Influencing Factors and Construction of a Predictive Model for Lower Extremity Deep Vein Thrombosis after Total Knee Arthroplasty

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ABSTRACT

Objective: To identify risk factors for deep vein thrombosis (DVT) following total knee arthroplasty (TKA) and to develop a predictive nomogram model.

Study Design: An observational study.

Place and Duration of the Study: Department of Orthopaedics, Nanjing Pukou People's Hospital, Liangjiang Hospital, Southeast University, Nanjing, China, from March 2018 to March 2022.

Methodology: Among the 1,015 eligible TKA patients, 457 developed postoperative DVT (DVT group), and 558 served as controls (non-DVT group). Risk factors were identified through univariate analysis and multivariate logistic regression.

Results: The DVT group showed significantly higher proportions of patients aged age ≥65 years, BMI ≥28 kg/m^2, female gender, history of diabetes, cemented prosthesis, operation duration ≥90 minutes, bed rest duration ≥72 hours, no mechanical thromboprophylaxis, D-dimer levels >0.545 mg/L, and von Willebrand factor (vWF) level >178.55 ng/mL (all $p < 0.05$) *vs*. the non-DVT group. Independent risk factors for DVT included age ≥65 years, BMI ≥28 kg/m^2, female gender, history of diabetes, cemented prosthesis, operation duration ≥90 minutes, bed rest duration ≥72 hours, no mechanical thromboprophylaxis, D-dimer >0.545 mg/L, and vWF >178.55 ng/mL. A predictive nomogram incorporated these variables using regression coefficients (*e.g.*, age × 1.128 ... vWF × 6.225; intercept = 4.545).

Conclusion: Key modifiable and non-modifiable factors influence the risk of DVT following TKA. The predictive validated nomogram demonstrates clinical utility for individualised risk stratification and prevention strategies.

Key Words: *Total knee arthroplasty, Deep vein thrombosis, Risk factors, Predictive model*.

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INTRODUCTION

The incidence of osteoarthritis has been increasing annually with improvements in medical standards and quality of life. Total knee arthroplasty (TKA) effectively treats end-stage osteoarthritis; however, patients face an increased risk of postoperative deep venous thrombosis (DVT) in the lower limbs. DVT—a peripheral vascular disease affecting lower limb veins—elevates the likelihood of complications, such as swelling, secondary varicose veins, stasis ulcers, pulmonary embolism, and long-term deep venous insufficiency, thereby impeding postoperative recovery.[1-3]

Clarifying the factors influencing DVT after TKA in elderly patients is clinically valuable for postoperative prevention,[4,5] although current research on these factors and their predictive models remains debated. This study aimed to identify independent risk factors for lower extremity DVT following TKA in elderly patients and to develop a predictive model to support clinical decision-making.

METHODOLOGY

This observational study received approval from the Ethics Review Committee of Nanjing Pukou People's Hospital, Nanjing, China (2018-SR-016), with a waiver of informed consent. Data were extracted exclusively from the hospital's electronic health records. Patients who underwent TKA at the Department of Orthopaedics, Nanjing Pukou People's Hospital, China, from March 2018 to March 2022 were included in the study.

Inclusion criteria were comprehensive preoperative imaging (knee MRI, full-length weight-bearing x-ray, and varus/valgus stress x-ray), absence of lower limb DVT on admission, no documented history of DVT or varicose veins, and complete clinical documentation.

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Exclusion criteria were prior lymphatic reflux disorders, coagulation dysfunction, surgery within the preceding week, malignancies, systemic lupus erythematosus (SLE), or thrombophilia-inducing conditions.

Diagnostic criteria for DVT were sudden onset of swelling and pain, pitting oedema in the affected limb, increased soft tissue tension, elevated skin temperature, tenderness in the posterior calf, medial thigh, femoral triangle, and ipsilateral iliac fossa, visible or dilated superficial veins in the affected limb, positive Homans' sign and Neuhof sign when the thrombus is located in the calf muscle venous plexus. B-mode ultrasound shows widening of the occluded vein's internal diameter, presence of thrombus echo, and inability to compress the vein lumen with probe pressure.[6]

Patients underwent routine preoperative assessments, including electrocardiography (ECG), blood tests, chest radiography, blood biochemistry analysis, coagulation studies, and venous ultrasound. All TKAs were performed by a single surgeon under general anaesthesia. The surgical team followed standardised protocols, with tourniquet application. Postoperatively, venous blood flow and luminal pressure were monitored using Doppler ultrasound. Fasting venous blood samples were collected, centrifuged, aliquoted, and analysed for D-dimer (*via* immunoturbi-dimetry) and von Willebrand factor (vWF) using enzyme-linked immunosorbent assay (ELISA). Multivariable logistic regression was employed to analyse factors influencing DVT development in elderly patients following TKA and to construct a predictive model.

General patient characteristics (age, gender, BMI, hypertension history, prosthesis type, alcohol use history, diabetes history, and corticosteroid therapy history), surgical parameters (operation duration, intraoperative blood loss, mechanical thromboprophylaxis, anaesthesia method, and postoperative bed rest duration), and postoperative laboratory markers (D-dimer and vWF levels) were recorded.

Statistical analyses were performed using SPSS 22.0 software. Categorical data were presented as frequencies (percentages). The Kolmogorov-Smirnov test assessed the normality of the distribution. Based on data characteristics, categorical variables were compared using the chi-square test. Variables with $p < 0.05$ in univariate analysis were entered into multivariate logistic regression. Factors with $p < 0.05$ in the final regression model were identified as independent risk factors for the lower extremity DVT following TKA. Nomograms were constructed using these independent predictors, with calibration curves and decision curve analysis subsequently generated to evaluate model performance.

RESULTS

Of the 1,211 initially screened TKA patients, 1,015 met the inclusion criteria. The cohort comprised 566 males and 449 females, aged 60–83 years (mean 68.3 ± 4.5), with BMI ranging from 19.0 to 32.2 kg/m^2 (mean 24.31 ± 4.65). Medical histories included diabetes (n = 535), smoking (n = 620), alcohol use (n = 602), and corticosteroid therapy (n = 576). Prosthesis types included cemented (n = 432) and cementless (n = 568). Postoperative DVT was identified in 457 patients, with 558 in the non-DVT group.

The DVT group demonstrated significantly higher proportions of patients who were aged ≥65 years, had a BMI ≥28 kg/m^2, were female gender, had a history of diabetes, or had cemented prostheses compared to the non-DVT group (all $p < 0.05$). No statistically significant differences were observed in smoking history, alcohol use history, or corticosteroid treatment history between groups ($p > 0.05$). Demographic and clinical characteristics are presented in Table I.

Table I: Comparison of general information of patients in the DVT group and the non-DVT group [n (%)].

Clinical parameters	DVT Group (n = 457)	Non-DVT Group (n = 558)	χ^2-value	p-values
Gender			23.103	<0.001
Male	217 (47.48)	349 (62.54)		
Female	240 (52.52)	209 (37.46)		
Age (year)			24.943	<0.001
<65	205 (44.86)	338 (60.57)		
≥65	252 (55.14)	220 (39.43)		
BMI / (kg/m^2)			10.665	0.001
<28	247 (54.05)	358 (64.36)		
≥28	210 (45.95)	200 (35.84)		
Prosthesis type			30.463	<0.001
Biological prosthesis	216 (47.26)	360 (64.52)		
Cement-based prosthesis	241 (52.74)	198 (35.48)		
Diabetes			26.222	<0.001
Yes	204 (44.64)	339 (60.75)		
No	253 (55.36)	219 (39.25)		
Smoking			1.403	0.236
Yes	270 (59.08)	350 (62.72)		
No	187 (40.92)	208 (37.28)		
Drinking			3.255	0.071
Yes	257 (56.24)	345 (61.83)		
No	200 (43.76)	213 (38.17)		
Hormone drug treatment			1.734	0.188
Yes	249 (54.49)	327 (58.60)		
No	208 (45.51)	231 (41.40)		

Note: Using the Chi-square test, p <0.05 was considered a statistically significant difference.

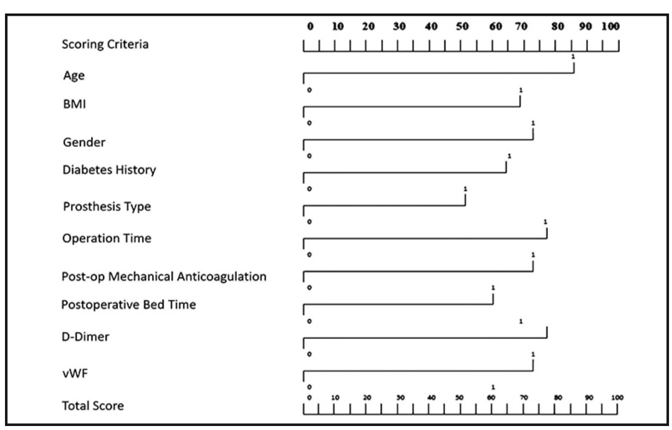

Figure 1: A predictive nomogram model for lower extremity DVT after TKA.

Table II: Comparison of surgical data between patients in the DVT group and the non-DVT group [n (%)].

Clinical parameters	DVT Group (n = 457)	Non-DVT Group (n = 558)	χ^2-value	p-values
Postoperative mechanical anticoagulation			117.181	<0.001
Yes	138 (30.20)	359 (64.34)		
No	319 (69.80)	199 (35.66)		
Operation time (minutes)			31.054	<0.001
<90	205 (44.86)	348 (62.37)		
≥90	252 (55.14)	210 (37.63)		
Intraoperative blood loss (mL)			0.009	0.923
<300	270 (59.08)	328 (58.78)		
≥300	187 (40.92)	230 (41.22)		
Postoperative bedtime (hours)			4.932	0.026
<72	246 (53.83)	339 (60.75)		
≥72	211 (46.17)	219 (39.25)		

Note: Using the chi-square test, p <0.05 was considered a statistically significant difference.

Table III: Comparison of laboratory test results of the patients in the DVT group and the non-DVT group [n (%)].

Clinical parameters	DVT Group (n = 457)	Non-DVT Group (n = 558)	χ^2-value	p-values
D-dimer (mg/L)			30.463	<0.001
≤0.545	216 (47.26)	360 (64.52)		
>0.545	241 (52.74)	198 (35.48)		
vWF (ng/mL)			28.181	<0.001
≤178.55	208 (45.51)	347 (62.19)		
>178.55	249 (54.49)	211 (37.81)		

Note: Using the chi-square test, p <0.05 was considered a statistically significant difference.

The DVT group demonstrated significantly higher proportions of patients who had an operation duration of ≥90 minutes, postoperative bed rest duration of ≥72 hours, and no mechanical thromboprophylaxis compared to the non-DVT group (all p <0.05). No statistically significant differences were observed in intraoperative blood loss between groups (p >0.05). Detailed characteristics are presented in Table II.

Patients with elevated D-dimer (>0.545 mg/L) and vWF (>178.55 ng/mL) levels were significantly more prevalent in the DVT group than in the non-DVT group (p <0.05; Table III).

Multifactor logistic regression analysis showed that age ≥65 years, female gender, BMI ≥28 kg/m^2, diabetes history, cemented prosthesis, operation duration ≥90 minutes, no mechanical thromboprophylaxis, postoperative bed rest duration ≥72 hours, D-dimer >0.545 mg/L, vWF >178.55 ng/mL were risk factors for DVT after TKA in elderly patients. The predictive model was formulated as: 4.545+age × 1.128 + BMI × 3.430 + gender × 2.948 + history of diabetes × 5.895 + prosthesis type × 3.429 + operation time × 5.744 + use of postoperative mechanical anticoagulation × 2.943 + postoperative bed time × 6.135 + D-dimer×1.123+vWF× 6.225 (Figure 1).

DISCUSSION

DVT primarily results from venous stasis, platelet aggregation, and fibrin deposition. Patients undergoing TKA face substantially elevated DVT risk. Notably, more than 70% of postoperative DVT cases present without typical symptoms, complicating early diagnosis and intervention. This diagnostic challenge underscores DVT prevention as a critical clinical priority.[7,8] This study retrospectively analyses the risk factors for DVT after TKA in elderly patients and develops a predictive nomogram model, aiming to identify high-risk patients and optimise targeted thromboprophylaxis strategies in this population.[9]

This study identified multiple independent risk factors for DVT following TKA in elderly patients: age ≥65 years, BMI ≥28 kg/m^2, female gender, cemented prostheses, history of diabetes, omission of postoperative mechanical thromboprophylaxis, operative duration ≥90 minutes, D-dimer >0.545 mg/L, vWF >178.55 ng/mL, and bed rest duration ≥72 hours.

The influence of the age factor is similar to the results of previous studies, suggesting that increasing age will increase the risk of DVT. The main reason is that increasing age leads to changes in the structure of the vascular intima, which also reduces vascular elasticity and increases vascular fragility, thereby triggering intimal ageing, and ultimately leading to an increased risk of DVT.[10-12]

A BMI ≥28 kg/m^2 means that the patient has accumulated a large amount of fat in the body, which causes the endogenous coagulation system to be rapidly activated, which in turn causes abnormalities in the fibrinolytic system. It also induces platelet activation and massive aggregation and adhesion, ultimately causing blood hypercoagulation and promoting thrombosis.[13]

The main reason why women are prone to DVT may be that their physical fitness is poorer than that of men. Women's tibial plateau osteotomy tends to be less stable, and tibial plateau prostheses are prone to fracture, which indirectly prolongs the patient's postoperative bed rest time, thereby increasing venous stasis in the patient's lower limbs and the risk of DVT.

The main reason why a history of diabetes increases the risk of postoperative DVT is that high blood sugar causes damage to the vascular endothelium, which in turn stimulates the release of a large amount of inflammatory factors, leading to special activation of the body's coagulation system, triggering blood hypercoagulation, and thus promoting thrombosis.[14]

Compared with biological prosthesis, cement-based prosthesis can cause damage to monocytes and granulocytes, promote the release of a large amount of proteolytic enzymes, and subsequently activate the body's complement system, ultimately accelerating the thrombosis process.

Excessive operation time can exacerbate the surgical trauma and the patient's stress response. This may cause damage to antioxidant function, thereby stimulating vascular coagulation and causing blood hypercoagulability, ultimately promoting the formation of thrombosis.[15]

The results of this study show that postoperative mechanical anticoagulation and prolonged bed rest can increase the risk of DVT. The main reason is that long-term immobilisation, prolonged sitting, and bed rest can cause blood stasis in the lower limbs, thereby increasing, the risk of DVT. Timely postoperative mechanical anticoagulant preventive interventions, such as plantar arteriovenous pumps, gradient elastic stockings, and lower limb venous pumps, can promote venous return, help reduce blood stasis, and thereby decrease the risk of DVT. If reasonable mechanical anticoagulation measures are not implemented after surgery, venous return may be impaired, thereby increasing the risk of DVT.[16,17]

D-dimer is a specific degradation product of cross-linked fibrin. It is a sensitive indicator reflecting the body's secondary hyperfibrinolysis and hypercoagulable state. It can be used as an indicator of thrombosis and enhanced fibrinolysis. Therefore, D-dimer is considered to be the main reason for increasing the risk of DVT. There is fibrinolysis and thrombosis in blood vessels, which activates the fibrinolytic system and causes an abnormal increase in D-dimer, which means the body is in a hypercoagulable state, thus promoting the formation of thrombosis.[18,19]

Some studies believe that increased vWF levels are significantly related to thrombosis and participate in the haemostasis process, confirming the feasibility of vWF levels as a variable influencing factor for DVT after TKA in elderly patients.[20] Compared with plasma fibre protein and other commonly used research indicators, there are relatively few studies related to vWF and thus DVT, and the selection of vWF has a certain novelty. Following vascular endothelial injury, platelets adhere to and aggregate at the injury site. vWF can exert an inducing effect by binding to platelet glycoprotein Ib, thereby indirectly promoting thrombosis, suggesting that vWF is a sensitive indicator of abnormal vascular endothelial function and could be used as a diagnostic marker for early DVT.

While this investigation incorporated numerous risk factors, several limitations warrant acknowledgement. First, the exclusion of anaesthesia modality as a variable represents a significant omission. Evidence suggests that epidural anaesthesia enhances lower limb perfusion through haemodilution effects, potentially mitigating hypercoagulability, whereas general anaesthesia may promote venous pooling and stasis due to vasodilation, consequently elevating DVT risk. Future studies should include anaesthesia technique as a critical covariate. Second, although a predictive model was developed for post-TKA DVT, its performance characteristics—including sensitivity, specificity, and discriminative capacity—require rigorous external validation. Subsequent research should prioritise model calibration and clinical utility assessment through prospective validation cohorts. Such refinement would strengthen the model's applicability in guiding thromboprophylaxis strategies for elderly TKA patients.

CONCLUSION

Multiple factors—including age, BMI, gender, history of diabetes, prosthesis type, operative duration, postoperative mechanical thromboprophylaxis, bed rest duration, D-dimer, and vWF levels—significantly influence the development of DVT following TKA in elderly patients. The predictive model incorporating these factors demonstrates clinical utility for risk stratification.

ETHICAL APPROVAL:
Ethical approval was obtained from the Ethical Review Committee of Nanjing Pukou People's Hospital, Jiangsu, China (2018-SR-016).

PATIENTS' CONSENT:
Informed consent was obtained from all individual participants included in the study.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
ZSG: Contribution to the conception and drafting of the manuscript.
BYW: Design of the study and drafting of the manuscript.
XQL: Contribution to the interpretation of the data and drafting of the manuscript.
All authors approved the final version of the manuscript to be published.

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