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Deep Vein Thrombosis and Pulmonary Embolism Following Unilateral and Simultaneous Bilateral Total Knee Arthroplasty

Mosaad Almegren*

Department of Medicine, Imam Mohammad Ibn Saud Islamic University, Riyadh, Saudi Arabia

**Corresponding e-mail: mosaad966@gmail.com*

ABSTRACT

Objective: *Venous thromboembolism (VTE), which comprises pulmonary embolism and deep vein thrombosis, is a known complication of total knee arthroplasty (TKA). However, data on the risk of VTE after simultaneous bilateral TKA, compared to that after single knee arthroplasty, is scarce.* ***Methods:*** *A retrospective study of electronic medical records of all adult patients who underwent simultaneous bilateral TKA or single unilateral TKA was conducted.* ***Results:*** *A total of 669 patients underwent TKA. Of these, 134 underwent simultaneous bilateral TKA while 535 underwent single unilateral TKA. All patients underwent pharmacological thromboprophylaxis for a median duration of 30 days. The incidence of confirmed VTE in all patients was 1.8% (95% confidence interval, CI: 0.9-3.0). VTE occurred in 8 of the 134 patients (6%, 95% CI: 2.2-10.4) who underwent simultaneous bilateral TKA and in 4 of the 535 patients (0.7%, 95% CI: 0.2-1.5) who underwent single unilateral TKA. The odds ratio of confirmed VTE was 8.42 (95% CI: 2.49-28.4; p=0.001).* ***Conclusion:*** *The risk of VTE is significantly higher following simultaneous bilateral TKA than following single unilateral TKA. Further studies are needed to evaluate high-risk patients and to determine the appropriate thromboprophylaxis regimen.*

Keywords: Venous thromboembolism, Thromboprophylaxis, Anticoagulation, Major orthopedic surgery

INTRODUCTION

Total knee arthroplasty (TKA) is a common orthopedic surgical procedure that can be performed as single unilateral, staged bilateral or simultaneous bilateral. The single mode of operation, anesthesia session, rehabilitation, and shorter duration of hospital stay are major advantages of simultaneous bilateral TKA [1]. However, published literature report increased risks of perioperative surgical site infection, cardiovascular complications, bleeding necessitating blood transfusion, and mortality [2,3].

Venous thromboembolism (VTE), which comprises pulmonary embolism (PE) and deep venous thrombosis (DVT), is a serious and potentially fatal complication of TKA [4]. The incidences of VTE following TKA without pharmacological thromboprophylaxis are 40% to 85% and 1.5% to 28% for DVT and PE, respectively [4-6]. Moreover, VTE was reported to be a common cause of re-hospitalization after joint arthroplasty [7]. These incidences can be reduced to less than 10% with the use of thromboprophylaxis [4,5]. A meta-analysis of randomized controlled trials showed a significant reduction in the frequency of post-discharge VTE with extended duration thromboprophylaxis compared to placebo or untreated controls [8]. Therefore, pharmacological thromboprophylaxis has become the standard of care for VTE prevention following TKA. The American College of Chest Physicians (ACCP) recommends extended pharmacological thromboprophylaxis of at least 10 days following TKA [4]. Several pharmacological agents have been approved for VTE prevention following TKA, and they include warfarin, low molecular weight heparin (LMWH), unfractionated heparin, fondaparinux, and direct oral anticoagulant agents [4,9-11].

The risk of VTE after simultaneous bilateral TKA is comparable to those after single unilateral TKA and staged bilateral TKA. In some studies, the risk of VTE was found to increase following simultaneous bilateral TKA compared to following single unilateral TKA or staged bilateral TKA while other recent studies reported no differences [2,12-14].

Data on the incidence of VTE following simultaneous bilateral TKA is scarce. Therefore, we aimed to evaluate the incidence of VTE, including DVT and/or PE, in patients who underwent simultaneous bilateral TKA compared to those who underwent single unilateral TKA.

MATERIALS AND METHODS

A retrospective comparative study was conducted at a single tertiary care center. Following approval from the institutional review board, medical records of all consecutive patients who underwent simultaneous bilateral TKA and single unilateral TKA between January 2010 and December 2015 were reviewed. We defined simultaneous bilateral TKA as a procedure in which the patient underwent 2-sided knee arthroplasty during the same operation. All patients who were older than 18 years of age and who underwent primary TKA were included in the study. The exclusion criteria were as follows: revision procedure, staged bilateral TKA, history of VTE or active cancer, and administration of therapeutic doses of anticoagulants.

Data were collected by reviewing paper-based and electronic medical records of each identified patient. The following data were collected: age, gender, type of TKA (single unilateral or simultaneous bilateral), type of anesthesia, length of hospital admission, type and duration of thromboprophylaxis regimen, and concurrent use of antiplatelet agents. Comorbidities and potential VTE risk factors such as chronic obstructive pulmonary disease, congestive heart failure, family history of VTE, and immobility were collected. Obesity was defined as a body mass index (BMI) of 30 or more. Follow-up data were collected from the day of the surgery to the day of last encounter, death, or end of the study.

The primary outcome of the study was the incidence of VTE, including PE, DVT, or both, within 90 days of knee arthroplasty in patients who underwent simultaneous bilateral TKA or single unilateral TKA. PE and DVT diagnoses were confirmed based on patient symptoms and signs documented in the medical records as well as imaging results. The intraluminal filling defect of pulmonary arteries on computed tomography pulmonary angiography (CTPA) or high-probability ventilation-perfusion scan was considered confirmatory of PE diagnosis. Lack of compressibility, the absence of Doppler flow, and direct visualization of thrombus in the deep venous system on Doppler ultrasound scans were considered confirmatory of DVT diagnosis. Ethical approval for this study was obtained from the King Abdullah International Research Center, Riyadh, Saudi Arabia.

Statistical Analysis

The demographic and clinical data of all the patients were collected from electronic medical records and inputted on a spreadsheet for analysis. We used Pearson's chi-square test or Fisher's exact test to compare differences between categorical variables and the Mann-Whitney U test was performed to test differences in continuous data. Odds ratios and confidence intervals were calculated using logistic regression analysis. The above-mentioned tests, as well as measures of central tendency (frequencies, mean, and median), were performed on IBM SPSS statistics for windows version 21 (IBM Corp, Armonk, NY). A 2-sided p-value<0.05 was considered significant throughout the analysis.

RESULTS

A total of 669 consecutive patients who underwent knee arthroplasty were identified. Of these, 134 (20%) underwent simultaneous bilateral TKA and 535 (80%) underwent single unilateral TKA. The baseline characteristics of the patients are shown in Table 1.

Table 1 Patient's demographics (N=669)

Characteristics	Single TKA=134 patients	Bilateral TKA=535 patients	Total	p-value
	n (%)	n (%)	n (%)	
Age [Mean (SD)]	63.8 (8.4%)	66.9 (9.3%)	64.4 (8.7%)	
<75	479 (89.5%)	104 (77.6%)	583 (87.1%)	<0.001
≥ 75	56 (10.5%)	30 (22.4%)	86 (12.9%)	<0.001
Sex				
Male	117 (21.9%)	44 (32.8%)	161 (24.1%)	0.008
Female	418 (78.1%)	90 (67.2%)	508 (75.9%)	
Comorbidities				
COPD				
No	534 (99.8%)	134 (100.0%)	668 (99.9%)	1
Yes	1 (0.2%)	0 (0.0%)	1 (0.1%)	

Heart failure				
No	533 (99.6%)	134 (100.0%)	667 (99.7%)	1
Yes	2 (0.4%)	0 (0.0%)	2 (0.3%)	
TKA: Total knee arthroplasty; SD: Standard deviation				

The group consisted of 508 female patients (76%) and 161 male patients (24%). The mean age of the patients was 64.4 years (standard deviation: 8.7 years). The length of hospital stay was longer in patients who underwent simultaneous bilateral TKA compared to those who underwent single unilateral TKA (median: 16.2 days versus 11.2 days, p=00.1). Patients who underwent simultaneous bilateral TKA were more obese and received more blood transfusions than patients who underwent single unilateral TKA (Table 2). The surgical procedures were conducted under general anesthesia in 44% of the patients that underwent simultaneous bilateral TKA compared to 33% of patients that underwent single unilateral TKA. The median follow-up time for all the patients was 15 months (range: 1-88 months).

Table 2 Clinical characteristics (N=669)

Characteristics	Single TKA n (%)	Bilateral TKA n (%)	Total n (%)	p-value
Length of hospital stay [Mean (SD%)]	11.2 (7.2%)	16.2 (7.3%)	12.2 (7.5%)	0.001
General Anesthesia				
No	357 (66.7%)	75 (56%)	432 (64.6%)	0.020
Yes	178 (33.3%)	59 (44%)	237 (35.4%)	
Regional Anesthesia				
No	93 (17.4%)	29 (21.6%)	122 (18.2%)	0.254
Yes	442 (82.6%)	105 (78.4%)	547 (81.8%)	
BMI				
<30	134 (25.2%)	45 (33.8%)	179 (27%)	0.046
≥ 30	397 (74.8%)	88 (66.2%)	485 (73%)	
Blood Transfusion				
No	479 (89.5%)	97 (72.4%)	576 (86.1%)	<0.001
Yes	56 (10.5%)	37 (27.6%)	9313.9	
Ambulation after Surgery				
≤ 2 days	534 (99.8%)	132 (98.5%)	666 (99.6%)	0.104
> 2 days	1 (0.2%)	2 (1.5%)	3 (0.4%)	
VTE				
No	531 (99.3%)	126 (94%)	657 (98.2%)	0.001
Yes	4 (0.7%)	8 (6%)	12 (1.8%)	
Starting Thromboprophylaxis after Surgery				
Day 0 + post op. day 1	500 (93.5%)	120 (89.6%)	620 (92.7%)	0.240
Post op. day 2 and after	14 (2.6%)	5 (3.7%)	19 (2.8%)	
Before surgery	21 (3.9%)	9 (6.7%)	30 (4.5%)	

Venous thromboprophylaxis was administered to 620 patients (92.75%) within 24 hours of the surgery to 19 patients (2.8%) more than 24 hours after the surgery, and to the remaining 30 patients (4.5%) before the surgery. Most of the patients (99%) were treated with 40 mg of enoxaparin once daily rather than with 30 mg of enoxaparin twice daily (Table 3). Unfractionated heparin was administered to 9 patients, fondaparinux to 1 patient, and dabigatran to 1 patient. Intermittent pneumatic compression (IPC) or graduated compression stocking (GCS) were not used in any patient. Aspirin was administered to patients who underwent simultaneous bilateral TKA more than patients who underwent single unilateral TKA (15.7% versus 7.7%, p=0.003). The median duration of venous thromboprophylaxis in all patient groups was 30 days (range: 4-90 days).

Table 3 Type of venous thromboprophylaxis

Type of Thromboprophylaxis	Single TKA n (%)	Bilateral TKA n (%)	Total n (%)	p-value
Enoxaparin				
No	5 (0.9%)	4 (3.0%)	9 (1.3%)	0.085
Yes	530 (99.1%)	130 (97.0%)	660 (98.7%)	

Enoxaparin				
Enoxaparin 40 mg	444 (85.1%)	96 (76.8%)	540 (83.5%)	0.026
Enoxaparin 30 mg	78 (14.9%)	29 (23.2%)	107 (16.5%)	
Fondaparinux				
No	534 (99.8%)	134 (100%)	668 (99.9%)	1.000
Yes	1 (0.2%)	0 (0%)	1 (0.1%)	
Unfractionated heparin				
No	531 (99.3%)	129 (96.3%)	660 (98.7%)	0.019
Yes	4 (0.7%)	5 (3.7%)	9 (1.3%)	
Dabigatran				
No	534 (99.8%)	134 (100%)	668 (99.9%)	1.000
Yes	1 (0.2%)	0 (0%)	1 (0.1%)	
Combined (ASA+enoxaparin)				
No	497 (92.9%)	115 (85.8%)	612 (91.5%)	0.009
Yes	38 (7.1%)	19 (14.2%)	57 (8.5%)	
ASA use				
No	494 (92.5%)	113 (84.3%)	607 (90.9%)	0.003
Yes	40 (7.5%)	21 (15.7%)	61 (9.1%)	
Plavix				
No	532 (99.6%)	133 (99.3%)	665 (99.6%)	0.490
Yes	2 (0.4%)	1 (0.7%)	3 (0.4%)	
ASA+Plavix				
No	534 (99.8%)	133 (99.3%)	667 (99.7%)	0.361
Yes	1 (0.2%)	1 (0.2%)	2 (0.3%)	

The overall confirmed incidence of VTE was 12 in 669 patients (1.8%, 95% CI: 0.9-3.0). VTE occurred in 8 of the 134 patients (6%, 95% CI: 2.2-10.4) who underwent simultaneous bilateral TKA and in 4 of the 535 patients (0.7%, 95% CI: 0.2-1.5) who underwent single unilateral TKA. The odds ratio of confirmed symptomatic VTE was 8.42 (95% CI: 2.49-28.4; p=0.001). PE was diagnosed in 6 of 134 patients (4.5%) who underwent simultaneous bilateral TKA and in 3 of 535 patients (0.6%) who underwent single unilateral TKA. DVT was diagnosed in 2 of 134 patients (1.5%) who underwent simultaneous bilateral TKA and in 1 of 535 patients (0.2%) who underwent single unilateral TKA. All VTE cases were diagnosed during hospital admission at a median postoperative interval of 4.5 days and there were no reports of bleeding as a complication.

None of the age, gender, BMI, type of anesthesia, blood transfusion, or dosage of enoxaparin (40 mg once daily versus 30 mg twice daily) was found in univariate analysis to be a predictor of VTE following TKA.

DISCUSSION

In this retrospective study, 669 patients with a mean age of 64.4 years and female predominance underwent single unilateral TKA and simultaneous bilateral TKA. The overall incidence of PE and DVT was 1.8% (12 events, 95% CI: 0.9-3.0). The odds ratio for VTE was 8 times higher in patients who underwent simultaneous bilateral TKA than in those who underwent single unilateral TKA. PE and DVT accounted for 2 in 3 and 1 in 3 VTE incidents, respectively. In this study, there was no fatal PE or major bleeding complication. Almost all the patients received venous thromboprophylaxis using LMWH, particularly enoxaparin. Mechanical thromboprophylaxis in the form of IPC or GCS was not used in our study population and all VTE cases were diagnosed during hospital admission.

The results of the study by Memtsoudis, et al., on the incidence of VTE after knee arthroplasty in 670,305 patients, were similar to ours. The study found that the incidence of VTE after simultaneous bilateral TKA was significantly higher than after single unilateral TKA (1.2% versus 0.72%, p<0.001) [15]. Barrett, et al., found that the incidences of PE after simultaneous bilateral TKA and single unilateral TKA in 104,389 patients were 1.44% and 0.8%, respectively (hazard ratio: 1.81; 95% CI: 1.49-2.20) [16]. In a case-control study of 365 patients who underwent simultaneous bilateral TKA and single unilateral TKA, the overall incidence of VTE was 1.9% (7 of 365 patients) and all the affected patients had undergone simultaneous bilateral TKA [17]. In a prospective observational study including patients who underwent total knee and hip arthroplasties, the incidence of symptomatic VTE was 2.8% in patients who underwent TKA [7]. However, DVT, rather than PE, accounted for the majority of the VTE cases. A large

retrospective study including 3,667 patients reported that the incidence of in-hospital PE after knee arthroplasty was 0.8%, which is consistent with reports of earlier studies [18]. The incidences of PE following single unilateral TKA and simultaneous bilateral TKA were reported to be 0.62% and 1.9% ($p<0.001$), respectively. The diagnosis of PE after arthroplasty has increased from 0.2% to 1.7% since the introduction of multidetector computed tomography [19]. PE was diagnosed in all the patients in our study using CTPA, which could explain the higher incidence of PE in our study compared to the earlier studies.

In contrast to this study, a retrospective analysis of 216 patients (72 underwent simultaneous bilateral TKA while 144 underwent single unilateral TKA) showed that the incidence of VTE was similar in both patient groups at 1.4% in patients who underwent simultaneous bilateral TKA and 2% in patients who underwent single unilateral TKA ($p=0.7$) [2]. A study that compared the complications of simultaneous bilateral TKA and single unilateral TKA in 462 patients did not show differences in the incidence of VTE between the patient groups [12]. In 2 other studies, no differences were found in the incidences of PE and DVT following simultaneous bilateral TKA and single unilateral TKA [20,21].

Our study results are consistent with those of large cohort studies that indicate that the risk of VTE, which includes PE and DVT, is probably at least 2 times higher after simultaneous bilateral TKA than after single unilateral TKA. However, these studies did not indicate the type or duration of the thromboprophylaxis regime. The ACCP and the American Academy of Orthopedic Surgeons released guidelines for VTE prevention in patients undergoing major orthopedic surgeries but there were no specific recommendations for patients undergoing TKA [4,22].

The limitations of this study include its retrospective design, that it was conducted in a single tertiary care center and the relatively low number of VTE events that prevented sub-analysis to identify the risk factors of VTE after simultaneous bilateral TKA and single unilateral TKA.

CONCLUSION

The incidence of VTE is higher after simultaneous bilateral TKA than after single unilateral TKA. Large prospective studies are needed to identify the risk factors of VTE and determine the appropriate thromboprophylaxis regime in high-risk knee arthroplasty patients.

DECLARATIONS

Conflict of Interest

The manuscript has no influence on the conflict of interest from all authors regarding the publication of the article.

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