianzhaoxing@163.com

©2025 Tohoku University Medical Press. This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License (CC-BY-NC-ND 4.0). Anyone may download, reuse, copy, reprint, or distribute the article without modifications or adaptations for non-profit purposes if they cite the original authors and source properly.

<https://creativecommons.org/licenses/by-nc-nd/4.0/>

ally between 2.9% and 14.0%. DVT is one of the common postoperative complications of TKA. If the condition continues to deteriorate without effective intervention, it may have a higher probability of developing fatal complication, that is, pulmonary embolism (Wenger et al. 2021). With the increasing maturity of TJA technique in joint surgery, the occurrence of postoperative DVT has been paid more attention.

Clinical studies showed that active prevention before operation can effectively reduce the incidence of postoperative DVT (Liu et al. 2016; Chai et al. 2021). In actual clinical practice, doctors need to understand which are the risk factors for postoperative DVT, or which patients are the high-risk group of postoperative DVT. These questions are the thorny problems in the field of joint orthopedics, and they are also important topics that need to be studied urgently. Therefore, this study retrospectively analyzed 113 patients with TJA, aiming to explore the incidence and potential risk factors of postoperative DVT, so as to provide an effective basis for identifying high-risk patients before operation and taking targeted measures.

Materials and Methods

Inclusion of the study sample

The clinical data of patients with TJA in Beijing JiShuiTan Hospital were analyzed retrospectively. The inclusion criteria are as follows: 1) Complete patient data; 2) The diagnosis of the patient's disease is definite and primary; 3) All patients were treated with TJA for the first time; 4) There were no symptoms of active infection, and there were no significant abnormalities in C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and blood routine examination before operation. The exclusion criteria are as follows: 1) Patients with DVT before operation; 2) Active hemorrhage or recent spontaneous intracranial hemorrhage; 3) Long-term use of anticoagulant medicine or accompanied by bleeding diseases; 4) severe hepatic and renal insufficiency; 5) Patients with contraindications to anticoagulation therapy. A total of 113 patients met the criteria, including 65 TKA patients and 48 THA patients.

This study was conducted in accordance with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Beijing JiShuiTan Hospital. Informed consent was obtained from all individual participants included in the study.

Perioperative treatment

1) 24 h before operation: All patients included in the study were examined by color Doppler ultrasound before operation, including intermuscular vein, anterior and posterior tibial vein, posterior popliteal vein of knee joint, femoral vein of thigh, etc. The standard for diagnosis of DVT is that vascular ultrasound shows the filling defects of the above veins.

2) 24 h after operation: All patients were operated by the same joint surgeon and his team, and each patient was

undergoing unilateral replacement for the first time. Anticoagulant therapy: rivaroxaban (10 mg) was taken orally once a day from 8 h after operation, and 10 mg each time from the first day after operation. Functional rehabilitation: standardize and guide early rehabilitation exercises and encourage patients to get out of bed properly in the early stage.

3) 72 h after operation: The treatment method is the same as before. The vein diameter, blood flow changes, lumen pressure, deep vein valve function and thrombosis of both lower limbs were detected by Doppler ultrasound.

Observation indicators

Preoperative information was collected, including age, sex, height, weight, smoking and drinking history, underlying diseases, disease type, American Society of Anesthesiologists (ASA) grade, operation duration, intraoperative blood loss and intraoperative blood transfusion. In addition, the indexes of antithrombin-III (AT-III), plasma protein C (PC), soluble platelet endothelial cell adhesion molecules-1 (SPECAM-1), endothelin-1 (ET-1), plasminogen activator inhibitor-1 (PAI-1) and tissue-type plasminogen activator (t-PA) were detected before surgery and 24 and 72 h after surgery, respectively.

Data analysis

SPSS 22.0 software and GraphPad Prism 7.0 software were used for data analysis and figures rendering. Quantitative data is expressed as mean \pm standard deviation (SD), and qualitative data is represented as n (%). T-test, Chi-square test or paired sample T-test was used for comparison between groups, or pairwise comparison within groups. The receiver operator characteristic (ROC) curve was performed to analyze the diagnostic accuracy of each index for DVT. $P < 0.05$ was considered as significant difference.

Results

Summary of preoperative information of 113 subjects with TJA

The information of 113 subjects involved in this study is summarized in Table 1. Of the 113 subjects, 62 were male and 51 were female, and their age range was 23-79 years, with a mean age of (57.65 \pm 12.25) years. Among them, 48 cases received THA, and 65 cases received TKA. There were 65 cases of knee osteoarthritis, 18 cases of hip osteoarthritis, 22 cases of femoral head necrosis and 8 cases of other diseases.

Trend of perioperative blood indexes in 113 patients with TJA

Table 2 summarized the changes of blood coagulation indexes (AT-III, PC), endothelial injury indexes (SPECAM-1, ET-1) and fibrinolysis indexes (PAI-1, t-PA) in 113 patients before and after TJA. The results showed that the levels of AT-III, SPECAM-1 and t-PA increased at

Table 1. Baseline data of all subjects.

Items	TJA patients (n = 113)
Sex (male/female)	62/51
Age (years)	57.65 ± 12.25
BMI (kg/m ²)	24.21 ± 1.51
Smoking history (n, %)	71 (62.8%)
Drinking history (n, %)	53 (46.9%)
Complications (n, %)	
Hypertension	50 (44.2%)
Diabetes	37 (32.7%)
Disease type (n, %)	
Knee osteoarthritis	65 (57.5%)
Hip osteoarthritis	18 (15.9%)
Osteonecrosis of the femoral head	22 (19.5%)
Others	8 (7.1%)
Type of operation (n, %)	
THA	48 (42.5%)
TKA	65 (57.5%)
Operation duration (min)	101.23 ± 39.76
Intraoperative bleeding loss (mL)	327.26 ± 265.27
Intraoperative blood transfusion (mL)	96.81 ± 140.58

BMI, body mass index; TJA, total joint arthroplasty; THA, total hip arthroplasty; TKA, total knee arthroplasty. $P < 0.05$ means significant difference.

Table 2. Changes of perioperative laboratory indicators in patients with TJA.

Indicators	1 day before TJA	24h after TJA	72h after TJA
AT-III (μg/mL)	70.03 ± 20.51	81.36 ± 24.93***	118.65 ± 34.61***/###
PC (μg/mL)	2.03 ± 0.66	1.20 ± 0.36***	0.88 ± 0.30***/###
SPECAM-1 (μg/L)	68.47 ± 26.14	107.42 ± 39.27***	156.40 ± 42.75***/###
ET-1 (ng/L)	39.26 ± 13.27	18.41 ± 5.95***	15.27 ± 5.64***/###
PAI-1 (ng/mL)	4.23 ± 1.53	3.57 ± 1.18***	2.49 ± 0.70***/###
t-PA (μg/L)	2.03 ± 1.03	2.53 ± 0.86***	2.87 ± 0.83***/###
D-dimer (mg/L)	0.49 ± 0.07	2.53 ± 0.95***	4.16 ± 2.03***/###
FIB (g/L)	3.23 ± 0.49	3.62 ± 2.32**	4.39 ± 2.24***/###

TJA, total joint arthroplasty; AT-III, antithrombin-III; PC, plasma protein C; SPECAM-1, soluble platelet endothelial cell adhesion molecules-1; ET-1, endothelin-1; PAI-1, plasminogen activator inhibitor-1; t-PA, tissue-type plasminogen activator; FIB, fibrinogen. ** $P < 0.01$, *** $P < 0.001$ vs. 1 day before TJA. ### $P < 0.001$ vs. 24 h after TJA.

24 h and 72 h after TJA, and the above indexes were significantly higher at 72 h compared with 24 h after TJA ($P < 0.001$). Additionally, compared with pre-operation, the levels of PC, ET-1 and PAI-1 at 24 h and 72 h after operation showed a decreasing trend, and these indexes decreased more at 72 h after operation than at 24 h after TJA ($P < 0.001$).

The incidence of DVT and the comparison of clinical information between the two groups

On the third day after TJA, the patients were examined by Doppler ultrasound of lower limbs, and 11 patients developed DVT. In this study, the incidence rate of DVT after TJA was 9.73%. As shown in Table 3, the clinical data

of 11 DVT patients and 102 non-DVT patients were analyzed, and it was found that the age of patients in the DVT group was significantly older than that in the non-DVT group, and the proportion of diabetes mellitus in the DVT group was significantly higher than that in the non-DVT group ($P < 0.05$). It was also observed that the average operation duration, average intraoperative blood loss and blood transfusion in the DVT group were significantly higher than those in the non-DVT group ($P < 0.05$). In addition, intra-group analysis of the blood indicators of the two cohorts found that the perioperative levels of AT-III, SPECAM-1, and t-PA in the two groups showed an increasing trend, while the perioperative levels of PC, ET-1 and PAI-1 showed a decreasing trend (Table 4, $P < 0.05$).

Table 3. Comparison of clinical information between DVT patients and non-DVT patients.

Items	Non-DVT group (n = 102)	DVT group (n = 11)	P
Sex (male/female)	57/45	5/6	0.540
Age (years)	56.65 ± 12.28	66.37 ± 8.10	0.004
BMI (kg/m ²)	24.17 ± 1.55	24.36 ± 0.92	0.693
Smoking history (n)	64	7	0.903
Drinking history (n)	46	7	0.343
Hypertension (n)	46	4	0.752
Diabetes (n)	29	8	0.005
Disease type (n)			0.627
Knee osteoarthritis	59	6	
Hip osteoarthritis	15	3	
Osteonecrosis of the femoral head	21	1	
Others	7	1	
Type of operation (n)			0.757
THA	44	4	
TKA	58	7	
Operation duration (min)	97.21 ± 33.54	138.55 ± 68.17	0.001
Intraoperative bleeding loss (mL)	309.61 ± 243.85	490.91 ± 393.58	0.030
Intraoperative blood transfusion (mL)	87.64 ± 136.03	181.82 ± 160.11	0.034
Site of thrombosis after TJA (n, %)			
Venae musculares	/	7 (63.6%)	
Venae tibiales posteriores	/	2 (18.2%)	
Venae tibiales anteriores	/	1 (9.1%)	
Common femoral veins	/	0 (0)	
Popliteal vein	/	1 (9.1%)	
Medication information (n, %)			
Enteric-coated aspirin	/	11 (100.0%)	
Low molecular weight heparin calcium	/	8 (72.7%)	

DVT, deep vein thrombosis; BMI, body mass index; THA, total hip arthroplasty; TKA, total knee arthroplasty. $P < 0.05$ means significant difference.

Furthermore, an intergroup comparison between the two cohorts showed that AT-III levels were significantly lower in the DVT group before and 24 hours after surgery than in the non-DVT group (Fig. 1A, $P < 0.05$). As shown in Fig. 1B, PC level in the DVT group was significantly lower than that in the non-DVT group 24 h after surgery ($P < 0.01$). For SPECAM-1, patients in the DVT group had significantly higher levels at 24 h and 72 h after surgery than those in the non-DVT group (Fig. 1C, $P < 0.05$). For ET-1, although the level in the DVT group was higher than that in the non-DVT group during the perioperative period, the difference was not significant (Fig. 1D, $P > 0.05$). As exhibited in Fig. 1E, the PAI-1 levels in DVT group were significantly higher than that in non-DVT group at 72 h after operation ($P < 0.05$). The level of t-PA in DVT group was significantly lower than that in non-DVT group at 24 h before operation, 24 h after operation and 72 h after operation (Fig. 1F, $P < 0.05$). In addition, compared with the 1 day before TJA, the expression level of D-dimer was observed to increase at 24 h and 72 h after TJA, and the

level in the DVT group was significantly higher than that in the non-DVT group at 24 h and 72 h after TJA (Fig. 1G, $P < 0.01$). For FIB level, it was observed that the expression level in DVT group was higher than that in non-DVT group at 72 h after operation (Fig. 1H, $P < 0.001$).

Risk factors for postoperative DVT in TJA patients

The indicators with significant differences between the DVT group and the non-DVT group were included in multivariate logistic regression analysis to evaluate the potential risk factors for the occurrence of DVT. The results in Table 5 showed that age, combined diabetes, increased D-dimer, decreased PC and reduced t-PA were risk factors for postoperative DVT in TJA patients ($P < 0.05$).

The value of PC and t-PA in the combined diagnosis of DVT at 24 h after surgery

ROC curves of blood indexes D-dimer, PC and t-PA, which had significant significance in multivariate regression analysis, were constructed to evaluate their clinical diag-

Table 4. Comparison of perioperative laboratory indexes between non-DVT group and DVT group.

Indicators	Group	1 day before TJA	24h after TJA	72h after TJA
AT-III (μg/mL)	Non-DVT (n = 102)	71.40 ± 20.58	83.25 ± 25.36**	119.78 ± 35.44***/###
	DVT (n = 11)	57.24 ± 15.27	63.82 ± 9.39*	108.20 ± 24.29***/###
PC (μg/mL)	Non-DVT (n = 102)	2.02 ± 0.66	1.23 ± 0.35***	0.89 ± 0.30***/###
	DVT (n = 11)	2.09 ± 0.59	0.93 ± 0.32***	0.83 ± 0.28***
SPECAM-1 (μg/L)	Non-DVT (n = 102)	67.90 ± 26.61	104.59 ± 36.16***	153.55 ± 39.54***/###
	DVT (n = 11)	73.75 ± 21.52	133.61 ± 56.79**	182.80 ± 61.93**/#
ET-1 (ng/L)	Non-DVT (n = 102)	38.65 ± 13.41	18.12 ± 6.01***	15.01 ± 5.75***/###
	DVT (n = 11)	44.88 ± 10.74	21.06 ± 4.86***	17.72 ± 3.89***
PAI-1 (ng/mL)	Non-DVT (n = 102)	4.15 ± 1.54	3.51 ± 1.19***	2.44 ± 0.68***/###
	DVT (n = 11)	4.97 ± 1.26	4.17 ± 1.01**	2.97 ± 0.74***/###
t-PA (μg/L)	Non-DVT (n = 102)	2.07 ± 1.07	2.61 ± 0.86***	2.94 ± 0.83***/###
	DVT (n = 11)	1.64 ± 0.39	1.83 ± 0.35*	2.24 ± 0.44**/##
D-dimer (mg/L)	Non-DVT (n = 102)	0.49 ± 0.07	2.61 ± 0.83***	3.98 ± 1.79***/###
	DVT (n = 11)	0.51 ± 0.07	3.22 ± 0.92***	6.45 ± 2.73***/###
FIB (g/L)	Non-DVT (n = 102)	3.22 ± 0.46	3.61 ± 2.08***	4.21 ± 2.11***/###
	DVT (n = 11)	3.31 ± 0.51	4.29 ± 2.68***	6.07 ± 2.74***/###

DVT, deep vein thrombosis; TJA, total joint arthroplasty; AT-III, antithrombin-III; PC, plasma protein C; SPECAM-1, soluble platelet endothelial cell adhesion molecules-1; ET-1, endothelin-1; PAI-1, plasminogen activator inhibitor-1; t-PA, tissue-type plasminogen activator; FIB, fibrinogen. **P* < 0.05, ***P* < 0.01, ****P* < 0.001 vs. 1 day before TJA. #*P* < 0.05, ##*P* < 0.01, ###*P* < 0.001 vs. 24 h after TJA.

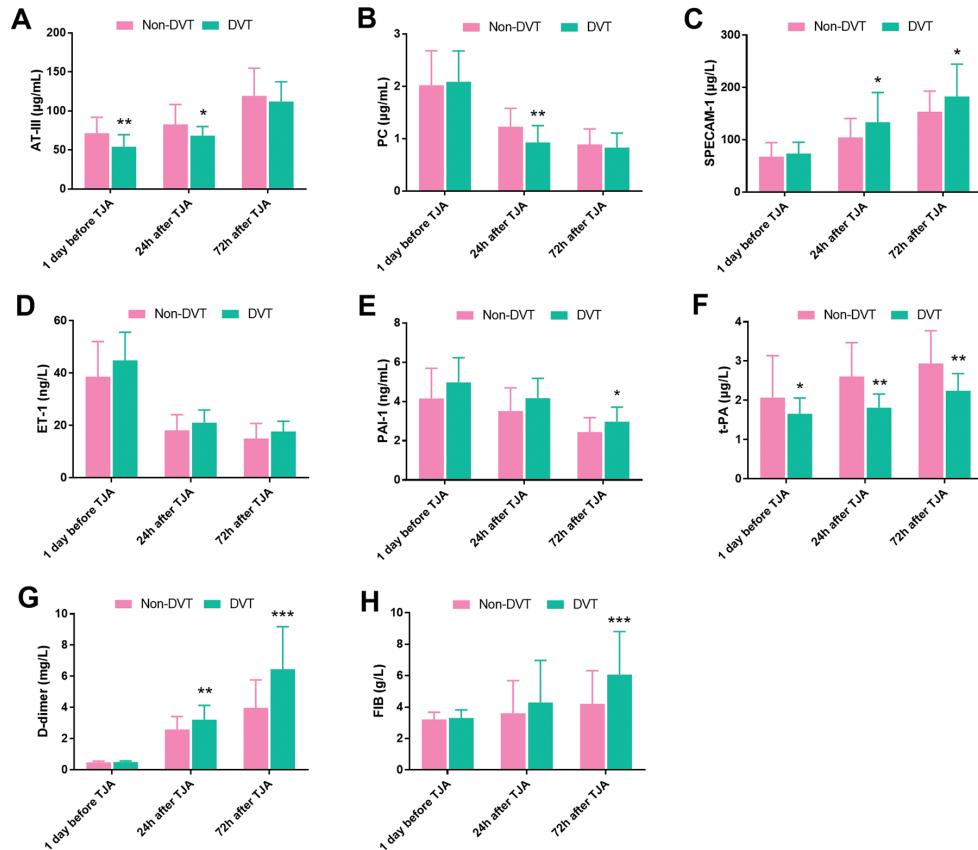


Fig. 1. Comparison of perioperative laboratory parameters between DVT group and non-DVT group. (A) The levels of anti-thrombin-III (AT-III) gradually increased during the perioperative period. (B) Plasma protein C. (C) Soluble platelet endothelial cell adhesion molecules-1 (SPECAM-1). (D) Endothelin-1 (ET-1). (E) Plasminogen activator inhibitor-1 (PAI-1). (F) Tissue-type plasminogen activator (t-PA). (G) D-dimer. (H) fibrinogen (FIB). **P* < 0.05, ***P* < 0.01, ****P* < 0.001 vs. Non-DVT group.

Table 5. Multivariate logistic regression analysis.

Items	95% CI	OR	<i>P</i>
Age (year)	3.524-23.138	7.975	0.008
Diabetes (n)	2.006-17.459	6.013	0.019
Operation duration (min)	0.624-7.936	3.983	0.137
Intraoperative bleeding loss (mL)	2.035-25.132	7.873	0.503
Intraoperative blood transfusion (mL)	0.886-16.609	3.006	0.369
AT-III ($\mu\text{g}/\text{mL}$)	0.053-3.123	0.573	0.515
PC ($\mu\text{g}/\text{mL}$)	0.009-0.703	0.069	0.027
SPECAM-1 ($\mu\text{g}/\text{L}$)	1.135-6.726	6.897	0.069
t-PA ($\mu\text{g}/\text{L}$)	0.009-0.516	0.030	0.016
D-dimer (mg/L)	1.162-14.857	7.335	0.011

OR: odds ratio; AT-III, antithrombin-III; PC, plasma protein C; SPECAM-1, soluble platelet endothelial cell adhesion molecules-1; t-PA, tissue-type plasminogen activator. $P < 0.05$ was a significant difference.

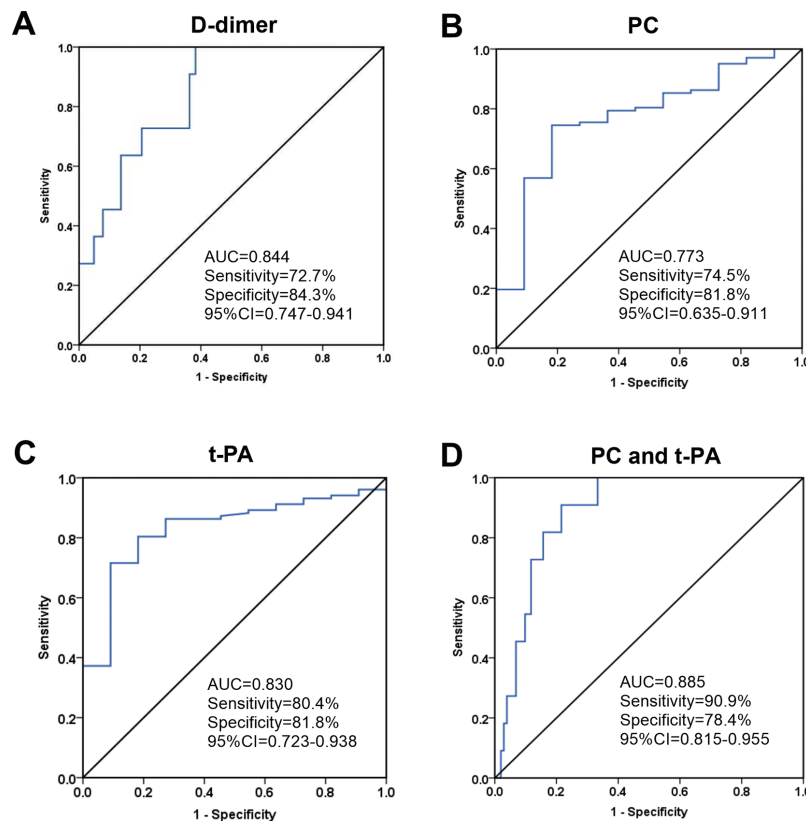


Fig. 2. The ability of DVT identification was evaluated by receiver operator characteristic (ROC) curves. (A) ROC curve of D-dimer. (B) The area under the ROC curve of plasma protein C is 0.773. (C) ROC curve of tissue-type plasminogen activator (t-PA). (D) ROC curve of PC combined with t-PA.

nostic value for DVT. As shown in Fig. 2A, the ROC curve shows that the sensitivity and specificity of D-dimer for distinguishing DVT patients from non-DVT patients are 72.7% and 84.3%, and the AUC value of ROC curve is 0.844. The results showed that for PC to distinguish DVT from non-DVT, the AUC of its ROC curve was 0.773, and the sensitivity and specificity were 74.5% and 81.8%, respectively (Fig. 2B, $P < 0.05$). For t-PA, the AUC of its

ROC curve was 0.830, the sensitivity was 80.4%, and the specificity was 81.8% (Fig. 2C, $P < 0.05$). The ROC curve constructed by PC combined with t-PA is shown in Fig. 2D. The AUC of this curve was 0.885, and the sensitivity and specificity were 90.9% and 78.4%, respectively. In summary, the combination of PC and t-PA has the highest diagnostic accuracy for DVT.

Discussion

Artificial joint arthroplasty has brought good news to patients with joint diseases, and greatly improved the quality of life. However, DVT is one of the most common serious complications after joint arthroplasty. Therefore, early diagnosis and treatment and active prevention of deep venous thrombosis are particularly important. In this study, the results showed that DVT occurred in 11 out of 113 patients with TJA, with an incidence rate of DVT was 9.73%. Multivariate regression analysis showed that age, diabetes, increased D-dimer and the reduction of PC and t-PA at 24 h after TJA were risk factors for DVT after TJA. ROC analysis showed that both PC and t-PA showed predictive value for distinguishing DVT from non-DVT, but the combination of PC and t-PA had the highest diagnostic accuracy for DVT.

The occurrence of DVT after TJA is a serious postoperative disease caused by the interaction of many reasons, among which the hypercoagulable state of blood, damaged vein wall and slow venous blood flow are the main reasons, which are also the three elements of Virchow thrombosis (Yao et al. 2023). In addition, postoperative limb immobilization or bed rest will promote blood stasis or slow down the flow rate, eventually change the metabolic environment, lead to local tissue hypoxia, and further promote the formation of DVT (Dai et al. 2021). In this study, the postoperative incidence of DVT in patients receiving TJA is about 9.73%, which was lower than that reported in previous studies (17.96%) (Zhang et al. 2017). In addition to the small sample size in this study, preoperative and postoperative care in different hospitals may also be another important factor leading to this difference.

A large number of basic and clinical studies showed that thrombosis is caused by the changes of vascular endothelial cells, platelets, coagulation, anticoagulation, fibrinolytic system and hemorheology, etc. (Furie and Furie 2008; Brill 2021). These factors have changed to varying degrees before thrombosis, and these changes have an important influence on the course and prognosis of the disease. Antithrombin system, protein C system and tissue factor pathway inhibitor are the three main anticoagulation systems in the human body (Segel and Francis 2000). AT-III and PC are important anticoagulant factors in vivo, and their congenital or acquired deficiency may lead to hypercoagulability and increase the risk of DVT formation (Suehisa et al. 2001; Elfaki et al. 2023). Fibrinolysis refer to the process by which fibrin or fibrinogen is hydrolyzed by fibrinolytic enzyme. PAI-1 and t-PA are two important indicators to measure fibrinolysis function. PAI-1 is an inhibitor of t-PA, which binds to t-PA in a ratio of 1:1 to inactivate t-PA (Mo et al. 2015). Therefore, an imbalance of PAI-1 and t-PA can lead to the abnormalities of fibrinolytic system, followed by bleeding due to the increase of fibrinolytic activity, or thrombosis due to the decrease of fibrinolytic activity. The damage of vascular endothelial

cells is one of the precursors of thrombosis. The damaged endothelial cells expose the basement membrane of blood vessels, and lead to platelet aggregation to thrombosis (Takahashi et al. 2010). After endothelial cell injury, factors such as ET-1 are released to activate platelets. Activated platelets can combined with exposed vascular basement membranes and endothelial cells, suggesting the expression of adhesion molecules such as SPECAM-1 that further promote thrombosis. On the basis, according to the mechanism of DVT, AT-III, PC, SPECAM-1, ET-1, PAI-1, and t-PA were selected as the main research indicators, and the patients included in the study were dynamically observed to analyze the relationship between these indicators and DVT.

In the present study, the AT-III expression in patients with DVT and non-DVT during perioperative period showed a gradual upward trend, while the expression of PC showed a downward trend. However, it is worth noting that the levels of AT-III and PC in the DVT group were significantly lower than those in the non-DVT group 24 h after TJA. Deficiency of AT-III is known to result in a hypercoagulable state of the body, increasing the risk of thromboembolism disease by 10-50 times (Ye et al. 2022). Similarly, a lack of PC can lead to insufficient inactivation of coagulation factors, increasing the risk of thrombosis and increasing the recurrence rate (Wang et al. 2021). In addition, this study demonstrated that the expression of SPECAM-1 increased and the level of ET-1 decreased in the two groups during the perioperative period. However, the expression level of SPECAM-1 in the DVT group was higher than that in the non-DVT group at 24 h and 72 h after TJA. During the perioperative period, PAI-1 decreased, while t-PA increased. In view of the dynamic change trend of the above indicators, the indicators and baseline indicators of the two groups at 24 h after TJA were included in logistic regression analysis to evaluate the risk factors affecting DVT. Multivariate analysis showed that age, combined diabetes, increased D-dimer, decreased PC and decreased t-PA were risk factors for DVT after TJA. As is known to all, with the increase of age, the curvature and hardness of blood vessels increase, and the acquired hypercoagulability of blood increases (Akrivou et al. 2022). Although age is controversial as a risk factor for DVT of lower limbs, it is generally believed that the risk of DVT increases with age (Crop et al. 2014). In addition, the high glucose may damage the vascular endothelium, induce the release of various inflammatory mediators and further activating the coagulation system (Kang et al. 2015). A retrospective study showed that diabetes mellitus is an independent risk factor for patients with DVT before TJA (Xiong et al. 2022). Therefore, for elderly and diabetic patients, DVT should be closely monitored and prevented before and after surgery.

The advantage of this study is to determine the predictive value of PC combined with t-PA for DVT after TJA by evaluating various perioperative blood indexes of TJA

patients. The limitations of this study are that: (1) This is a retrospective study with a limited sample size, and a prospective study with a large sample size can better identify the risk factors of DVT after TJA; (2) Since almost all the indicators included in this study were general anesthesia, we have not yet evaluated the influence of anesthesia on DVT formation; (3) The ultrasound images of the subjects included in this study were all completed during hospitalization. However, the risk of DVT formation within 3 months after TJA is also high, it means that some patients may develop DVT after discharge, which may affect the calculation of the incidence of DVT.

In summary, as one of the important complications after TJA, DVT of the lower extremity still has a high incidence rate in current clinical practice. Elderly people or people with diabetes mellitus are high risk groups for DVT after TJA. Meanwhile, decreased PC level and decreased t-PA production at 24 h after TJA are also risk factors for DVT after TJA. Reasonable evaluation of surgical risk, active detection of postoperative indicators and intervention measures are helpful for prevention and treatment of DVT.

Conflict of Interest

The authors declare no conflict of interest.

References

- Akrivou, D., Perlepe, G., Kirgou, P., Gourgoulis, K.I. & Malli, F. (2022) Pathophysiological Aspects of Aging in Venous Thromboembolism: An Update. *Medicina (Kaunas)*, **58**, 1078.
- Brill, A. (2021) Multiple Facets of Venous Thrombosis. *Int. J. Mol. Sci.*, **22**, 3853.
- Chai, Y.N., Luo, M., Liang, W.J., Qiu, J.L., Li, D., Wang, L.C., Tu, X., Liu, C.Y., Qin, C.Z. & Li, D.L. (2021) The safety and effectiveness of salvianolate in preventing perioperative venous thromboembolism in China: A PRISMA-compliant meta-analysis based on RCTs. *Medicine (Baltimore)*, **100**, e25639.
- Crop, M.J., Siemes, C., Berendes, P., van der Straaten, F., Willemsen, S. & Levin, M.D. (2014) Influence of C-reactive protein levels and age on the value of D-dimer in diagnosing pulmonary embolism. *Eur. J. Haematol.*, **92**, 147-155.
- Dai, X., Wang, X., Huang, Z., Wang, K. & Ding, W. (2021) Exact Association Between Preoperative Blood Viscosity and Postoperative Deep Venous Thrombosis Risk in Knee Osteoarthritis Patients: A 10-Year Retrospective Study. *Clin. Appl. Thromb. Hemost.*, **27**, 10760296211048896.
- Elfaki, E.M., Algarni, A., Yousif, T.Y.E., Hamza, A., Abdalhabib, E.K., Elzein, H.O., Habiballah, E.M., Ahmed, O.A.B., Osman, H.A., Kumar, P., Babker, A.M.A., Alfeel, A.H. & Saboor, M. (2023) Protein C and protein S deficiencies are associated with increased risk of deep vein thrombosis in pregnant women using oral contraceptives. *Blood Coagul. Fibrinolysis*, **34**, 446-450.
- Ferraro, D., Siegler, S., Belvedere, C., Ruiz, M. & Leardini, A. (2021) Effect of artificial surface shapes and their malpositioning on the mechanics of the replaced ankle joint for possible better prosthesis designs. *Clin. Biomech. (Bristol)*, **90**, 105489.
- Furie, B. & Furie, B.C. (2008) Mechanisms of thrombus formation. *N. Engl. J. Med.*, **359**, 938-949.
- Ginnetti, J.G., O'Connor, M.I., Chen, A.F. & Myers, T.G. (2022) Total Joint Arthroplasty Training (Prehabilitation and Rehabilitation) in Lower Extremity Arthroplasty. *J. Am. Acad. Orthop. Surg.*, **30**, e799-e807.
- Kang, J., Jiang, X. & Wu, B. (2015) Analysis of Risk Factors for Lower-limb Deep Venous Thrombosis in Old Patients after Knee Arthroplasty. *Chin. Med. J. (Engl)*, **128**, 1358-1362.
- Liu, Z., Han, N., Xu, H., Fu, Z., Zhang, D., Wang, T. & Jiang, B. (2016) Incidence of venous thromboembolism and hemorrhage related safety studies of preoperative anticoagulation therapy in hip fracture patients undergoing surgical treatment: a case-control study. *BMC Musculoskelet. Disord.*, **17**, 76.
- Mo, J.W., Zhang, D.F., Ji, G.L., Liu, X.Z. & Fan, B. (2015) Detection of targets and their mechanisms for early diagnosis of traumatic deep vein thrombosis. *Genet. Mol. Res.*, **14**, 2413-2421.
- Navarrete, S., Solar, C., Tapia, R., Pereira, J., Fuentes, E. & Palomo, I. (2023) Pathophysiology of deep vein thrombosis. *Clin. Exp. Med.*, **23**, 645-654.
- Nicol, M., Sun, Y., Craig, N. & Wardlaw, D. (2009) Incidence of thromboembolic complications in lumbar spinal surgery in 1,111 patients. *Eur. Spine J.*, **18**, 1548-1552.
- Rachidi, S., Aldin, E.S., Greenberg, C., Sachs, B., Streiff, M. & Zeidan, A.M. (2013) The use of novel oral anticoagulants for thromboprophylaxis after elective major orthopedic surgery. *Expert. Rev. Hematol.*, **6**, 677-695.
- Scales, D.C., Riva-Cambrin, J., Wells, D., Athaide, V., Granton, J.T. & Detsky, A.S. (2010) Prophylactic anticoagulation to prevent venous thromboembolism in traumatic intracranial hemorrhage: a decision analysis. *Crit. Care*, **14**, R72.
- Segel, G.B. & Francis, C.A. (2000) Anticoagulant proteins in childhood venous and arterial thrombosis: a review. *Blood Cells Mol. Dis.*, **26**, 540-560.
- Suehisa, E., Nomura, T., Kawasaki, T. & Kanakura, Y. (2001) Frequency of natural coagulation inhibitor (antithrombin III, protein C and protein S) deficiencies in Japanese patients with spontaneous deep vein thrombosis. *Blood Coagul. Fibrinolysis*, **12**, 95-99.
- Takahashi, M., Yamashita, A., Moriguchi-Goto, S., Sugita, C., Matsumoto, T., Matsuda, S., Sato, Y., Kitazawa, T., Hattori, K., Shima, M. & Asada, Y. (2010) Inhibition of factor XI reduces thrombus formation in rabbit jugular vein under endothelial denudation and/or blood stasis. *Thromb. Res.*, **125**, 464-470.
- Waheed, S.M., Kudaravalli, P. & Hotwagner, D.T. (2025) Deep Vein Thrombosis. In *StatPearls*, Treasure Island (FL).
- Wang, W., Liang, X., Liu, X., Bai, J., Zhang, W., Li, W., Wang, T., Li, M., Wu, Z., Chen, L., Yang, H., Gu, Y., Tao, Y., Zhou, J., Wang, H., et al. (2022) NOX4 blockade suppresses titanium nanoparticle-induced bone destruction via activation of the Nrf2 signaling pathway. *J. Nanobiotechnology*, **20**, 241.
- Wang, W., Sun, P., Han, F. & Qu, C. (2021) Sex Differences in Risk Factors for Transient Ischemic Attack in a Chinese Population. *Front. Neurol.*, **12**, 615399.
- Wenger, N., Sebastian, T., Engelberger, R.P., Kucher, N. & Spirk, D. (2021) Pulmonary embolism and deep vein thrombosis: Similar but different. *Thromb. Res.*, **206**, 88-98.
- Wu, H., Cheng, W.D. & Jing, J. (2020) Total hip arthroplasty by direct anterior approach in the lateral position for the treatment of ankylosed hips. *Eur. J. Orthop. Surg. Traumatol.*, **30**, 993-1001.
- Xiong, X., Li, T. & Cheng, B. (2022) Association between glycosylated hemoglobin, diabetes mellitus, and preoperative deep vein thrombosis in patients undergoing total joint arthroplasty: a retrospective study. *J. Orthop. Surg. Res.*, **17**, 430.
- Yao, M., Ma, J., Wu, D., Fang, C., Wang, Z., Guo, T. & Mo, J. (2023) Neutrophil extracellular traps mediate deep vein thrombosis: from mechanism to therapy. *Front. Immunol.*, **14**, 1198952.
- Ye, M., Fang, R., Lun, S. & Fang, J. (2022) The association of AT-III and D-Dimer with unexplained recurrent spontaneous abortion and their diagnostic value for prethrombotic state.

Am. J. Transl. Res., **14**, 2350-2355.
Zhang, H., Mao, P., Wang, C., Chen, D., Xu, Z., Shi, D., Dai, J.,
Yao, Y. & Jiang, Q. (2017) Incidence and risk factors of deep

vein thrombosis (DVT) after total hip or knee arthroplasty: a
retrospective study with routinely applied venography. *Blood
Coagul. Fibrinolysis*, **28**, 126-133.
