

Venous thromboembolism after total knee and hip arthroplasty

A retrospective study

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ABSTRACT

الأهداف: تقييم عوامل الخطر ومدى الإصابة بالجلطات الوريدية الدموية بعد جراحة استبدال مفصل الركبة وجراحة استبدال مفصل الورك.

الطريقة: أجرينا دراسة إسترجاعية للمرضى من خلال السجلات الطبية الإلكترونية بين عامي 2010م و2015م الذين خضعوا لجراحة استبدال مفصل الركبة أو جراحة استبدال مفصل الورك في مدينة الملك عبد العزيز الطبية، الرياض، المملكة العربية السعودية.

النتائج: كان معدل حدوث أعراض الجلطات الوريدية الدموية 1.9% (17 حالة، 95% CI: 1.1–2.8) في 756 مريض من الذين خضعوا إلى 889 عملية جراحية. جميع حالات الجلطات الوريدية الدموية حدثت قبل الخروج من المستشفى. اثنا عشر مريض (1.4%) أصيبوا بجلطة الشريان الرئوي، و5 مرضى (0.6%) أصيبوا بخثار الوريد العميق. خضع الغالبية من 557 مريضاً (62.7%) لعملية جراحية لاستبدال مفصل ركبة واحد، و138 (15.5%) من المرضى خضعوا لعملية استبدال المفاصل الثنائية. واستناداً إلى تحليل المخاطر وحيد المتغير، كانت جراحة استبدال المفاصل الثنائية هي المنتبئ المحتمل الوحيد للجلطات الوريدية الدموية بعد الجراحة.

الخاتمة: معدل الجلطات الوريدية الدموية في السكان السعوديين بعد جراحة استبدال المفاصل منخفض وقابل للمقارنة مع البيانات الدولية. ومع ذلك، هناك حاجة لمزيد من الجهود والمزيد من التجارب لتحسين تدابير الوقاية من الجلطات الوريدية في المستشفى.

Objectives: To evaluate the incidence and risk factors of Venous thromboembolism (VTE) among total knee arthroplasty (TKA) and total hip arthroplasty (THA) patients following surgery.

Methods: We conducted a retrospective review of electronic medical records of consecutive patients

between January 2010 and January 2015 who underwent TKA or THA at King Abdulaziz Medical City (KAMC), Riyadh, Saudi Arabia.

Results: The incidence of symptomatic VTE was 1.9% (17 events, 95% CI: 1.1–2.8) in 756 patients who underwent 889 surgeries. All VTE cases developed before hospital discharge. Twelve (1.4%) patients developed pulmonary embolism, and 5 (0.6%) patients developed deep vein thrombosis. The majority of patients (n=557, 62.7%) underwent surgery for single TKA, and 138 (15.5%) patients underwent bilateral arthroplasty. Based on univariate risk analysis, bilateral arthroplasty was the only potential predictor for VTE after surgery.

Conclusion: The rate of symptomatic VTE in a Saudi population following arthroplasty is low and comparable to the international data. However, efforts and more trials are needed to further improve in-hospital thromboprophylaxis measures.

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Venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE), are major complications following total knee arthroplasty (TKA) and total hip arthroplasty (THA).¹ In the absence of thromboprophylaxis use, the incidence of DVT following a major orthopedic surgery has been noted to be as high as 40-60% after THA and 40-85% after TKA.² These rates could be reduced to 1-10% with routine use of pharmacological thromboprophylaxis.^{1,2} Additionally, the incidence of PE without prophylaxis varies from 0.9-28% after THA and from 1.5-28% after TKA with a mortality rate of approximately 15%.^{1,3,4} Moreover, in a comparison cohort THA was associated with an increased risk of VTE up to one year after surgery compared with the risks of the general population.⁵ Furthermore, VTE was found to be the most common cause of emergency readmission following lower limb arthroplasty.⁶ However, the incidence of symptomatic VTE after THA and TKA was found to be reduced by extended thromboprophylaxis compared with no outpatient thromboprophylaxis.^{7,8}

Reducing the rate of VTE via the use of mechanical and pharmacological prophylaxis will certainly reduce the overall mortality rate from fatal PE.⁹ In a cohort of 936 cases of consecutive primary TKA, fatal PE was rare with the routine use of graded elastic stockings and early mobilization.¹⁰ The use of pharmacological thromboprophylaxis up to 35 days after THA and for at least 10 days after TKA is recommended by the American College of Chest Physicians (ACCP) guidelines.¹ Hypercoagulable state usually starts on the operating table and persists for up to 12 weeks after surgery.¹¹ A meta-analysis of data from randomized trials found that extended-duration prophylaxis after THA or TKA significantly reduced the frequency of post-discharge symptomatic VTE compared with placebo or untreated controls.⁸

Although VTE after lower limb arthroplasty is a recognized complication following the surgery, different study populations may exhibit variability in their outcomes. Data on the incidence of VTE after major orthopedic surgery in Asian populations are conflicting. While some studies have demonstrated comparable events in Asian and Western population populations,^{12,13} recent data revealed a lower incidence of VTE events in Asians compared with Western populations.^{14,15}

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Data about VTE after TKA or THA in Saudi populations are lacking. We therefore aimed to evaluate the incidence and risk factors of symptomatic VTE following TKA/THA and to assess the safety and efficacy of thromboprophylaxis in patients at King Abdulaziz Medical City (KAMC), Riyadh, Saudi Arabia.

Methods. All consecutive patients older than 18 who underwent primary TKA or THA with or without hip fracture at KAMC between January 2010 and January 2015 were retrospectively selected. Patients operated on for revision hip or knee arthroplasty were excluded. After applying the agreed-upon exclusion criteria, 756 patients who underwent 889 orthopedic procedures involving both THA and TKA were included in the study.

A data collection sheet was created that included demographic data, body mass index (BMI), length of in-hospital stay, type of THA and TKA (unilateral, bilateral), type of anesthesia, and follow up after hospital discharge. Follow-up data were extracted from the day of surgery to the last clinic visit, death, or end of the study. Potential risk factors of VTE including obesity, immobility, a history of VTE, chronic obstructive pulmonary disease (COPD), congestive heart failure, and active cancer were documented. Body mass index was calculated, and patients were classified as obese (BMI ≥ 30) or not obese (BMI < 30). The use and duration of thromboprophylaxis as recommended by the ACCP guidelines, whether it was pharmacological, mechanical (intermittent pneumatic compression (IPC), graduated compression stocking (GCS), or both, were identified.

The primary study outcome was the incidence of VTE within 3 months of surgery manifested as PE, lower extremity deep vein thrombosis, or both. Pulmonary embolism was classified as fatal and non-fatal, and deep vein thrombosis was classified as either distal (thrombosis limited to infrapopliteal veins) or proximal (thrombosis involving popliteal veins and above). A VTE diagnosis was confirmed by the patient's clinical symptoms documented in their medical records combined with diagnostic imaging (such as computed tomography pulmonary angiography (CTPA) or ventilation perfusion scan (V/Q) for a PE diagnosis and Doppler Ultrasounds (US) for a DVT diagnosis). Secondary outcomes included VTE risk factors, mortality rate, and the event of major bleeding as defined by the International Society on Thrombosis and Hemostasis (ISTH). The institutional review board at KAMC approved the study.

Statistical analysis. All of the clinical data were collected from the patient's medical record and put into

a spreadsheet, which was then used for further analysis. We used IBM SPSS Statistics for Windows Version 21 (IBM Corp, Armonk, NY) to carry out all the statistical analysis, including calculating frequencies and central tendency. We used logistic regression to calculate odds ratios (ORs). A value of $p < 0.05$ was taken as being statistically significant.

Results. Overall, 756 patients underwent 889 surgeries between January 2010 and January 2015 at KAMC. The mean age of the population was 65.0 ± 11.6 years; 624 of the patients (82.5%) were younger than 75. There were more women 531 (70.2%) than

men 225 (29.8%). Ten (1.3%) patients had a previous history of VTE (Table 1). The majority of patients (557; 62.7%) underwent surgery for single TKA. Surgery was performed for THA on 76 patients (8.5%). Bilateral arthroplasty was carried out on 138 patients (15.5%). Bilateral TKA was carried out on 136 patients, and bilateral THA was carried out on 2 patients only. One hundred and eighteen patients (13.3%) underwent THA with fracture. The median time of follow up of this cohort was 14 months (range: 1-88 months).

Surgeries were conducted under regional anesthesia in 60% of cases; this rate was higher for TKA than THA patients (Table 2). One hundred and forty-three patients

Table 1 - Demographic data and comorbidities of 756 patients underwent surgeries.

Characteristics	TKA n=565	THA n=73	THA+fracture n=118	Total n=756
Age (mean±SD) (years)	64.7 ± 8.8	52.0 ± 17.1	70.1 ± 13.5	65 (11.6)
<75	485 (85.8)	67 (91.8)	72 (61.0)	624 (82.5)
≥75	80 (14.2)	6 (8.2)	46 (39.0)	132 (17.5)
Gender				
Male	142 (25.1)	39 (53.4)	44 (37.3)	225 (29.8)
Female	423 (74.9)	34 (46.6)	74 (62.7)	531 (70.2)
Comorbidities				
Previous VTE	5 (0.9)	2 (2.7)	3 (2.5)	10 (1.3)
COPD	2 (0.4)	0 (0)	3 (2.5)	5 (0.7)
Congestive heart failure	2 (0.4)	1 (1.4)	1 (0.8)	4 (0.5)
Atrial fibrillation	13 (2.3)	3 (4.1)	6 (5.0)	22 (3.9)
Cancer	2 (0.5)	4 (5.5)	4 (3.4)	10 (1.1)

TKA - total knee arthroplasty, THA - total hip arthroplasty, BMI - body mass index, VTE - venous thromboembolism, COPD - chronic obstructive pulmonary disease, CHF -

Table 2 - Clinical characteristics of 889 patients.

Characteristics	TKA n=693	THA n=78	THA+fracture n=118	Total n=889
Length of hospital stay (mean±SD)	12.4±7.5	17.5±25.0	20.8±24.8	13.9±13.7
Anesthesia				
General	243 (35.0)	58 (74.4)	52 (44.0)	353 (39.7)
Regional	450 (65.0)	20 (25.6)	66 (56.0)	536 (60.3)
Bilateral joint arthroplasty	136 (19.6)	2 (2.5)	0	138 (15.5)
BMI ≥30	503 (73.1)	38 (50.7)	35 (31.3)	576 (65.0)
Blood transfusion	98 (14.1)	25 (32.1)	20 (16.9)	143 (16.0)
Ambulation within 48 hours after surgery	689 (99.4)	78 (100)	113 (97.4)	880 (99.0)
Venous thromboembolism	12 (1.7)	1 (1.3)	4 (3.4)	17 (1.9)
Starting thromboprophylaxis after surgery				
≤24 hours	638 (92.1)	64 (82.1)	45 (38.1)	747 (84.0)
>24 hours	20 (2.9)	6 (7.7)	9 (7.6)	35 (4.0)
Before surgery	35 (5.1)	8 (10.3)	64 (54.2)	107 (12.0)
Mechanical (IPC+GCS)	1 (0.1)	0	0	1 (0.1)
Aspirin use	63 (9.1)	8 (10.7)	38 (32.2)	109 (12.2)
Clopidogrel use	3 (0.4)	0	7 (5.9)	10 (1.1)
Aspirin + Clopidogrel	2 (0.3)	0	5 (4.2)	7 (0.8)

TKA - total knee arthroplasty, THA - total hip arthroplasty, BMI - body mass index, IPC - intermittent pneumatic compression, GCS - graduated compression stocking

(16%) required a blood transfusion. Ninety-nine percent of patients started to ambulate within 48 hours of their surgery. Almost two thirds of the patients were obese with a BMI of ≥ 30 . The mean hospital stay was 13.9 ± 13.7 days.

All the patients received thromboprophylaxis: 747 (84%) started within 24 hours of the surgery, 35 (4%) started more than 24 hours after surgery, and the remaining 107 (12%) were on thromboprophylaxis before the surgery. Pharmacological thromboprophylaxis with enoxaparin was used in 853 (96%) procedures (Table 3). The dose was administered as 40 mg once daily in 684 (77%) procedures and 30 mg twice daily in 146 (16.5%) procedures. A direct oral anticoagulant (Dabigatran) was used in only 2 patients. One hundred and nine (12.2%) patients were on aspirin, 10 (1.1%) were on clopidogrel, and 7 (0.8%) were on both clopidogrel and ASA. All patients who were on an antiplatelet (aspirin/clopidogrel) were managed with enoxaparin as thromboprophylaxis. Only one patient was on combined thromboprophylaxis (mechanical and pharmacological) after the surgery. The median duration of administration of thromboprophylaxis was 30 days.

The overall rate of confirmed symptomatic VTE during the study period was 1.9% (17 events, 95% CI: 1.1-2.8). The rate was 1.7% in patients undergoing total knee replacement, 1.3% in patients undergoing total hip replacement, and 3.4% in patients undergoing total hip replacement with fracture. Twelve (1.4%) patients developed PE, and 5 (0.6%) patients developed DVT (4 proximal and 1 distal); 3 were at the same site of the surgery, 1 was bilateral DVT, and 1 was a left side distal DVT in a patient who underwent bilateral TKA. Of the 17 patients who developed VTE, only 1 (6%) patient had a history of congestive heart failure, and 11 (65%) were obese. None of the patients who had a history of previous thrombosis developed VTE. All VTE cases were diagnosed before hospital discharge a median of 5 days after surgery.

Table 4 - Univariate risk analysis of potential risk factors for VTE (n=17).

Risk factors	Odds ratio	95% CI	P-value
Age ≥ 75 versus <75	1.47	0.47-4.58	0.507
Female versus male	2.00	0.57-7.04	0.278
BMI ≥ 30 versus <30	1.15	0.39-3.33	0.804
General anesthesia; yes versus no	2.20	0.83-5.84	0.112
Regional anesthesia; yes versus no	0.54	0.19-1.48	0.229
THA versus TKA	0.74	0.09-5.75	0.771
Bilateral joint arthroplasty; yes versus no	5.12	1.94-13.51	0.001
Blood transfusion; yes versus no	2.22	0.77-6.39	0.141
Enoxaparin 40 mg versus 30 mg	1.07	0.12-9.21	0.952

95% CI - 95% confidence intervals, TKA - total knee arthroplasty, THA - total hip arthroplasty, VTE - venous thromboembolism

One patient had major bleeding that occurred 10 days after the surgery. Nine (1.2%) patients died during the follow up. Death was related to myocardial infarction, cardiac arrest, and sepsis; no fatalities were related to VTE. Based on univariate analysis, bilateral joint arthroplasty was the only predictor of symptomatic VTE during the study period (Table 4).

Discussion. In this retrospective cohort, 756 patients with the mean age of 65.0 ± 11.6 years who underwent 889 major orthopedic procedures involving TKA, THA, and THA with a fracture in a large tertiary care institution. The overall incidence of VTE was 1.9% (17 events, 95% CI: 1.1-2.8). Pulmonary embolism accounted for 70% of all VTE events, and DVT accounted for 30%. None of the PE cases were fatal. The highest rate of VTE occurred in patients who underwent THA with fracture (3.4%), followed by patients who underwent TKA (1.7%) and THA (1.3%). Low molecular weight heparin (LMWH), particularly enoxaparin, was the thromboprophylaxis of choice (96%) in our cohort for a median of 30 days for all types of surgeries. Direct oral anticoagulants (DOACs) and mechanical prophylaxis (IPC, GCS)

Table 3 - Types of thromboprophylaxis.

Characteristics	TKA n=693	THA n=78	THA+fracture n=118	Total n=889
Heparin	3 (0.4)	0 (0)	0 (0)	3 (0.3)
Enoxaparin	673 (97.1)	74 (95.0)	106 (89.8)	853 (96.0)
Enoxaparin 40 mg	552 (82.0)	52 (70.3)	80 (75.5)	684 (77.0)
Enoxaparin 30 mg	110 (16.4)	18 (24.3)	18 (17.0)	146 (16.5)
Unknown enoxaparin dose	11 (1.6)	4 (5.4)	8 (7.5)	23 (2.5)
Fondaparinux	2 (0.3)	0	2 (1.7)	4 (0.5)
Warfarin	13 (1.9)	4 (5.0)	10 (8.5)	27 (3.0)
Dabigatran	2 (0.3)	0	0	2 (0.2)

Values are presented by number and percentages (%), TKA - total knee arthroplasty, THA - total hip arthroplasty

were underused in our study. All of the patients who developed PE or DVT were diagnosed before hospital discharge.

Injectable LMWHs (namely, enoxaparin), were prescribed as a 30 mg twice a day in 146 (16.5%) patients or as a 40 mg given once a day in 684 (77%) patients. Most of the patients (84%) received thromboprophylaxis within 24 hours after the surgery; only 4% started >24 hours after surgery. Our results are consistent with those of a previously published FOTO trial, a prospective observational study that included 1080 patients and evaluated the incidence of symptomatic VTE 3 months following TKA/THA.⁶ The overall incidence of VTE was 1.8%; the rate was higher in patients who underwent TKA (2.8%). An extended duration of thromboprophylaxis (>14 days) and the use of injectable anticoagulants were common measures in both studies. In contrast to our study, PE accounted for 0.2% of VTE events and DVT accounted for 1.7% of VTE events.⁶ Parvizi et al¹⁶ found an increase in PE diagnosis following arthroplasty from 0.21% during the era of ventilation-perfusion (V/Q) scan to 1.7% during the time of multidetector computed tomography (CT). All of the PE patients in our study were diagnosed using CTPA. The sensitivity of CTPA compared with VQ scans in detecting clinically nonsignificant PE such as subsegmental PE may explain the high rate of PE in our study.

Previous studies have reported a range of incidences of VTE events in orthopedic patients. In a retrospective study of 346 patients who were managed with LMWH as thromboprophylaxis for 14 days, the incidence of symptomatic DVT and PE was as high as 13%.¹⁷ In another retrospective study, the in-hospital incidence of PE was 4.6%.¹⁸ Wells et al showed a high incidence of VTE following arthroplasty in a retrospective study of 3195 patients.¹⁹ The rate was significantly higher (3.9%) in the group of patients managed with thromboprophylaxis for fewer than 14 days compared with patients who received thromboprophylaxis for more than 14 days (1.4%) ($p < 0.0001$).

The current ACCP guidelines recommend thromboprophylaxis after TKA or THA for at least 10-14 days and suggest extended thromboprophylaxis lasting up to 35 days over short-duration thromboprophylaxis.²⁰ This recommendation is supported by the findings of several clinical trials and meta-analyses.^{7,8} Eikelboom et al⁸ identified 9 randomized controlled trials (RCTs) comparing extended-duration thromboprophylaxis (30 days) to a placebo or untreated patients and found a significant reduction in symptomatic VTE (1.3% versus

3.3%, OR 0.38; 95% CI 0.24-0.61) without an increase in major bleeding. An RCT comparing enoxaparin with a placebo after 10 days of thromboprophylaxis in patients who underwent TKA or THA found a significant reduction in symptomatic VTE events after THA but not TKA.⁷

Several risk factors are known to be associated with VTE following major orthopedic surgery. These factors include a previous history of PE, cardiovascular disease,²¹ or high BMI.²² In a prospective study of 569 patients who underwent primary THA or TKA, increased age, undergoing a knee arthroplasty, recent surgery, general anesthesia, a shorter operation time, non-receipt of blood transfusion and differences in surgical practice were significant risk factors for DVT following arthroplasty.²³ In our study, the univariate risk analysis revealed that bilateral joint arthroplasty was the only potential predictor for VTE after surgery; age, gender, BMI, type of anesthesia, site of the surgery, and the dose of enoxaparin were not predictors of VTE after surgery. These findings may be explained by the relatively small number of VTE events in our study.

The retrospective nature and involvement of a single center were limitations to this study. Furthermore, the sample size and the total number of VTE events were both relatively small and prevented us from performing subgroup analysis to identify, in particular, VTE risk factors after arthroplasty.

In conclusion, in this retrospective study of a Saudi population undergoing arthroplasty, the use of thromboprophylaxis was consistent with international guidelines for the dose and duration after surgery. However, direct oral anticoagulants and mechanical measures are underused at our institution. The incidence of symptomatic VTE with appropriate thromboprophylaxis was similar to that noted in Western data. Given that all VTE cases developed in-hospital, it is necessary to focus on improving thromboprophylaxis during hospitalization.

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