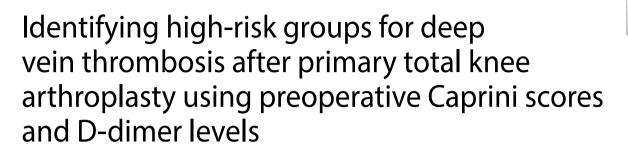
RESEARCH ARTICLE

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Abstract

Background Caprini score and D-dimer are well-recognized markers in deep vein thrombosis (DVT) assessment. However, their utility in guiding post-arthroplasty DVT risk is hampered by susceptibility to various post-operative factors, limiting their effectiveness as reminders. Conversely, these markers exhibit greater stability in the preoperative setting. Despite this, research on the pre-operative predictive value of Caprini score and D-dimer for DVT following primary total knee arthroplasty (TKA) remains scarce.

Methods In a retrospective study, we analyzed data from patients who underwent primary TKA, between August 2015 and December 2022. Upon admission, Caprini scores were assessed, and comprehensive blood panels were obtained from fasting blood samples. For all patients, lower limb vascular Doppler ultrasonography was performed pre-operatively to exclude those with pre-existing DVT, and all patients underwent DVT examination again post-operatively.

Results Our study included 2,873 patients, averaging 67.98 ± 7.54 years, including 676 men and 2,197 women. In this study, 303 (10.55%) patients developed postoperative DVT, and 57 (1.98%) cases presented with lower limb symptoms. DVT incidence in patients with pre-operative Caprini scores of 1–2 (6.50%), 3 (10.28%), and ≥ 4 (18.05%) showed significant differences (P < 0.05). DVT rates were 14.80% in patients with pre-operative D-dimer levels of ≥ 1 mg/L, higher than the 8.98% in those with levels of < 0.5 mg/L, and 10.61% in those with levels 0.5-1 mg/L (P < 0.05). In patients with Caprini scores of 1–2 and D-dimer levels ≤ 0.5 mg/L, the occurrence rate of postoperative DVT was only 5.84%. For patients with Caprini scores ≥ 4 and D-dimer levels ≥ 1.0 mg/L, the postoperative DVT occurrence rate soared to 24.81%, with the OR(odds ratio) was 4.744 compared to the former group.

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Conclusion Patients with preoperative higher Caprini scores and D-dimer are more likely to develop DVT after TKA. Additionally, those with a preoperative Caprini score ≥ 4 and D-dimer level ≥ 1.0 mg/L have a significantly increased risk (24.81%) of developing DVT, identifying them as a high-risk group for DVT following TKA. These findings hold significant value for DVT risk stratification in primary TKA patients and the formulation of preoperative interventions to mitigate the risk of DVT.

Keywords Caprini score, D-dimer, Deep vein thrombosis (DVT), Total knee arthroplasty (TKA)

Introduction

Primary total knee arthroplasty (TKA) is a widely employed surgical intervention for alleviating pain and enhancing quality of life in patients with end-stage osteoarthritis [1, 2]. Despite its benefits, TKA comes with potential complications, including deep vein thrombosis (DVT), which poses a significant challenge for both healthcare providers and patients [3].

Individual biological factors contribute to varying probabilities of DVT development in patients. Researchers have conducted multifactorial analyses to identify key risk factors associated with DVT after TKA, including age, BMI (body mass index), D-dimer, and the history of tumor or VTE (venous thromboembolism) [4, 5]. However, evaluating numerous risk factor indicators poses challenges for clinicians in accurately assessing DVT risk. To address this issue, the Caprini risk assessment model (RAM) has been developed based on clinical experience and medical evidence. This model has proven to be an effective, simple, feasible, economical, and practical tool for predicting the risk of DVT [6, 7]. Additionally, our preliminary research indicates that the modified postoperative Caprini RAM is highly effective in predicting the development of DVT after joint arthroplasty [8]. However, DVT risk assessment should begin as soon as the patient is admitted. Early detection of high-risk patients allows for the timely implementation of individualized preventive measures. On the other hand, in the context of joint arthroplasty, a score of 5 in itself elevates the Caprini score to a very high-risk category, potentially obscuring its role in providing early warning [9]. Similarly, postoperative D-dimer levels are significantly influenced by surgical trauma, with some studies even suggesting a lack of pronounced correlation with DVT [10, 11]. Conversely, these markers exhibit relative stability in the preoperative setting. Despite this, research on the predictive value of preoperative Caprini score and D-dimer for DVT following primary knee arthroplasty remains limited. To clarify the predictive value of preoperative Caprini score and D-dimer levels for DVT, we first excluded patients with pre-existing DVT. Subsequently, we analyzed these factors as independent risk factors for DVT and evaluated their combined predictive effectiveness.

Patients and methods

The retrospective data collection from patients was approved by the Ethics Committee of the Clinical Institution, and all participants provided informed consent prior to data collection. Patients aged \geq 50 years who underwent primary unilateral total knee arthroplasty, between August 2015 and December 2022 were considered. Exclusions applied to those with incomplete baseline information, absence of preoperative or postoperative lower extremity vascular color Doppler ultrasound examination, preoperative DVT diagnosis, severe renal or organ dysfunction, immune or hematologic disorders. Initial analysis included 3135 patients who underwent primary TKA. After excluding 262 patients with pre-existing DVT, a total of 2,873 patients were included in the study.

Upon admission, Caprini scores were assessed, and fasting blood samples were obtained for a comprehensive blood panel examination. The 2013 Caprini RAM [6] was employed, and dedicated personnel collected and assessed all data. D-dimer was measured using the latex-enhanced immunoturbidimetric method, with a normal range of <0.5 mg/L. Vascular Doppler ultrasonography of the bilateral lower limbs was performed one day before and 3–5 days after the operation using the SonoSite M-Turbo machine. Symptomatic DVT was characterized by symptoms such as swelling, pain, tenderness, warmth, or color change in the affected area.

Surgical management and anticoagulation protocol

All surgeries were performed by surgeons of similar experience and skill. All patients received general anesthesia and had a tourniquet applied. They were administered 1 g of TXA intravenously before the surgery and another 1 g of TXA injected into the joint cavity at the end of the surgery. To prevent DVT post-operatively, it was recommended that all patients undergoing TKA, unless contraindicated, commence treatment with low molecular weight heparin (4000 IU/day) or rivaroxaban (10 mg/day) from the evening following surgery. Physical preventive measures, such as compression stockings and ankle pump exercises, were also actively recommended starting the evening after surgery. Additionally, patients were encouraged to engage in early mobilization and rehabilitation exercises under the guidance of professional physiotherapists.

Table 1 Lo	cations and	numbe	r of DVT
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Number of Cases		
2(0.66%)		
1(0.33%)		
1(0.33%)		
301(99.34%)		
2(0.66%)		
3(0.99%)		
3(0.99%)		
1(0.33%)		
292(96.37%)		
303(100%)		

DVT, deep vein thrombosis.

Statistical analysis

Descriptive statistics were employed to analyze demographic data. *T-tests* analyzed age, BMI (body mass index), PT (prothrombin time), INR (international normalized ratio), APTT (activated partial thromboplastin time), TT (thrombin time), FIB (fibrinogen), hemoglobin, HCT (hematocrit), platelets, Caprini score, operation duration and intraoperative bleeding. *Chi-square or Fisher tests* were performed for gender, hypertension, diabetes, CRP(C-reactive protein) positivity(>8 mg/L), D-dimer (\geq 0.5 mg/L) positivity, and all Caprini RAM risk factors. Statistical significance was set at *p*<0.05. IBM SPSS software version 25 (IBM, Armonk, NY, USA) and GraphPad Prism 9.0 (La Jolla, CA, USA) were used for statistical analyses.

Result

Patients demographics and DVT locations

Our study encompassed 2,873 patients, averaging 67.98±7.54 years of age, including 676 men and 2,197 women. Before surgery, each patient underwent lower extremity vascular color Doppler ultrasonography. To ensure higher accuracy, this study excluded patients who had pre-existing DVT. A total of 303 patients (10.55%) developed DVT following surgery. Interestingly, only 57 (1.98%) of these cases presented with lower limb symptoms, indicating 246 (8.56%) asymptomatic DVTs. Detailed analysis of DVT cases identified 2 proximal DVTs involving 1 femoral vein and 1 popliteal vein. Additionally, there were 301 distal DVTs, which included thromboses in the peroneal and muscular veins (2 cases), posterior tibial vein (3 cases), posterior tibial and muscular veins (3 cases), and a combination of posterior tibial, peroneal, and muscular veins (1 case). The remaining 292 instances were muscular vein thromboses, as depicted in Table 1.

Table 2 The comparison of basic information, preoperative laboratory tests, and preoperative Caprini score between the DVT group and the non-DVT group

<u> </u>	DVT(n=303)	Non-	t /x²value	Р
		DVT(n=2570)		value
Age(year)	69.55 ± 7.36	67.79±7.54	3.852	< 0.001
BMI	27.19 ± 3.88	26.97 ± 3.86	0.951	0.342
Women	259(85.48%)	1938(75.41%)	15.275	< 0.001
Diabetes	50(16.50%)	459(17.85%)	0.343	0.558
Hypertension	176(58.09%)	1342(52.22)	3.745	0.053
PT(second)	11.15 ± 1.20	11.03 ± 1.94	1.053	0.292
INR	0.97 ± 0.11	0.96 ± 0.08	2.027	0.043
APTT(second)	26.68 ± 2.93	26.66 ± 2.88	0.106	0.916
TT(second)	18.10 ± 1.02	17.96 ± 1.72	1.446	0.148
FIB(g/L)	2.88 ± 0.64	2.96±0.81	1.548	0.122
Hemoglobin(g/L)	127.31±12.38	129.07 ± 14.06	2.057	0.040
HCT (%)	38.56 ± 3.65	38.77±3.81	0.904	0.366
Platelet (10^ ⁹ /L)	211.14 ± 59.68	209.82 ± 62.52	0.348	0.728
CRP positivity (>8 mg/L)	30(9.90%)	299(11.63%)	0.803	0.370
D-dimer positiv- ity (≥0.5 mg/L)	159(52.48%)	1110(43.19%)	9.475	0.002
Caprini score	3.26 ± 1.14	2.83±0.91	6.376	< 0.001
Operation dura- tion (min)	111.38±25.26	112.84±26.02	0.922	0.357
Intraoperative bleeding(ml)	151.19±93.02	146.18±96.27	0.848	0.396

DVT, deep vein thrombosis, BMI: body mass index, PT: prothrombin time, INR: international normalized ratio, APTT: activated partial thromboplastin time, TT: thrombin time, FIB: fibrinogen, HCT: hematocrit, CRP: C-reactive protein

Comparison between the DVT group and the non-DVT group

The DVT group had a higher mean age, women proportion, INR, D-dimer positivity rates, and Caprini scores (P<0.05), while exhibiting lower hemoglobin (P<0.05). However, factors such as BMI, diabetes, hypertension, PT, APTT, TT, FIB, HCT, platelets, CRP positivity, operation duration and intraoperative bleeding demonstrated no significant differences between the groups (P>0.05), as detailed in Table 2.

A multiple regression analysis was performed on factors that showed significant differences between the groups. This analysis identified women, D-dimer positivity, and Caprini score as independent risk factors for DVT following TKA. The resulting OR (odds ratios) were 2.011, 1.342, and 1.525, respectively (p < 0.05, Table 3).

Symptomatic DVT in comparison

Among the 303 patients diagnosed with DVT, 57 (18.81%) presented with symptoms, while the remaining 246 (81.19%) were asymptomatic. There was no significant difference between the two DVT groups in terms of women, D-dimer positivity and Caprini score (P>0.05). However, asymptomatic DVT patients exhibited a higher proportion of women compared to non-DVT patients

Risk factors	В	SE	Wals	OR	Exp(B) 95% Cl	P value
Age(year)	0.002	0.010	0.031	0.998	0.978-1.019	0.860
Women	0.699	0.184	14.442	2.011	1.403-2.884	< 0.001
INR	0.889	0.639	1.937	2.433	0.696-8.506	0.164
Hemoglobin(g/L)	0.001	0.005	0.018	0.999	0.989-1.00-	0.893
D-dimer positivity (≥0.5 mg/L)	0.280	0.131	4.604	1.342	1.025-1.710	0.032
Caprini score	0.422	0.073	33.332	1.525	1.322-1.761	< 0.001

Table 3 Logistic regression analysis to identify independent risk factors

B: regression coefficient, SE: standard error, Wals: wald test, OR: odds ratios, INR: international normalized ratio

Table 4 The comparison of risk factors among patients with symptomatic DVT, asymptomatic DVT, and those without DVT

Risk factors	Symptom- atic DVT (n=57)	Asymptom- atic DVT (n=246)	Non-DVT (<i>n</i> = 2570)	P value		
Women	48(84.21%)	211(85.77%)**	1938(75.41%)	< 0.05		
D-dimer positiv-	34(59.65%)*	125(50.81%)*	1110(43.19%)	< 0.05		
ity (≥0.5 mg/L)						
Caprini score	3.46±1.50**	3.22±1.04**	2.83 ± 0.91	< 0.05		

DVT, deep vein thrombosis, *= $\rho{<}0.05,$ compared with non-DVT group, **= $\rho{<}0.001,$ compared with non-DVT group

(P<0.001). Both D-dimer positivity and Caprini score levels were elevated in both DVT groups compared to non-DVT patients (P<0.05), as illustrated in Table 4.

DVT at different Caprini scores

Preoperative Caprini scores in TKA patients ranged from 1 to 9, predominantly 2–4, with higher scores correlating with increased postoperative DVT incidence, as demonstrated in Fig. 1. Stratified scoring (1–2 points, 3 points, and \geq 4 points) indicated a significantly elevated DVT incidence (18.05%) in patients scoring \geq 4, in comparison

to scores of 1–2 (6.50%) and 3 (10.28%) (P<0.05), as depicted in Fig. 2.

The Caprini RAM includes scores for numerous factors, some of which are specifically related to knee arthroplasty. The study found that age 41–60 years, age \geq 75 years, 25<BMI \leq 40, BMI>40, diabetes requiring insulin and history of thrombosis showed statistically significant differences between the DVT and non-DVT groups (*P*<0.05), as demonstrated in Table 5.

DVT in different D-dimer range

Preoperative D-dimer levels varied amongst the study population. The majority of patients (1,604, 55.83%) had normal levels below 0.5 mg/L. An additional 688 patients (23.95%) had levels between 0.5 mg/L and 1 mg/L, while 581 patients (20.22%) had levels exceeding 1 mg/L. Notably, the incidence of DVT increased significantly (p<0.05) as D-dimer levels rose above the normal range. DVT rates were 8.98% for patients with levels below 0.5 mg/L, 10.61% for those between 0.5 and 1 mg/L, and climbed to 14.80% for those with levels exceeding 1 mg/L, as illustrated in Fig. 3.

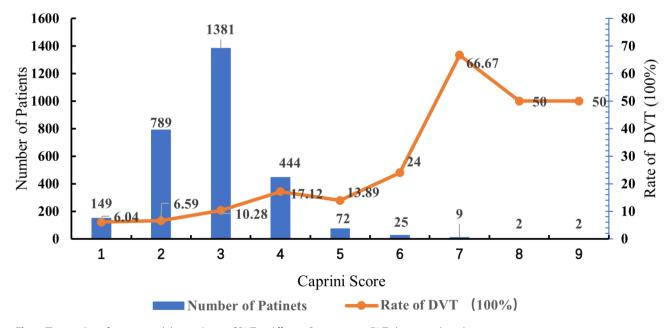


Fig. 1 The number of patients and the incidence of DVT at different Caprini scores. DVT, deep vein thrombosis

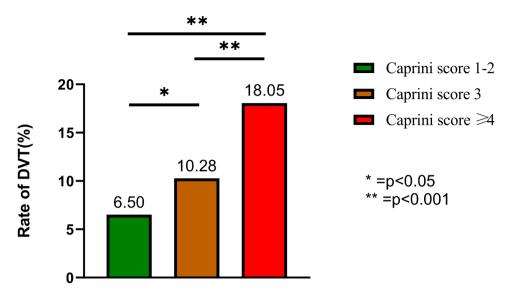
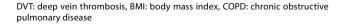


Fig. 2 The rate of DVT at different range of Caprini scores. DVT, deep vein thrombosis, *=P < 0.05, **=P < 0.001

Relative Risk Factors	Risk Score	DVT(n=303)	Non- DVT(<i>n</i> = 2570)	X ²	P value
Age 41–60 years	1	35(11.55%)	430(16.73%)	5.362	0.021
Age 61–74 years	2	186(61.39%)	1666(64.82%)	1.399	0.237
Age≥75 years	3	82(27.06%)	474(18.44%)	12.901	< 0.001
25 < BMI ≤ 40	1	231(76.24%)	1702(66.23%)	12.342	< 0.001
BMI > 40	2	5(1.65%)	6(0.23%)	10.790	0.001
Visible vari- cose veins	1	7(2.31%)	43(1.67%)	0.643	0.423
History of inflamma- tory Bowel disease	1	1(0.33%)	2(0.08%)	-	0.284
Swollen legs (current)	1	0(0.00%)	2(0.08%)	-	1.000
Congestive heart failure	1	1(0.33%)	8(0.31%)	-	1.000
Lung disease (e.g., em- physema or COPD)	1	2(0.66%)	7(0.27%)	-	0.244
Smoking	1	12(3.96%)	79(3.07%)	0.694	0.405
Diabetes requiring insulin	1	21(6.93%)	67(2.61%)	17.065	< 0.001
Current or past malignancies	2	7(2.31%)	66(2.57%)	0.073	0.787
History of	3	12(3.96%)	9(0.35%)	48.686	< 0.001



blood clots

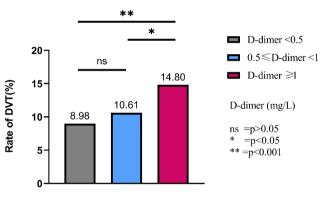


Fig. 3 The rate of DVT at different range of D-dimer. DVT, deep vein thrombosis, ns = P > 0.05, *=P < 0.05, **=P < 0.001

Caprini scores combined with D-dimer

To gain a deeper understanding of DVT risk, we further analyzed the combined effect of Caprini scores and D-dimer levels. Patients with the lowest risk profile (Caprini scores of 1–2 and D-dimer levels ≤ 0.5 mg/L) exhibited a remarkably low DVT occurrence rate of only 5.84%. Conversely, the DVT rate rose significantly as both Caprini scores and D-dimer values increased. In the highest risk category (Caprini scores≥4 and D-dimer levels \geq 1.0 mg/L), the DVT occurrence rate increased to a concerning 24.81%. A detailed breakdown of these findings is presented in Fig. 4. From Table 6, it is evident that patients with Caprini scores of 3 and 4 have significantly higher DVT incidence rates compared to those with scores of 1-2, with OR values of 1.648 and 3.167, respectively (P < 0.05). Additionally, the highest DVT incidence rate is observed in patients with Caprini scores \geq 4 and D-dimer levels \geq 1.0 mg/L, with an OR of 4.744 (*P*<0.001).

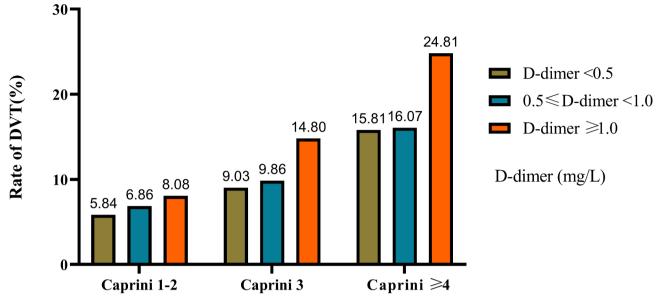


Fig. 4 The incidence of DVT in patients across different Caprini scores and D-dimer ranges. DVT, deep vein thrombosis

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	DVT %	OR	Exp(B) 95% Cl	P vale		
Caprini1-2	6.50	-	-	-		
Caprini 3	10.28	1.648	1.206-2.252	0.002		
Caprini≥4	18.05	3.167	2.259-4.440	< 0.001		
Caprini≥4+D-Dimer<0.5 mg/L	15.81	2.700	1.763–4.134	< 0.001		
Caprini≥4+0.5 mg/L≤D- Dimer<1 mg/L	16.07	2.753	1.692–4.479	< 0.001		
Caprini≥4+D-Dimer≥1 mg/L	24.81	4.744	2.961-7.601	< 0.001		
DVT, deep vein thrombosis, OR: odds ratios						

The OR were compared to the Caprini 1–2 group, and the p value for all groups were < 0.05

Discussion

DVT remains a frequent postoperative complication following knee arthroplasty [12]. In this study, we report an incidence of 10.55% for DVT with symptomatic DVT representing 1.98% of these cases. The significance of preventing DVT to reduce thrombotic events after TKA cannot be overstated, thus making the implementation of preventive strategies more crucial than their treatment. To mitigate postoperative thrombotic complications, clinicians typically employ comprehensive methods that includes a variety of preventive measures, such as the use of pneumatic pumps, elastic socks, and anticoagulant medications [13, 14]. However, DVT prevention should commence immediately after surgery, or even before surgery. Therefore, preoperative markers and scoring models that identify individuals at high risk can facilitate more proactive preventive measures. Our analysis identified women, preoperative D-dimer positivity, and preoperative Caprini score as independent risk factors for DVT after TKA. The increased risk in women can be attributed to a combination of factors such as older average age, estrogen level fluctuations, higher body fat percentage, and an increased prevalence of immunerelated diseases among women patients, leading to an elevated incidence of thrombotic events [15]. Our study indicates a significantly higher proportion of women among asymptomatic DVT patients. This suggests that while women are at a heightened risk of developing DVT after surgery, the resulting DVT is more likely to be asymptomatic. While asymptomatic DVT exerts a lesser impact on patients compared to symptomatic DVT, there remains a potential for its progression to post-thrombotic syndrome (PTS), warranting attention and not to be disregarded [16]. Extensive research within the academic community has consistently demonstrated that female gender is a notable risk factor for the development of DVT [17–19], and TKA is predominantly performed on women patients. To better prepare for the potential occurrence of DVT, this study underscores the predictive value of preoperative Caprini score and D-dimer levels for DVT following TKA.

The well-validated Caprini RAM score has been shown to effectively predict DVT risk and guide preventive measures across various surgeries [7, 20, 21]. Conducting a preoperative evaluation using the Caprini score can provide more accurate risk stratification, aid in identifying high-risk individuals early, and facilitate the prompt implementation of preventive measures. As an important content of Caprini RAM, age option shows its difference between the DVT group and the non-DVT group. Age is a significant risk factor for postoperative DVT in patients undergoing joint arthroplasty [5]. In the multifactorial regression analysis, as the Caprini score already encompasses age-related risks, age consequently demonstrates itself as a non-independent risk factor. Several factors contribute to the increased risk of DVT with advancing age. These include heightened activity of coagulation factors in the blood, reduced calf muscle pumping function leading to enhanced venous stasis, and declining estrogen levels in women patients [22]. Besides age, statistically significant differences were observed in BMI>25, BMI>40, diabetes requiring insulin, and a history of thrombosis. Interestingly, in univariate comparisons, the average BMI and prevalence of diabetes did not show statistical differences. This further underscores the scientific rigor of assessing DVT using the Caprini score, which proves more insightful compared to conventional risk factors.

D-dimer, a well-known marker for DVT [23, 24], is highly sensitive but can be influenced by various factors and fluctuate rapidly [25]. The association between postoperative D-dimer levels and DVT is subject to debate due to the multitude of influencing factors affecting D-dimer levels [10, 11, 26]. Preoperative D-dimer level offer a more accurate assessment of an individual's underlying risk for developing thrombosis and other related conditions. This is because it's not influenced by the trauma of surgery, which can temporarily elevate D-dimer levels. Studies have also shown that preoperative D-dimer levels can be highly predictive of postoperative survival and recurrence outcomes in patients with cancer [27, 28]. Additionally, preoperative D-dimer has shown noninferiority to serum C-reactive protein in the diagnosis of periprosthetic joint infection [29]. After excluding acute injuries and joint inflammation as confounding factors, for patients with knee osteoarthritis who are undergoing primary TKA, preoperative D-dimer level is a valuable tool for assessing DVT risk. Consequently, patients with preoperative D-dimer positivity are at a higher risk of experiencing DVT following surgery. Moreover, when D-dimer levels reach two-fold reference $(\geq 1 \text{ mg/L})$, the incidence rate of DVT after surgery will further increase.

Previous studies have indicated that the combination of postoperative Caprini score and D-dimer levels provides valuable guidance for predicting DVT in patients with thoracolumbar fractures and those undergoing laparoscopic radical surgery for colon cancer [30, 31]. Our study is the first to apply this combined approach in the context of TKA, and it utilizes preoperative indicators. The Caprini RAM is a dynamic tool that requires multiple adjustments during hospitalization [32], and we should identify high-risk DVT patients upon admission. By evaluating both preoperative Caprini score and D-dimer levels, we can identify high-risk patients earlier, allowing for more timely interventions and ultimately leading to a reduced incidence of DVT. The ACCP (American College of Chest Physicians) guideline for DVT prevention after TKA still advocate for a comprehensive prevention strategy that combines physical and pharmacological methods [33]. However, with the recent development of enhanced recovery protocols, more potential anticoagulation strategies and individualized prevention measures have been proposed [34–36]. Caprini JA suggested that low-risk patients could be managed with aspirin, while high-risk patients should receive more robust chemoprophylaxis, both of which can effectively prevent DVT [37]. In future research, we can also use preoperative higher Caprini scores and D-dimer levels to identify high-risk DVT patients earlier and provide individualized anticoagulant therapy after surgery.

Our study has several advantages. First and foremost, the study paid particular attention to the occurrence of symptomatic and asymptomatic DVT, a finding that contributes to our understanding and prevention of asymptomatic DVT, an area often overlooked in previous research. Secondly, all patients underwent DVT screening both before and after surgery, ensuring a more accurate assessment of new DVT development following surgery. Finally, this study is the first to investigate the combined effect of preoperative Caprini scores, D-dimer levels, and DVT incidence after primary TKA. Identifying these predictive factors has the potential to improve risk stratification and guide the development of more effective preventive measures.

In addition, it is important to acknowledge the limitations of our study. Firstly, age is universally recognized as a critical risk factor for the development of DVT. In this study, we did not consider age as an independent risk factor due to its substantial impact on the Caprini score. Secondly, most of the DVT events identified in our study were classified as muscular vein thrombosis. Some researchers might argue that these events bear limited clinical significance. Nevertheless, it is vital to note that muscular vein thrombosis can act as an overall indicator of the body's thrombotic state and is strongly associated with a predisposition for clot formation [38]. Thirdly, our focus was on screening for DVT during the hospital stay, specifically 3-5 days post-surgery. While DVT can occur up to three months after knee arthroplasty, existing literature suggests that DVT primarily takes place within the initial four days following surgery [39]. Meanwhile, we also acknowledge that preoperative factors significantly influence the incidence of in-hospital DVT following TKA. Conversely, the occurrence of DVT post-discharge is primarily dictated by patient activity levels and the duration of anticoagulant medication usage.

Conclusion

Patients with preoperative higher Caprini scores and D-dimer are more likely to develop DVT following primary TKA. Our study found that individuals with elevated preoperative Caprini scores (\geq 4) and D-dimer (\geq 1.0 mg/L) exhibited a significantly increased risk (24.81%) of DVT compared to those with lower scores, identifying them as a high-risk group for DVT following TKA. These findings hold significant value for DVT risk stratification in primary TKA patients and the formulation of preoperative interventions to mitigate the risk of DVT.

Acknowledgements

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Author contributions

QJ, ZHX designed and guided this project. XKY, GJZ analyzed and interpreted the patient data regarding the Deep Vein Thrombosis after Total Knee Arthroplasty. DXW, HkT gathered preoperative patient profiles, blood test indexes, and Caprini scores. LQ, YY were major contributors in writing the manuscript. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Consent for publication

Informed consent to publication of research was obtained from all participants in this study.

Competing interests

The authors declare no competing interests.

Ethical approval and consent to participate

All methods were performed in accordance with the Declaration of Helsinki. Approval from the Medical Ethics Committee of Nanjing University Medical Affiliated Drum Tower Hospital was obtained for this study. Informed consent was obtained from all patients to participate in the study.

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References

- González-Sáenz-de-Tejada M, Quintana JM, Arenaza JC, et al. Long-term health related quality of life in total knee arthroplasty. BMC Musculoskelet Disord. 2023;24:327. https://doi.org/10.1186/s12891-023-06399-6.
- Giustra F, Bosco F, Cacciola G, et al. No significant differences in clinical and radiographic outcomes between PCL retained or sacrificed kinematic aligned medial pivot total knee arthroplasty in Varus knee. J Clin Med. 2022;11:6569. https://doi.org/10.3390/jcm11216569.
- Januel JM, Chen G, Ruffieux C, et al. Symptomatic in-hospital deep vein thrombosis and pulmonary embolism following hip and knee arthroplasty among patients receiving recommended prophylaxis: a systematic review. JAMA. 2012;307:294–303. https://doi.org/10.1001/jama.2011.2029.
- Zhang H, Mao P, Wang C, et al. 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. 2017;28:126–33. https://doi.org/10.1097/mbc.0000000000556.
- Xu H, Zhang S, Xie J, et al. A nested case-control study on the risk factors of deep vein thrombosis for Chinese after total joint arthroplasty. J Orthop Surg Res. 2019;14:188. https://doi.org/10.1186/s13018-019-1231-9.
- Cronin M, Dengler N, Krauss ES, et al. Completion of the updated Caprini Risk Assessment Model (2013 version). Clin Appl Thromb Hemost. 2019;25:1076029619838052. https://doi.org/10.1177/1076029619838052.
- Krauss ES, Segal A, Dengler N, et al. Utilization of the Caprini score for risk stratification of the Arthroplasty patient in the Prevention of postoperative venous thrombosis. Semin Thromb Hemost. 2022;48:407–12. https://doi.org/ 10.1055/s-0042-1742739.
- Qiao L, Yao Y, Wu D, et al. The validation and modification of the Caprini Risk Assessment Model for evaluating venous thromboembolism after Joint Arthroplasty. Thromb Haemost. 2024;124:223–35. https://doi. org/10.1055/a-2122-7780.
- Bateman DK, Dow RW, Brzezinski A, et al. Response to the letter to the editor on correlation of the Caprini score and venous thromboembolism incidence following primary total joint arthroplasty-results of a single-Institution Protocol. J Arthroplasty. 2018;33:2698–9. https://doi.org/10.1016/j.arth.2018.03.064.
- 10. An TJ, Engstrom SM, Oelsner WK, et al. Elevated d-Dimer is not predictive of symptomatic deep venous thrombosis after total joint arthroplasty. J Arthroplasty. 2016;31:2269–72. https://doi.org/10.1016/j.arth.2016.02.059.
- Rafee A, Herlikar D, Gilbert R, et al. D-Dimer in the diagnosis of deep vein thrombosis following total hip and knee replacement: a prospective study. Ann R Coll Surg Engl. 2008;90:123–6. https://doi.org/10.1308/0035884 08x261627.
- Matharu GS, Kunutsor SK, Judge A, et al. Clinical effectiveness and safety of aspirin for venous thromboembolism Prophylaxis after total hip and knee replacement: a systematic review and Meta-analysis of Randomized clinical trials. JAMA Intern Med. 2020;180:376–84. https://doi.org/10.1001/ jamainternmed.2019.6108.
- Liu J, Zhao J, Yan Y, et al. Effectiveness and safety of rivaroxaban for the prevention of thrombosis following total hip or knee replacement: a systematic review and meta-analysis. Med (Baltim). 2019;98:e14539. https://doi. org/10.1097/md.00000000014539.
- Lippi G, Favaloro EJ, Cervellin G. Prevention of venous thromboembolism: focus on mechanical prophylaxis. Semin Thromb Hemost. 2011;37:237–51. https://doi.org/10.1055/s-0031-1273088.
- 15. Thachil R, Nagraj S, Kharawala A, et al. Pulmonary embolism in women: a systematic review of the current literature. J Cardiovasc Dev Dis. 2022;9:234. https://doi.org/10.3390/jcdd9080234.
- Wille-Jørgensen P, Jorgensen LN, Crawford M. Asymptomatic postoperative deep vein thrombosis and the development of postthrombotic syndrome. A systematic review and meta-analysis. Thromb Haemost. 2005;93:236–41. https://doi.org/10.1160/th04-09-0570.
- 17. Migita K, Bito S, Nakamura M, et al. Venous thromboembolism after total joint arthroplasty: results from a Japanese multicenter cohort study. Arthritis Res Ther. 2014;16:R154. https://doi.org/10.1186/ar4616.
- Lee SY, Ro du H, Chung CY, et al. Incidence of deep vein thrombosis after major lower limb orthopedic surgery: analysis of a nationwide claim registry. Yonsei Med J. 2015;56:139–45. https://doi.org/10.3349/ymj.2015.56.1.139.
- Zhang Z-h, Shen B, Yang J, et al. Risk factors for venous thromboembolism of total hip arthroplasty and total knee arthroplasty: a systematic review of evidences in ten years. BMC Musculoskelet Disord. 2015;16:24. https://doi. org/10.1186/s12891-015-0470-0.
- 20. Krauss ES, Cronin M, Dengler N, et al. Lessons learned: using the Caprini Risk Assessment Model to provide safe and

efficacious Thromboprophylaxis following hip and knee arthroplasty. Clin Appl Thromb Hemost. 2020;26:1076029620961450. https://doi. org/10.1177/1076029620961450.

- 21. Krauss ES, Segal A, Cronin M, et al. Implementation and validation of the 2013 Caprini score for risk stratification of Arthroplasty patients in the Prevention of venous thrombosis. Clin Appl Thromb Hemost. 2019;25:1076029619838066. https://doi.org/10.1177/1076029619838066.
- 22. Wilkerson WR, Sane DC. Aging and thrombosis. Semin Thromb Hemost. 2002;28:555–68. https://doi.org/10.1055/s-2002-36700.
- Pulivarthi S, Gurram MK. Effectiveness of d-dimer as a screening test for venous thromboembolism: an update. N Am J Med Sci. 2014;6:491–9. https:// doi.org/10.4103/1947-2714.143278.
- Riva N, Attard LM, Vella K, et al. Diagnostic accuracy of D-dimer in patients at high-risk for splanchnic vein thrombosis: a systematic review and meta-analysis. Thromb Res. 2021;207:102–12. https://doi.org/10.1016/j. thromres.2021.09.016.
- Siragusa S, Terulla V, Pirrelli S, et al. A rapid D-dimer assay in patients presenting at the emergency room with suspected acute venous thrombosis: accuracy and relation to clinical variables. Haematologica. 2001;86:856–61.
- Shimoyama Y, Sawai T, Tatsumi S, et al. Perioperative risk factors for deep vein thrombosis after total hip arthroplasty or total knee arthroplasty. J Clin Anesth. 2012;24:531–6. https://doi.org/10.1016/j.jclinane.2012.02.008.
- Lin GS, Lu J, Lin J, et al. Value of the preoperative D-Dimer to albumin ratio for survival and recurrence patterns in gastric Cancer. Ann Surg Oncol. 2023;30:1132–44. https://doi.org/10.1245/s10434-022-12625-7.
- Shiina Y, Nakajima T, Yamamoto T, et al. The D-dimer level predicts the postoperative prognosis in patients with non-small cell lung cancer. PLoS ONE. 2019;14:e0222050. https://doi.org/10.1371/journal.pone.0222050.
- Tarabichi S, Goh GS, Baker CM, et al. Plasma D-Dimer is noninferior to serum C-Reactive protein in the diagnosis of Periprosthetic Joint infection. J Bone Joint Surg Am. 2023;105:501–8. https://doi.org/10.2106/jbjs.22.00784.
- Zhang W, Sun R, Hu X, et al. Caprini risk assessment model combined with D-dimer to predict the occurrence of deep vein thrombosis and guide intervention after laparoscopic radical resection of colorectal cancer. World J Surg Oncol. 2023;21:299. https://doi.org/10.1186/s12957-023-03183-7.
- 31. Wang H, Lv B, Li W, et al. Diagnostic performance of the Caprini Risk Assessment Model Combined with D-Dimer for preoperative deep vein thrombosis in patients with Thoracolumbar fractures caused by high-energy

injuries. World Neurosurg. 2022;157:e410–6. https://doi.org/10.1016/j. wneu.2021.10.106.

- Tafur AJ, Caprini JA. Dissecting the rationale for thromboprophylaxis in challenging surgical cases. J Thromb Haemost. 2024;22:613–9. https://doi. org/10.1016/j.jtha.2023.12.033.
- Falck-Ytter Y, Francis CW, Johanson NA, et al. Prevention of VTE in orthopedic surgery patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2012;141:eS278–e325. https://doi.org/10.1378/ chest.11-2404.
- Johnson SA, Jones AE, Young E, et al. A risk-stratified approach to venous thromboembolism prophylaxis with aspirin or warfarin following total hip and knee arthroplasty: a cohort study. Thromb Res. 2021;206:120–7. https:// doi.org/10.1016/j.thromres.2021.08.009.
- Peng HM, Chen X, Wang YO, et al. Risk-stratified venous thromboembolism Prophylaxis after Total Joint Arthroplasty: low Molecular Weight Heparins and Sequential Aspirin vs aggressive chemoprophylaxis. Orthop Surg. 2021;13:260–6. https://doi.org/10.1111/os.12926.
- Landy DC, Bradley AT, King CA, et al. Stratifying venous thromboembolism risk in Arthroplasty: do high-risk patients exist? J Arthroplast. 2020;35:1390–6. https://doi.org/10.1016/j.arth.2020.01.013.
- Caprini JA, Cronin M, Dengler N, et al. A new chapter regarding thrombosis Risk Assessment in total joint replacement patients. Thromb Haemost. 2024;124:236–8.
- Gonzalez Della Valle A, Shanaghan KA, Nguyen J, et al. Multimodal prophylaxis in patients with a history of venous thromboembolism undergoing primary elective hip arthroplasty. Bone Joint J. 2020;102–B:71–7. https://doi. org/10.1302/0301-620X.102B7.BJJ-2019-1559.R1.
- Yamaguchi T, Hasegawa M, Niimi R, et al. Incidence and time course of asymptomatic deep vein thrombosis with fondaparinux in patients undergoing total joint arthroplasty. Thromb Res. 2010;126:e323–326. https://doi. org/10.1016/j.thromres.2010.03.018.

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