Is Routine Chemical Thromboprophylaxis Necessary in Patients Undergoing Unicompartmental Knee Arthroplasty?

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Abstract
Background This study aimed to determine the prevalence of venous thromboembolism (VTE) in patients undergoing unicompartmental knee arthroplasty (UKA) 3 days and 3 months postoperatively and figure out whether routine chemical thromboprophylaxis was necessary.

Methods The medical records of 146 patients who underwent unilateral UKA at our institution were reviewed. The length of hospital stays after the surgery of the patients was 5.6 ± 2.7 days (3–23 days). All patients underwent pneumatic leg compression, rehabilitation exercises, pain management, and chemical deep vein thrombosis (DVT) prophylaxis from the day of surgery to 3 days after the surgery. From the fourth day to discharge, chemical prophylaxis was stopped. After discharge, only rehabilitation exercises were encouraged. All patients underwent bilateral venography or ultrasound preoperatively and 3 days postoperatively to detect DVT. They completed the follow-up review 3 months after the surgery; 108 patients had ultrasound tests again.

Results DVT was detected in 9 (6.2%) of the 146 patients 3 days after the surgery and in 8 (7.4%) of the 108 patients 3 months after the surgery. No symptomatic or proximal DVT was observed. No patient exhibited pulmonary embolism–related symptoms. After discharge, six DVTs (66.7%) dissolved, and 6 (5.6%) were newly formed. No significant difference in demographics and surgery-related factors was detected between DVT and no-DVT groups at both time points.

Conclusions Routine chemical thromboprophylaxis in patients undergoing UKA with pain management and rehabilitation exercises may not be necessary.

Introduction
Venous thromboembolic (VTE) disease, including deep venous thrombosis (DVT) and pulmonary embolism (PE), is a serious complication after lower limb arthroplasty (1–3). The prevalence of VTE varied in different studies, ranging from 33–46% (4, 5). Given the risk of VTE, thromboprophylaxis remains an important issue. Chemoprophylaxis and mechanical compression were recommended by the American College of Chest Physicians (ACCP) and the American Academy of Orthopaedic Surgeons (AAOS) as two main prophylaxis strategies for VTE after lower limb arthroplasty (6–8). However, the efficacy, safety, and cost of various chemical thromboprophylaxis strategies remain a concern (9, 10).
No consensus exists regarding the duration of chemical prophylaxis (8, 11). It is meaningful to decrease the risk of pharmacologic agents by minimizing their administration to the shortest time without attenuating valid therapeutic benefits.

Unicompartmental knee arthroplasty (UKA) has become increasingly popular nowadays (12). Compared with total knee arthroplasty (TKA), UKA has several advantages such as less invasiveness and faster recovery time. Patients undergoing UKA are generally younger and more active compared with patients undergoing TKA. Actually, the prevalence of symptomatic VTE in patients receiving routine pharmacological thromboprophylaxis after UKA is significantly lower than that after TKA (13). However, no well-accepted recommendation with regard to the length of administration time in patients undergoing UKA has been established. Studies suggested that extended prophylaxis might not be needed, as the majority of PE cases occurred early in the postoperative course (14). This retrospective study was conducted to investigate whether routine chemical thromboprophylaxis was necessary for patients after UKA.

Materials And Methods

Patient selection

This study was approved by the ethical committee of the hospital. The medical records of patients who underwent unilateral UKA between July 2014 and April 2019 at the institution were reviewed. The exclusion criteria were as follows: patients with incomplete demographic data or incomplete thrombus testing outcomes preoperatively or 3 days postoperatively; and patients with preexisting coagulopathy or history of VTE, or newly diagnosed VTE at the preoperative evaluation.

Surgery and postoperative treatment

All patients underwent mobile-bearing UKAs by a standard procedure under general anesthesia using the Oxford partial knee system (Biomet, IN, USA). A tourniquet that inflated to 300 mm Hg was applied during the surgery. No patient received a blood transfusion during or after the surgery. The treatment strategies after the surgery were as follows (Fig. 1). In brief, the patients were encouraged to start rehabilitation exercises, including ankle pump movement, ambulation, muscle strength exercises, and exercises with a gradually increasing range of motion. A pneumatic leg compression
wrapping the legs and feet with inflatable sleeves were continually used during the first 24 h after the patients returned to their wards, and were intermittently applied up to 8 h per day during their stay in the hospital. Further, 10 mg rivaroxaban was administered every night during the first 3 days in the hospital postoperatively. All patients underwent bilateral venography (before September 2015) or ultrasound preoperatively and 3 days postoperatively to detect DVT by two experienced sonographers. Chest computed tomography angiography (CTA) was applied if anyone exhibited the symptoms of PE. Effective pain control was achieved using injectable non-steroidal anti-inflammatory drugs (NSAIDs) Oral opioids were used for rescue analgesia. The rehabilitation exercises were continued after discharge without pneumatic leg compression or any pharmacologic prophylaxis agent. Subsequently, the patients were followed up after 6 weeks, 3 months, 6 months, and 1 year. Besides, every patient had free access to a dedicated phone line of the institution for advice regarding any possible complication and rehabilitation exercise procedures. The third ultrasound test was performed at their second follow-up visit 3 months postoperatively.

Data collection
The demographic data, including age, sex body mass index, and medical comorbidity (hypertension, diabetes mellitus, coronary artery disease, and so on), were collected. The surgical factors, including operation time and tourniquet time, were recorded. Both the whole length of hospital stay and hospital stay after the surgery were recorded. The venography and ultrasound test results were recorded. DVT was classified as either proximal or distal. The thrombus in the femoral, iliac, or popliteal veins was considered proximal.

Statistical analysis
Statistical analysis was performed with IBM SPSS Statistics 16 (IBM Corporation, NY, USA). Descriptive statistics were used to summarize the quantitative variables. Before statistical analysis, the data were tested for normality distribution and homogeneity of variance. The normality distribution was checked with the Shapiro–Wilk test, and the homogeneity of variance was tested using the Levene statistic. Then, the unpaired t test and Mann–Whitney U test were applied according to the result of normality distribution and homogeneity of variance. The statistical significance between differences for each
categorical variable and the statistical significance of VTE incidence between 3 days and 3 months postoperatively were tested using the chi-square ($c^2$) test. A value of $P$ less than 0.05 was considered to be statistically significant for all tests.

**Results**

A total of 146 patients (111 female and 35 male; mean age 64.9 years; range 47–79 years) were included in the present study. All patients underwent venography or ultrasound preoperatively and 3 days postoperatively. All patients accomplished their second follow-up visit 3 months postoperatively, and 108 patients underwent the third ultrasound test at this time point. The other 38 patients refused because no VTE-related symptoms were detected. No chest CTA was applied because no patients had suspicious symptoms.

DVT was detected in 9 (6.2%) of the 146 patients 3 days postoperatively and in 8 (7.4%) of the 108 patients 3 months postoperatively (Fig. 2). No significant difference was observed in the DVT incidence rate between these two time points ($P = 0.6951$). All DVTs were asymptomatic and distal (Fig. 3). After discharge, six DVTs (66.7%) dissolved, and six (5.6%) were newly formed. As for all the demographic and surgical factors, no significant difference was detected between DVT and no-DVT groups at both time points. No significant differences were observed in the length of hospital stay between the two groups (Table 1).

**Discussion**

This study reported an overall prevalence of DVT of 6.2% in patients undergoing UKA using 10 mg rivaroxaban (3 days) for chemical DVT prophylaxis after the surgery during hospitalization. The prevalence of DVT was 7.4% in patients undergoing UKA 3 months after discharge without any specific DVT prophylaxis treatment. No symptomatic DVT or PE was detected during the whole length of hospital stay or the whole 3-month follow-up. No proximal DVT was observed in the present study. The ninth ACCP guideline recommends pharmacologic DVT prophylaxis for Total hip arthroplasty (THA) and TKA for a minimum of 10–14 days and up to 35 days, respectively (8). However, no recommendation was made for the duration of chemical prophylaxis in patients undergoing UKA. It is desirable to reduce the pharmacologic administration period because chemical prophylaxis is
associated with several complications such as infection, wound problems, and hematoma formation (9, 15). A study published in 2016 explored whether routine thromboprophylaxis was necessary for Korean patients undergoing UKA by determining the prevalence of VTE without chemical prophylaxis (16). Their results showed that the overall prevalence of VTE was 26%, although no symptomatic DVT or PE was detected (16). The prevalence of VTE of 26% was higher than the prevalence of VTE of 0–5% following UKA in the present study and some other previous studies (17–19). However, only with symptomatic VTE who received routine pharmacological prophylaxis were evaluated in previous studies (17–19). In this study, the prevalence of VTE was examined among asymptomatic patients. Hence, it was believed that the prevalence of 6.2% and 7.4% in the present study was really low. This study suggested that 3-day chemical thromboprophylaxis was sufficient in patients undergoing UKA. The results showed that six of nine DVTs (66.7%) dissolved 3 months postoperatively after discharge. Previous studies showed the complete resolution of VTEs without thrombolysis in patients after TKA, regardless of size or location (3, 20). The aforementioned study conducted by Korean scholars demonstrated the complete resolution of all VTEs during the postoperative 6-month follow-up (16). Therefore, it was suggested that therapeutic thrombolytic treatment might not be necessary for patients undergoing UKA who had only asymptomatic DVTs. Six of 108 patients (5.6%) were detected with newly formed DVTs 3 months after discharge in the present study. Several studies suggested that VTEs might occur in people without surgery (21, 22). In 2017, a study evaluated 322 patients admitted for TKA and found that 56 patients (17.4%) were diagnosed with preoperative DVT (21). Another study showed that the prevalence of DVT was 8% before TKA (22). The results of the present study suggested that abandoning specific DVT prophylaxis after discharge did not increase the prevalence of VTEs.

The pneumatic leg compression, effective pain management, and rehabilitation exercises, including ankle pump movement, ambulation, range-of-motion exercises, and muscle strength development, also played a pivotal role in DVT prophylaxis after UKA. Several studies emphasized the importance of pneumatic compression (23–25). A study showed that intermittent pneumatic compression might be an effective and safe method for preventing VTE after total hip arthroplasty (23). Another study
demonstrated that intermittent compression applied during exercise could result in increased limb blood flow (24), contributing to DVT prophylaxis. A meta-analysis study including 22 trials revealed that the combination of pneumatic compression and pharmacological prophylaxis could reduce the incidence of symptomatic PE from 2.92–1.20%, compared with pharmacological prophylaxis alone (25). The duration of chemical prophylaxis administration and pneumatic leg compression in the present study was supported by a previous study comprising a large cohort of patients undergoing total joint arthroplasty, which demonstrated that 81% of symptomatic PE cases occurred within the first three postoperative days (26). It was also presumed that rehabilitation played a positive role toward DVT prophylaxis, as vein circulation in the lower limb could be promoted. A study showed that active ankle movements might prevent the formation of lower-extremity DVT after orthopedic surgery (27). One study showed that active movement of the ankle joint yielded better results in DVT prevention compared with passive movement (28). Effective pain management was essential for active rehabilitation exercise.

The present study had several limitations. First was the use of ultrasound in majority of patients to detect DVT. The sensitivity of using ultrasound to detect DVT was between 88% and 100%, although venography was considered the gold standard to detect DVT (29, 30). Ultrasound is technician dependent, which might affect the sensitivity to detect DVT. Both the sonographers in the present study had experience of handling about 2000 cases of DVT each year at the institution. Also, the use of duplex ultrasound was less expensive, less invasive, and more convenient compared with venography. Second was the relatively small sample size. Only 146 patients were enrolled in this study, and all participants were Chinese. A multi-ethnic study enrolling a large number of patients is still needed. Third, a risk screening approach for patient stratification was not used to further diverge the duration of chemical prophylaxis. Further, only one kind of pharmacological thromboprophylaxis agent was used in the present study.

Conclusion
In conclusion, the results of this study suggested that routine chemical thromboprophylaxis might not be necessary in patients undergoing UKA with proper pain management and rehabilitation exercises.
Abbreviations
VTE: venous thromboembolism; UKA: unicompartmental knee arthroplasty; DVT: deep vein thrombosis; PE: pulmonary embolism; ACCP: American College of Chest Physicians; AAOS: American Academy of Orthopaedic Surgeons; TKA: total knee arthroplasty; CTA: Chest computed tomography angiography (CTA); NSAIDS: non-steroidal anti-inflammatory drugs; THA: total hip arthroplasty

Declarations

Ethics approval and consent to participate
The study was approved by the ethical committee of the participating institutions, and informed consent was obtained from all subjects. IRB approval was signed by the corresponding author and all other authors.

Consent for publication
All the authors agree to the publication of this manuscript.

Availability of data and material
Please feel free to contact us for all the raw data or materials we used in the present study.

Competing interests
All authors state that they have no conflict of interest related to this study.

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Authors' contributions
(I) Conception and design: Dongquan Shi, Qing Jiang, Xingquan Xu; (II) Surgery perform: Dongyang Chen, Zhihong Xu; (III) Administrative support: D Shi, Q Jiang; (IV) Collection and assembly of data: Xingquan, Xu, Yao Yao, Jia Xu; (V) Data analysis and interpretation: Wenqiang Yan, Wenjin Yan; (VI) Manuscript writing: Xingquan Xu; (VII) Final approval of manuscript: All authors.

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Table
Table 1. Comparison of demographic and surgical factors between DVT and No-DVT groups
| Variables                                      | 3 Days postoperatively | 3 Months postoperatively |
|-----------------------------------------------|------------------------|--------------------------|
|                                               | DVT (n = 9)            | No-DVT (n = 137)         | P value |
|                                               |                        |                          |         |
| Demographic factors                           |                        |                          |         |
| Age, year                                     | 67 ± 4                 | 65 ± 7                   | 0.3785  |
|                                               | 67 ± 6                 | 65 ± 7                   | 0.3785  |
| No. and proportion of patients aged ≥65 year, | 6 (66.7%)              | 73 (53.3%)               | 0.4351  |
|                                               | 4 (50%)                | 73 (53.3%)               | 0.4351  |
| Sex (female, %)                               | 7 (77.8%)              | 104 (75.9%)              | 0.8990  |
|                                               | 7 (87.5%)              | 104 (75.9%)              | 0.8990  |
| Body mass index, kg/m²                        | 26.5 ± 2.9             | 26.5 ± 3.5               | 0.9912  |
|                                               | 25.7 ± 2.3             | 26.5 ± 3.5               | 0.9912  |
| No. and proportion of patients with           | 1 (11.1%)              | 22 (16.1%)               | 0.6931  |
| body mass index ≥30 kg/m², %                  | 1 (12.5%)              | 22 (16.1%)               | 0.6931  |
| Medical comorbidity (present, %)              | 4 (44.4%)              | 79 (57.7%)               | 0.4379  |
|                                               | 3 (37.5%)              | 79 (57.7%)               | 0.4379  |
| Whole length of hospital stay                 | 11.1 ± 2.3             | 11.0 ± 4.8               | 0.9351  |
|                                               | 9.5 ± 2.2              | 11.0 ± 4.8               | 0.9351  |
| Hospital stay after surgery                   | 5.3 ± 1.6              | 5.6 ± 2.8                | 0.7394  |
|                                               | 5.3 ± 1.5              | 5.6 ± 2.8                | 0.7394  |
| Surgical factors                              |                        |                          |         |
| Operation time, min                           | 100.7 ± 11.8           | 101.9 ± 18.9             | 0.6337  |
|                                               | 99.3 ± 18.8            | 101.9 ± 18.9             | 0.6337  |
| Tourniquet time, min                          | 63.3 ± 10.6            | 63.8 ± 12.1              | 0.6647  |
|                                               | 56.6 ± 11.1            | 63.8 ± 12.1              | 0.6647  |

Figures
| Pre-operation | Venography or ultrasound test (n=146) |
|---------------|-------------------------------------|
| Post-operation (hospitalization) | Operation day to first Day (n=146) | Second day (n=146) | Third day (n=146) | Fourth day to discharge (n=146) |
|               | 1. Rehabilitation exercises          | 1. Rehabilitation exercises          | 1. Rehabilitation exercises          | 1. Rehabilitation exercises          |
|               | 2. Pain management                    | 2. Pain management                    | 2. Pain management                    | 2. Pain management                    |
|               | 3. Pneumatic compression (24 hours)   | 3. Pneumatic compression (8 hours)    | 3. Pneumatic compression (8 hours)    | 3. Pneumatic compression (8 hours)    |
|               | 4. 10mg rivaroxaban per day           | 4. 10mg rivaroxaban                   | 4. 10mg rivaroxaban                   | 4. Venography or ultrasound           |
| Post-discharge | Regular rehabilitation exercises without pneumatic leg compression or any pharmacologic prophylaxis | |
| Follow-up (three-months) | Ultrasound test (n=108) |

**Figure 1**

Scheme of DVT assessment and postoperatively treatment strategies.

**Figure 2**

Incidence of DVT 3 days and 3 months postoperatively.
Figure 3

Characteristics of distal DVTs observed by ultrasound. (A) Ultrasound screening showed hypoechoic signals in the longitudinal view (white arrow). (B) the ultrasound screening showed a hypoechoic signalscan and can not be compressed in the transverse view (white arrow). (C) Little blood flow signal can be visualized on color Doppler ultrasound (white arrow).