Original article

Impact of anesthesia modality and mechanical venous thromboembolism prophylaxis on the incidence of symptomatic deep venous thrombosis after TKA[☆]

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ABSTRACT

Background: Venous thromboembolic events (VTE) are a common complication of total knee arthroplasty (TKA). Prior studies have discussed the utility of mechanical VTE prophylaxis as a monotherapy for low-risk TKA patients. We assess the incidence of clinically significant deep venous thrombosis (DVT) or pulmonary embolism (PE) in low-risk TKA patients who receive mechanical VTE prophylaxis and undergo spinal, epidural, or general anesthesia for their surgery.

Methods: A retrospective study was performed on consecutive low-risk patients who received a TKA between July 2002 and June 2015 with spinal anesthesia ($n = 65$), epidural and general anesthesia ($n = 154$), or general anesthesia alone ($n = 152$). Patients with spinal anesthesia had mechanical VTE prophylaxis until 15 h postoperatively, when remobilization was permitted. Patients who received epidural or general anesthesia had mechanical VTE prophylaxis for 2 h postoperatively. Notable outcomes included development of clinically symptomatic DVT or PE, patient demographics, and perioperative lab values. Statistical analysis was performed using SPSS 22, with chi-squared and Fisher's exact tests for categorical variables and the Kruskal–Wallis test with Scheffe's method for continuous variables.

Results: No clinically symptomatic DVT or PE was diagnosed. Patient demographics were equivocal. A statistically significant decrease in prothrombin and activated partial thromboplastin times were noted in the general anesthesia group, but all measurements were within the normal range.

Conclusions: A short course of mechanical VTE prophylaxis may be appropriate for low-risk patients who can immediately mobilize.

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1. Introduction

Total knee arthroplasty (TKA) is a successful procedure that significantly improves the quality of the patient's life. Venous thromboembolic events (VTEs) are common complications of TKAs. Postoperative VTEs can be prevented through the utilization of pharmacologic agents and mechanical devices, although an ideal method for thromboprophylaxis does not exist.

Intermittent pneumatic compression devices such as the venous foot pump have been found to decrease venous stasis, accelerate the emptying of the venous system,¹ release endothelial-delivered relaxing factor,¹ and increase systemic and local fibrinolysis.² Some papers hypothesized that patients with no risk factors, who can be mobilized early,^{3,4} or who are using risk stratification^{5,6} could be managed with the use of mechanical methods of prophylaxis alone. However, two papers reported negative outcomes of intermittent plantar compression alone on the prevention of VTEs in patients undergoing TKAs.^{7,8}

Anesthesia may be one of the factors that necessitate VTE prophylaxis. Regional anesthesia was reported to improve total hip arthroplasty and TKA patient outcomes in a recent meta-analysis, which included a reduced incidence of VTEs.⁹ Some papers compared the antithrombotic efficacies of epidural,^{10,11} spinal,¹² and general anesthesia in TKAs. To the best of our knowledge, no

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comparison of the complications of VTEs between these three kinds of anesthesia has been conducted.

The purpose of the present study is to retrospectively evaluate the effects of spinal, epidural, and general anesthesia on the incidence of symptomatic deep venous thromboses (DVT) and pulmonary embolisms (PE) of consecutive low-risk primary TKA patients during the 6-month perioperative period who were treated with mechanical compression devices alone. Our hypothesis is that regional anesthesia might lead to better outcomes with respect to the incidence of symptomatic DVTs and PEs in those TKA patients who were low risk and treated with mechanical compression devices alone.

2. Materials and methods

From July 2002 to June 2015, 301 consecutive patients (372 knees) underwent primary hybrid TKAs (cemented tibia, un-cemented femur) with 6-month post-operative follow-up. One patient (1 knee) was excluded from this study because he died after an unexpected accident 2 months after surgery. Our local institutional review board approved this study. Informed consent was waived by the institutional review board because of the retrospective study design.

The anesthesia technique changed over time. The initial 65 knees received spinal anesthesia (SA). The next 154 knees received an epidural plus general anesthesia (EGA). The final 152 knees received general anesthesia alone (GA). All patients were considered low risk, as all of them were categorized as American Society of Anesthesiologists (ASA) Class I or II, and did not have a history of a DVT. Sixty-two patients took aspirin, aspirin-containing compounds, or any other antiplatelet medication. They were asked to discontinue taking these drugs 7 days before surgery and they started taking them again 3 days after surgery. The clinical characteristics of the patients in each anesthesia treatment group are summarized in Tables 1 and 2.

The New Jersey LCS total knee system (DePuy, Warsaw, IN, USA) was used on all patients. All TKAs were performed using a unilateral procedure. An MT-720 tourniquet system (Mizuho-Ika, Tokyo, Japan),¹³ which adjusts its pressure in synchrony with the systolic blood pressure (SBP), was used to prevent excessive intraoperative hemorrhage. The tourniquet was initially inflated based on the SBP recorded before the skin incision, and it maintained a pressure 100 mmHg greater than the systolic blood pressure of the patient during surgery. One senior surgeon (YI) performed all TKAs using a standardized technique, including the necessary soft tissue releases for proper gap balancing. The surgical technique that was employed is described in detail in a previous report.¹⁴ A bulky compression

Table 1
Patient demographic and surgical characteristics.

Anesthesia (knees) Mean (SD)	Spinal (65)	General + epidural (154)	General (152)	p value
Gender (male/female)	8/57	24/130	21/131	0.836
Age (year)	73 (7)	72 (7)	73 (8)	0.867
Diagnosis (OA/RA)	63/2	145/9	149/3	0.227
Body length (cm)	151 (7)	152 (7)	151 (7)	0.678
Body weight (kg)	58 (9)	59 (11)	61 (12)	0.270
BMI (kg/m ²)	25 (3)	25 (4)	26 (4)	0.084
Anesthesia time (min)	84 (12)	84 (13)	90 (12)	<0.001*1
Op time (min)	52 (9)	56 (12)	57 (10)	0.020*2
Tourniquet time (min)	56 (9)	59 (11)	59 (10)	0.076
Anticoagulation (yes/no)	10/55	23/131	29/123	0.620
Smoker (yes/no)	3/62	10/144	9/143	0.958
ASA* grade (I/II)	7/58	21/133	20/132	0.897

OA: osteoarthritis; RA: rheumatoid arthritis; BMI: body mass index; ASA*: American Society of Anesthesiologists.

*1 Spinal vs general, $p < 0.001$; general + epidural vs general, $p < 0.001$.

*2 Spinal vs general, $p = 0.003$.

Table 2

Preoperative coagulative and serum laboratory values.

Variables	Spinal	General + epidural	General	p value
RBC ($\times 10^4/\mu\text{l}$)	421 (42)	426 (42)	431 (38)	0.270
Ht (%)	40.2 (3.9)	39.9 (3.9)	40.4 (3.6)	0.468
Hb (g/dl)	13.2 (1.6)	12.9 (1.4)	13.3 (1.3)	0.285
Platelets ($\times 10^4/\mu\text{l}$)	23.3 (6.0)	24.1 (6.8)	24.0 (5.0)	0.555
TP (g/dl)	7.3 (0.5)	7.2 (0.5)	7.3 (0.5)	0.469
TG (mg/dl)	136 (66)	144 (87)	141 (71)	0.774
T-Chol (mg/dl)	208 (31)	207 (32)	209 (34)	0.988
PT (s)	11.1 (1.1)	11.2 (0.6)	10.5 (0.6)	<0.001*1
APTT (s)	28.1 (3.7)	28.0 (3.1)	27.1 (3.3)	0.009*2

RBC: red blood cell count; Ht: hematocrit; Hb: hemoglobin; TP: total protein; TG: tri-glyceride; T-Chol: total cholesterol; PT: prothrombin time; APTT: activated partial thromboplastin time.

*1 Spinal vs general, $p < 0.001$; general + epidural vs general, $p < 0.001$.

*2 General + epidural vs general, $p = 0.013$.

dressings was applied. The venous foot pump device (A-V impulse system, Novamedix Ltd., Andover, UK) was applied to both feet of all patients and started immediately after they returned to the ward. The device was maintained until the patient's first dressing change (approximately 15 h) on the first postoperative day in the SA group, or until clear mentation was confirmed approximately 2 h postoperatively in the EGA and GA group. After taking off the foot pump, all patients were asked to continue self-directed exercises of the ankle joint and toes to prevent venous thrombosis of the calf and plantar regions.

The postoperative treatment included the drop and dangle technique described by Kumar et al.¹⁵ After the first dressing change on the first postoperative day, weight-bearing as-tolerated with a cane was permitted under the supervision of a therapist, and the additional exercises as below were allowed. Passive range of motion (ROM) exercises were performed daily beginning 1 week after surgery. Patients received at least 2 h of daily physical therapy that consisted of isometric exercises, passive ROM, active-assisted ROM, quadriceps and hamstring strengthening, and gait training including ascending and descending stairs. Functional electrical stimulation was used in all patients.

The incidence of symptomatic DVTs and PEs was retrospectively evaluated using chart notes written at the time of discharge, 1, 3, and 6 months postoperatively. A DVT was considered clinically symptomatic when increased swelling, tenderness and redness over what one would expect following a TKA was noted. A symptomatic PE was characterized by unexpected tachypnea, tachycardia, a drop in blood pressure, or acute anemia.

2.1. Statistical analysis

The rate of symptomatic DVTs or PEs was compared between the three anesthesia techniques using the chi-square and Fisher's exact test. Before the study, the required sample size for the study was estimated using a power analysis with a power level of 0.8 and a small effect size of 0.2 at an α -level of 0.05. It was estimated that a total of 241 samples were required for this study. After a large enough number of patients could be recruited, the incidence of symptomatic DVTs or PEs was compared between the three groups. After the study, a post hoc power analysis was performed based on the sample size.

Patient demographics were compared between three groups using the chi-square and Fisher's exact test for discrete variables, and the Kruskal–Wallis test with Scheffe's method for multiple comparisons of continuous variables. Continuous variables were expressed as a mean and standard deviation. All statistical analyses were performed using SPSS Statistics 22 (IBM Japan Ltd., Tokyo, Japan).

3. Results

Although all patients had various degrees of swelling, tenderness and redness of their surgical knees, this improved during the 6 months following their TKA. No clinically symptomatic DVTs or PEs were noted in any patient at discharge, 1, 3, or 6 months postoperatively. There was therefore no statistically significant difference in the incidence of DVTs or PEs between the three groups.

Demographics were similar between the three groups except for anesthesia time and operative time, which showed statistically significant differences between three groups (Table 1). Regardless, the mean operative and tourniquet times of the three groups were less than 1 h.

With respect to preoperative coagulative and serum laboratory values, the prothrombin (PT) and the activated partial thromboplastin (APTT) times were significantly different among the three groups (Table 2). However, these values all fell within the normal range, since the normal range for the PT is 9.4 and 12.2 min, and the normal APTT range is between 25.1 and 39.8 min.

A post hoc power analysis calculated a power of 0.94 based on the existing sample sizes.

4. Discussion

The most important finding in this study is that no clinically symptomatic DVT or PE was noted in any anesthesia group at discharge or at the 1, 3, and 6 month postoperative follow-up. Since we believe that the prevention of fatal pulmonary emboli, not asymptomatic deep vein thrombosis, is the main goal of prophylaxis against postoperative thromboembolic complications, isolated mechanical thromboembolic prophylaxis for low risk patients might be recognized as safe and effective following a TKA.

Regarding anesthesia for patients undergoing a TKA, two prior papers compared the antithrombotic efficacy of epidural anesthesia vs GA^{10,11} and SA vs GA¹² in TKA surgeries. Regional anesthesia had a better antithrombotic efficacy than GA in these papers. The authors proposed possible reasons for the positive effect of regional anesthesia against symptomatic DVT and PE, which included altered coagulability, an increased volume of blood flow to the lower limbs, an improved ability to breathe without pain, and a reduced surgical stress response^{16,17} when compared with GA. According to the current study, no advantage of any anesthesia technique was noted with regard to the incidence of symptomatic DVTs and PEs. Pugely et al.¹² reported that patients who underwent TKA with GA had a small but significant increase in the complication rate compared with patients who were managed with SA. However, their observed differences were <1%, and the clinical importance of such a small gap is therefore not clear. The difference in complications was greatest for patients with multiple comorbidities, and spinal anesthesia may have a greater benefit in that group. It is therefore important to recognize that general anesthesia remains a reasonable choice for many patients who receive a TKA. Since the patients in this study were lower risk without serious comorbidities, these differences might not be evident.

Patients undergoing TKA could be managed with the use of mechanical methods of prophylaxis alone.^{3–6} The duration and frequency of the application of mechanical VTE varied from 2 to 14 days,^{4,5,18} which was reported as the length of hospital stay. However, considering that the incidence of venous thrombosis following a unilateral TKA was diagnosed in 86% of affected patients during the first 24 h,¹⁹ the effectiveness of the longer application of mechanical VTE remains controversial. In this study, the venous foot pump device was applied and started upon the patient's return to the ward, and maintained until the first dressing change (approximate 15 h) on the first postoperative day in the SA

group, and until 2 h postoperatively in the EGA and GA group. Taking into account that no symptomatic DVT or PE was diagnosed in any group, the application of a foot pump during the first 2 h postoperatively might be enough only if it was followed by self-directed exercises of the ankle joint and toes, and full weight-bearing on the first postoperative day. An early mobilization protocol that allows full weight-bearing might play a similar role to the continuous foot pump during the hospital stay, since the foot pump was originally developed to reproduce the longitudinal stretching of a large venous plexus in patients who are unable to bear weight.¹ Furthermore, a major criticism of pneumatic compression has been the lack of patient compliance.²⁰ Charalambous et al.²¹ reported on the gradual decline in the effective utilization rate of mechanical VTE that occurs as time passes after an operation. They suggest that foot pumps should be used in the first 24 h post-operatively when the patient is confined to the bed and the risk of bleeding from the surgical wound is high.

Finally, various risk factors for DVTs in patients receiving a TKA have been reported, such as a history of DVT or blood clots,^{5,22–24} female gender,^{7,8,25} increased BMI,^{4,23,25} a longer operative or tourniquet time,^{25,26} bilateral simultaneous surgeries,^{18,25,27} prolonged immobilization,²⁵ hyperlipidemia,²³ and the Caucasian population.^{4,28} This suggests the presence of genetic factors when assessing patient predisposition for a DVT. Since few patients in this study had these risk factors, it may be expected that no clinically symptomatic DVT and PE may occur.

There are several limitations to this study. First and foremost, this was a retrospective chart and database review, which has inherent limitations. Second, this study did not use a randomized design, and instead relied on consecutive cases stratified by the three kinds of anesthesia that were employed. However, the baseline patient characteristics of each group, including preoperative laboratory blood testing, seemed to be comparable. In addition, the number of patients analyzed is relatively small, although their numbers were sufficient to detect a significant correlation between anesthesia techniques, as indicated by our post hoc power analysis. Third, the mechanical prophylaxis times between the spinal, epidural + GA, and GA alone groups were different, although ideally it should be consistent to evaluate the effects on the clinical outcomes in each anesthesia group. Furthermore, we did not perform either standard Doppler ultrasonography or venography to detect asymptomatic DVTs. This is because no patients developed clinical findings that led us to suspect the presence of symptomatic DVT or PE during the follow-up period. The usefulness of routine postoperative screening for DVTs after TKA is controversial.²² In this series, taking into account various degrees of swelling, tenderness, and redness of the patient's operative knee, we acknowledge that asymptomatic DVTs may have developed. However, we believe that such DVTs might have spontaneously resolved without progressing to a symptomatic DVT or a fatal pulmonary embolus. Previous studies support this speculation. Kim et al.^{4,23,28,29} reported that all calf thrombi, regardless of their site or size, resolved completely and spontaneously without causing symptomatic PE. In addition, other reports have suggested that thrombi in the calf, whether large or small, are unlikely to produce symptomatic PE. Therefore, these patients do not require anticoagulation.^{30–32} To the best of our knowledge, this is the first study to evaluate the effects of three kinds of anesthesia on the incidence of symptomatic DVTs and PEs in patients who underwent a primary TKA, were classified as low risk, and treated with only mechanical compression devices.

5. Conclusions

In conclusion, the mechanical compression device might be sufficient to prevent the development of a symptomatic DVT in

lower risk patients who undergo a TKA using any of the three kinds of anesthesia discussed here, although we recognize that the current study concerned a specific population based on ethnicity. We agree with the perspective of Callaghan et al.²² that the surgeon's experience and discretion appear to be the most essential component in establishment of an individual postoperative DVT prophylaxis protocol. The current study suggests that prophylaxis using only a mechanical device should be recognized as an appropriate protocol for low-risk patients who undergo a primary TKA, although exclusion of chemoprophylaxis is not accepted by a large number of surgeons at the present time.

Ethical review committee statement

The local institutional review board approved this study. All patients provided informed consent.

Conflicts of interest

The authors have none to declare.

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