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Aspirin versus rivaroxaban in postoperative bleeding after total knee arthroplasty: a retrospective case-matched study

Varah Yuenyongviwat[1] · Pakjai Tuntarattanapong[1] · Chaiwat Chuaychoosakoon[1] · Chavalit Iemsaengchairat[2] · Khanin Iamthanaporn[1] · Theerawit Hongnaparak[1]

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Abstract

Background Venous thromboembolic disease (VTE) is a complication not uncommon following total knee arthroplasty. Postoperative bleeding-related complications are a concern in many guidelines. The authors aimed to compare the amount of postoperative drainage from closed suction drainage, transfusion rate, and postoperative complications between aspirin and rivaroxaban as VTE prophylaxes after total knee arthroplasty.

Methods This study was a retrospective case-matched study of 155 patients. The data were collected between 2008 and 2015 from patients who had total knee arthroplasty using aspirin or rivaroxaban as the VTE prophylaxis. Seventy-nine patients received aspirin, and 76 patients received rivaroxaban. A single surgeon operated on all patients with the same surgical technique and patient care protocol.

Results The total closed suction drainage outputs at 48 h were not significantly different between the aspirin and rivaroxaban groups ($p = 0.10$). Eighteen percent of patients in the aspirin group and 25% of patients in the rivaroxaban group received blood transfusions ($p = 0.37$). There were no bleeding-related complications or VTE in either group.

Conclusions Aspirin and rivaroxaban were effective and safe as VTE chemoprophylaxis in total knee arthroplasty.

Keywords Total knee replacement · Aspirin · Rivaroxaban · VTE

Abbreviations

VTE	Venous thromboembolic disease
BMI	Body mass index (BMI)
ASA classification	The American Society of Anesthesiologists classification

✉ Varah Yuenyongviwat
varahortho@gmail.com

Pakjai Tuntarattanapong
suttop@hotmail.com

Chaiwat Chuaychoosakoon
chaiwat.c@psu.ac.th

Chavalit Iemsaengchairat
st_bank@hotmail.com

Khanin Iamthanaporn
ikhanin@psu.ac.th

Theerawit Hongnaparak
theerawit.h@gmail.com

[1] Department of Orthopedics, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand

[2] Department of Orthopedics, Ratchaburi Hospital, Ratchaburi 70000, Thailand

Introduction

Total knee arthroplasty is a very successful operation. Total knee arthroplasty during the last 20 years has become increasingly common [1]. However, venous thromboembolic disease (VTE) is not an uncommon complication following total knee arthroplasty. VTE can affect the postoperative outcome and can be fatal from pulmonary embolism [2, 3]. The most recent recommendations for VTE prophylaxis include patient evaluation, a mechanical compressive device, and pharmacological agents [4]. Pharmacological agents that claim to decrease VTE events include aspirin, warfarin, dabigatran, low molecular weight heparin, and rivaroxaban [5, 6]. However, there is no consensus on which one is the best pharmacological agent for VTE prophylaxis.

Postoperative bleeding-related complications such as wound hematoma, major organ bleeding, or wound infection in patients who take a VTE prophylactic agent are a concern in the American Academy of Orthopaedic Surgeons (AAOS) guideline [7]. Aspirin is used in the AAOS guideline for VTE prevention especially in patients who have elevated risk of bleeding [8]. The use of aspirin is also supported by

much evidence which showed a decreased rate of VTE after total joint arthroplasty [9, 10].

Oral factor Xa inhibitors, including rivaroxaban, are increasingly popular and used widely by many surgeons for VTE prophylaxis because of ease of use by oral administration and no need to monitor blood coagulation. Rivaroxaban was reported to be effective in VTE prevention, but concerns were raised related to bleeding complications, such as wound hematoma which requires further surgical removal or major organ bleeding [11].

In a previous study, all patients who received rivaroxaban on days 1–5 were then randomized into two groups on day 6 to receive either rivaroxaban or aspirin. The results found no difference in postoperative bleeding or complications [12].

However, there is limited evidence on postoperative bleeding and complications that compare aspirin to rivaroxaban started on the day after the operation. We hypothesized that patients who use aspirin for VTE prophylaxis started on the day after the operation should have less bleeding and fewer complications compared to rivaroxaban after total knee arthroplasty.

Materials and methods

This study was a retrospective case-matched study. The data were extracted from the electronic hospital database of patients who had total knee arthroplasty by a single surgeon between January 2008 and December 2015. Between January 2008 and December 2011, the surgeon used rivaroxaban for VTE prophylaxis, and between January 2012 and December 2015, aspirin was used for VTE prophylaxis in all patients who had no contraindication to anticoagulants such as coagulation disorder or active bleeding in the gastrointestinal tract or hemorrhagic stroke. This study was approved by the local Ethics Committee and Institutional Review Board. The recruited patients were those who had total knee replacement for primary osteoarthritis and used aspirin or rivaroxaban. The exclusion criteria were patients who used an anticoagulant prior to total knee replacement, history of coagulation disorder, previous knee surgery, preoperative hematocrit less than 30%, history of myocardial infarction, and chronic renal or liver disease. Finally, the study patients were placed into either the aspirin group or rivaroxaban group.

A single surgeon operated on all patients with the same surgical technique and patient care protocol. The surgeon used the medial parapatellar approach in all patients. A cemented posterior stabilized total knee prosthesis [NexGen® Complete Knee Solution Legacy® Posterior Stabilized (LPS) LPS-Flex Fixed Knee Bearing; Zimmer Inc., Warsaw, IN, USA] was used in all patients. A pneumatic tourniquet was inflated throughout the operation from the initial incision until skin closure with 350 mmHg of pressure. Prophylaxis antibiotic was injected 30 min before the initial incision (cefazolin or clindamycin in the case of penicillin or cephalosporin allergy). Intramedullary guide was used for the femoral cut. The proximal tibia was cut with an extramedullary guide. A closed suction drain was applied before capsular closure.

The patients received one paracetamol (500 mg) tablet every 6 h and an intravenous injection of morphine (3 mg) every 3 h for pain control if the patient had a verbal numerical pain score more than 4. A daily prescription of one 300-mg tablet of aspirin or one 10-mg tablet of rivaroxaban was prescribed the day after the operation until 14 days after surgery. Quadriceps isometric exercise and ankle pumping were done immediately after the operation. Rehabilitation protocol for range of motion exercise and ambulation with a walker was applied on the day after the operation. Closed suction drainage was placed for 48 h after the operation, and the drainage outputs were recorded every 8 h. The patients received blood transfusion if the hematocrit was less than 30% and the patient had symptoms of anemia. The patients were followed up at day 14 and at 6 weeks after surgery for a clinical evaluation and for any signs of complications. The patients who were clinically suspected of deep vein thrombosis, such as unilateral swollen limb and pain, received duplex ultrasonography for a definite diagnosis of deep vein thrombosis. Spiral chest computed tomography was performed in patients who had blood oxygen desaturation and were suspected of pulmonary embolism.

Statistical analyses

R version 3.1.0 software (R Foundation for statistical computing, Vienna, Austria) was used to analyze the data. Patient demographic data, such as age, weight, height, body mass index (BMI), preoperative hemoglobin level, preoperative hematocrit, platelet count, and operative times, were evaluated between the groups with independent t test. Pearson's χ^2 test was used for comparisons of patient sex, side of operation, American Society of Anesthesiologists (ASA) classification, and transfusion rates. Closed suction drainage output was evaluated with the Mann–Whitney U test. Statistical significance was assumed when $p < 0.05$.

Demographics and description of study population

A total of 155 patients met the study criteria. Aspirin and rivaroxaban were used as the VTE prophylactic agents in 79 and 76 patients, respectively. There were no differences in the patient demographic data between the two groups (Table 1). There were no significant differences in patient age, sex, side of operation, body weight, height, BMI, ASA classification, preoperative hemoglobin level,

Table 1 Demographic data

Characteristic	Group 1 (aspirin) $N=79$	Group 2 (rivaroxaban) $N=76$	p value
Age (years)	70.08 ± 5.22*	71.41 ± 6.17*	0.15
Sex (male/female)	10:69	9:67	0.88
Side (right/left)	35:44	37:39	0.59
Weight (kg)	66.79 ± 11.7*	65.7 ± 9.18*	0.28
Height (cm)	152.32 ± 8.29*	153.61 ± 6.46*	0.11
BMI (kg/m^2)	28.82 ± 4.03*	27.73 ± 4.04*	0.09
ASA classification (II/III)	67:12	67:9	0.54
Pre-op hemoglobin (g/dL)	12.68 ± 1.49*	12.26 ± 1.31*	0.07
Pre-op hematocrit (%)	38.90 ± 4.49*	37.64 ± 3.62*	0.06
Platelet count (× 10^3/μL)	254.25 ± 66.99*	270.49 ± 65.06*	0.13
Operative time (min)	117.15 ± 22.11*	120.06 ± 17.23*	0.52

*Values are expressed as mean ± SD unless indicated otherwise

Table 2 Closed suction drainage output

Characteristic	Aspirin group $N=79$	Rivaroxaban group $N=76$	p value
0–8 h	145 (92.5–295)	160 (100–290)	0.29
8–16 h	115 (70–198.75)	110 (80–200)	0.61
16–24 h	50 (40–83.75)	70 (30–100)	0.25
24–48 h	90 (60–137.5)	70 (30–120)	0.04
Total drainage	490 (372.5–600)	540 (410–695)	0.10

Data are shown as median (interquartile range) (mL)

preoperative hematocrit, platelet count, or operative time between the two groups.

Closed suction drainage output at 0–8 h, 8–16 h, and 16–24 h was not significantly different between the aspirin group and the rivaroxaban group ($p=0.29$, 0.61, and 0.25, respectively). The authors found that the aspirin group had a median drainage output of 90 mL (interquartile range 60–137.5) at 24–48 h which was significantly higher than the rivaroxaban group which was 70 mL (interquartile range 30–120) ($p=0.04$). However, the total drainage amounts were not significantly different between the two groups ($p=0.10$) (Table 2).

Blood transfusions were received in 18.99% (15/79) of the patients in the aspirin group and in 25% (19/76) of the patients in the rivaroxaban group. However, this difference was not statistically significant ($p=0.37$).

There were no bleeding-related complications, such as wound hematoma, which required further treatment or any major organ bleeding in any of the cases. There was no incidence of deep vein thrombosis or pulmonary embolism in either group. However, there was a superficial wound infection in one patient in the aspirin group which was treated successfully with dressing and oral antibiotic.

Discussion

There are many pharmacological agents that can prevent VTE after total knee arthroplasty. Aspirin is recommended by the AAOS as the VTE chemoprophylactic agent [13]. One systematic review and meta-analysis stated that patients using aspirin as the VTE chemoprophylactic agent had a low rate of VTE and low risk of major bleeding complications [9]. Aspirin was also a cost-effective VTE chemoprophylactic agent because of low cost and effective VTE prevention [14].

Rivaroxaban was approved as an effective VTE chemoprophylaxis agent by the National Institute of Clinical Excellence and the American College of Chest Physicians [15, 16]. A report showed that rivaroxaban could significantly reduce symptomatic VTE. However, the complication of major bleeding was the major concern of this medication [11].

Our study showed that the total amounts of closed suction drainage output were not different between the aspirin and rivaroxaban groups. Similarly, a randomized study by Colleoni et al. [17], that compared aspirin and rivaroxaban for VTE prophylaxis in 32 patients with total knee arthroplasty, reported no differences between the 24-h and 48-h drainage outputs. Blood transfusion rates in our study were lower in the aspirin group compared with the rivaroxaban group without statistical significance. A previous study by Bala et al. [18], that compared the effectiveness and safety of four anticoagulants for VTE prophylaxis, found that aspirin had the lowest incidence of blood transfusion followed by factor Xa inhibitors, warfarin, and enoxaparin (7%, 9%, 12%, and 13%, respectively).

The incidences of postoperative VTE were not different between the groups in our study. However, this contradicted the results of previous studies. Bala et al. [18] reported that the incidences of deep vein thrombosis and pulmonary

embolism were the lowest with factor Xa inhibitors compared with aspirin, warfarin, and enoxaparin. Also, Zou et al. [19] found factor Xa inhibitors had the lowest rate of deep vein thrombosis compared with aspirin and low molecular weight heparin.

The authors found in this study that the incidence of bleeding-related complications was the same in the aspirin and rivaroxaban groups. This result was supported by previous studies that reported no differences in the incidence of bleeding-related complications between aspirin (1.2%), factor Xa inhibitors (1.4%), warfarin (1.5%), and enoxaparin (1.5%) [18]. Also, a study by Zou et al. [19] found no bleeding-related complications in patients who used aspirin, factor Xa inhibitors, or low molecular weight heparin as a VTE chemoprophylactic agent.

This study has some limitations. First, this study was a retrospective study in which the patients were not randomized and the patients and evaluator were not blinded. However, the authors tried to decrease bias by selecting the patients of a single surgeon who used the same surgical technique and patient care protocol during the study period. Furthermore, all of the electronically recorded data were easily tracked with a limited amount of lost data. Second, the incidence of complications in this study was reviewed from the outpatient records; therefore, some complications were possibly not mentioned in the outpatient record form. Finally, the authors could not determine patient compliance with the intake of the prescribed aspirin or rivaroxaban.

Conclusions

This study found no differences in drainage output from closed suction drainage, rate of blood transfusion, incidence of VTE event, or bleeding-related complications. Either aspirin or rivaroxaban is an effective and safe VTE chemoprophylaxis in total knee arthroplasty.

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Authors' contributions VY designed the study and performed the analysis and manuscript preparation; TH designed the study and performed the data analysis; PT, CC, and CI collected data; KI designed the study and reviewed the manuscript. All authors read and approved the final manuscript.

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Compliance with ethical standards

Conflict of interests The authors declare that they have no competing interests.

Ethics approval This study was approved by the Ethics Committee and Institutional Review Board of the Faculty of Medicine, Prince of Songkla University (EC 58-261-11-1).

Informed consent Consent was waived by the ethics committee. The hospital gave permission to extract information from the database.

Availability of data and materials The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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