Clamping drainage is unnecessary after minimally invasive total knee arthroplasty in patients with tranexamic acid
A randomized, controlled trial
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Abstract

Background: Drainage and tranexamic acid (TXA) have been widely used in total knee arthroplasty (TKA). However, it remains unclear whether it is necessary to clamp the drain after minimally invasive TKA (MIS-TKA) when TXA is used. We therefore conducted a randomized controlled trial to compare the effects of clamping versus not clamping drainage following MIS-TKA in patients in whom TXA was used.

Methods: From January 2015 to December 2015, 121 patients undergoing unilateral primary MIS-TKA were enrolled and randomly divided into 2 groups. In the clamping group (N = 60), drainage was clamped for the 1st 4 postoperative hours. In the nonclamping group (N = 61), drainage was not clamped. All patients underwent a minimivastus approach and received 10 mg/kg TXA intravenously before tourniquet deflation. We recorded the total blood loss, drainage volume, and transfusion requirements in the postoperative period. We also measured the hemoglobin (Hb) and hematocrit (Hct) levels on postoperative days 1, 3, and 5. Other factors, including range of motion (ROM), visual analog scale (VAS), and occurrence of wound-related complications, deep vein thrombosis (DVT), and pulmonary embolism (PE) were recorded at the time of discharge and 1 and 6 months postoperatively. No statistically significant differences were found between the 2 groups with regard to age, gender, weight, BMI, preoperative Hb and Hct levels, preoperative ROM, VAS, duration of surgery, anesthesia method, and the American Society of Anesthesiologists classification.

Results: The clamping group experienced better drainage volume results than the nonclamping group (P < 0.001). There were no statistically significant differences in TBL and transfusion requirements (P = 0.105 and 0.276, respectively); Hb and Hct levels on postoperative days 1, 3, and 5 were similar between the 2 groups. No significant differences were found for ROM, VAS, DVT, PE, wound-related complications, and hospital length of stay in the postoperative follow-up.

Conclusion: Based on our findings, clamping drainage is unnecessary after routine MIS-TKA using TXA.

Abbreviations: DVT = deep vein thrombosis; Hb = hemoglobin; Hct = hematocrit; MIS = minimally invasive surgical; PBV = patient’s blood volume; PE = pulmonary embolism; ROM = range of motion; TBL = total blood loss; TKA = total knee arthroplasty; TXA = tranexamic acid; VAS = visual analog scale.

Keywords: blood loss, complications, minimally invasive, total knee arthroplasty, transfusion

1. Introduction

Osteoarthritis (OA) is the most common form of arthritis that affects approximately 27 million adults in the United States and 25% of the population aged 25 to 74, suffer from OA with pain and deformity.\textsuperscript{11} Total knee arthroplasty (TKA) has become a common orthopedic procedure performed more than 400,000 times each year in the United States.\textsuperscript{2} However, TKA is often complicated by postoperative bleeding, which can lead to significant postoperative anemia and transfusion requirements.\textsuperscript{3,4} Transfusions can carry the risks of immunological reactions, transfusion-associated circulatory overload, transfusion-related acute renal failure, and even death.\textsuperscript{5,6} To date, several methods for controlling bleeding have been successfully employed in an effort to reduce postoperative blood loss and transfusions; these include tourniquets, drain clamping, and tranexamic acid (TXA), among others.\textsuperscript{1,3–7} The routine clamping of drains used in TKA has been advocated by some but remains a controversial topic even among surgeons who still use postoperative drains.\textsuperscript{7,8} Theoretically, clamping the drainage system can result in temporary hemostasis by creating a tamponade effect in the joint, which effectively results in less blood loss, less hemodynamic disturbance, and a lower transfusion rate.\textsuperscript{11} Meanwhile, the use of a nonclamping drainage system is considered to be effective in reducing hematoma formation, postoperative pain and swelling, and resulting in better wound outcomes.\textsuperscript{10} Several studies have compared the difference in results between the 2 procedures.\textsuperscript{11–13} However, these studies reported data on patients using only the traditional surgical approach. Recently, minimally invasive surgical (MIS) approaches
for TKA have become increasingly popular for orthopedic surgeons. The potential benefits of MIS techniques include less soft tissue trauma, faster recovery, and less postoperative pain. Moreover, most of the previous studies on drains and drain clamping were conducted prior to the routine use of MIS surgery and TXA; it is unclear whether drains or clamping have any benefit in modern TKA techniques. Therefore, we conducted a randomized controlled trial to determine the effects of a clamping drainage system compared to a no-clamping drainage system following MIS-TKA using TXA.

2. Materials and methods

This randomized controlled trial was registered in the Chinese Clinical Trial Registry (ChiCTR-INR-16009093) and was approved by the Institutional Review Board of West China Hospital (No: 201302007); informed consent was obtained before participation in the study. Randomization was blind and performed with the use of sealed envelopes at a ratio of approximately 1:1 to be opened just prior to surgery. The computer-generated numbers were used to generate the stratified randomization schedule. The patients and principal investigator were blinded to whether the drainage was clamped during the surgery. The random allocation sequence was performed by the nurses. From January 2015 to December 2015, all patients undergoing unilateral primary MIS-TKA for end-stage osteoarthritis were enrolled in our hospital. The exclusion criteria were as follows: acute or chronic infection, a history of deep vein thrombosis (DVT) or pulmonary embolism (PE), hematologic diseases, cancer, and a preoperative hemoglobin (Hb) level below 100 g/L. In the clamping group (N=60), drainage was clamped for the 1st 4 postoperative hours. In the nonclamping group (N=61), drainage was not clamped. All TKA procedures were performed under general anesthesia by 1 senior orthopedic surgeon. The minimally invasive technique was performed using mini-midvastus approach with a less than 12 cm skin incision. The vastus medialis was split (2 cm) with a medial parapatellar arthroscopy, and the patella was not everted. A tourniquet was applied at 250 mm Hg to all patients prior to the skin incision and released after the prosthesis was in place. All patients received 10mg/kg TXA intravenously 10 minutes before tourniquet deflation using the TXA administration method described by Patel et al. Electrocautery hemostasis was used to control all active bleeding after the tourniquet was released. The PFC Sigma PS (DePuy Orthopedics Inc., Warsaw, IN) prosthesis was used in all patients. All wounds were closed in approximately 45° of knee flexion. The arthroscopy closure was performed using an interrupted figure-of-eight #1 Ethibond (Ethicon, Somerville, NJ), a subdermal closure using interrupted buried simple 2-0 Monocryl (Ethicon) and staples for skin closure. The drain was removed 24 hours after surgery if the drain blood loss was less than 300 mL; otherwise it was continued until the quantity was less than 30 mL. All patients were mobilized and full-weight-walking was allowed on postoperative day 1. All patients were treated with a half dose of low molecular-weight heparin (LMWH) (0.2 mL, 2000 IU) at 6 hours after surgery and a full dose of (0.4 mL, 4000 IU) at 24-hour intervals in the subsequent days until discharge. Patients continued to receive oral rivaroxaban (10 mg) for 30 days after discharge to prevent DVT and PE. Furthermore, intermittent pneumatic compression device was routinely applied on the calves of patients until 3rd days after the operation.

The primary outcomes were total blood loss (TBL), drainage volume, and postoperative transfusion requirements. The secondary outcomes were Hb level, hematocrit (Hct) level, range of motion (ROM), and visual analog scale (VAS). DVT or PE, length of hospital stay, and wound-related complications were also recorded. Hb and Hct levels were routinely tested in the hospital on postoperative days 1, 3, and 5. ROM, VAS, and wound-related complications were assessed by the attending surgeon in the office at the time of discharge and at the 1 and 6 month postoperative appointments. Patients received transfusions if their Hb level was <80 g/L or if they experienced symptoms of anemia (such as mental status changes or palpitations) as determined by the senior orthopedic surgeon.

The size of the study was calculated as follows. According to a previous study, a power analysis with 95% confidence interval was performed by Jung et al. who found that a difference in the amount of blood loss of 300 mL was regarded as clinically meaningful between the continuous and intermittent wound drainage groups. To obtain a power of 0.80 and an alpha value of 0.05, 50 cases were required in each group. Accounting for potential exclusions, more than 50 cases were enrolled in each group in our study. The statistical analyses were performed with SPSS version 20.0 software (SPSS Inc., Chicago, IL). A series of demographic values were presented as percentage (%), standard deviation, and frequency. Student t test was used for normally distributed numerical variables such as TBL, drainage volume, Hb and Hct levels, ROM, and VAS. If the numerical variable was non-normally distributed or of unequal variance, the Mann–Whitney U test was used. The Pearson chi-square test or Fisher exact test was used to analyze categorical variables such as transfusion requirements, DVT, PE, and wound-related complications. A P value of less than 0.05 was considered to be statistically significant.

3. Results

During the study period from January 2015 to December 2015, a total of 131 patients with end-stage osteoarthritis requiring unilateral primary MIS-TKA were enrolled and followed. Of these patients, 10 patients were excluded for the following reasons: 4 patients declined to participate, 2 patients had a current chronic infection, 1 patient had a history of DVT, 1 patient had cancer, and 2 patients had hematologic diseases. Thus, 121 patients were ultimately eligible for data analysis, with 60 patients randomized to the clamping group and 61 patients to the nonclamping group (flow diagram). There were no statistically significant differences between the 2 groups with regard to age, gender, weight, BMI, preoperative Hb and Hct levels, preoperative ROM, VAS, duration of surgery, anesthesia
method, and the American Society of Anesthesiologists classification. The baseline characteristics of the 2 groups are shown in Table 1.

The average drainage volume in the clamping group was 148.4 ± 59.9 mL, compared to 275.8 ± 62.6 mL in the nonclamping group, which was statistically significant ($P < 0.001$). Although the TBL in the clamping group was 980.7 ± 213.8 mL, slightly less than the 1040.4 ± 208.5 mL in the nonclamping group, no significant difference was found between the 2 groups ($P = 0.105$) (Table 3). Among the 121 total patients, 2 patients (3.3%) in the clamping group and 5 patients (8.2%) in the nonclamping group required blood transfusion; this difference failed to reach statistical significance ($P = 0.276$). The Hb and Hct levels on postoperative days 1, 3, and 5 were similar in the 2 groups; however, patients in both groups experienced a significant drop in Hb and Hct levels after surgery. There were no significant differences in ROM and VAS at the time of discharge and 1 and 6 months postoperatively between the groups (Table 2). The hospital length of stay was 5.4 ± 1.3 days in the clamping group and 5.2 ± 1.6 days in the nonclamped group ($P = 0.452$) (Table 1).

Two asymptomatic DVT were detected by the Doppler ultrasound examination at the time of discharge in the clamping group ($P = 0.296$), which was treated with antithrombosis medication during the 1-month follow-up. At the final 6-month follow-up, there were 7 wound-related complications in the clamped group (4 wound ooze, 2 superficial infections, and 1 hematoma formation) and 3 wound-related complications in the nonclamped group (1 wound ooze, 2 superficial infections, and 2 blistering). All wound-related complications were ultimately cured by wound care, dressing reinforcement, and antibiotics. No deep infections or PE were observed in any of the patients (Table 3).

### Table 1

| Demographics | Clamping group (N = 60) | Nonclamping group (N = 61) | P |
|--------------|------------------------|---------------------------|---|
| Age, year    | 65.2 ± 6.8             | 64.9 ± 7.4                | 0.827 |
| Gender (M/F) | 24/36                  | 19/41                     | 0.314 |
| Side (R/L)   | 39/21                  | 35/26                      | 0.492 |
| Weight, kg   | 66.3 ± 10.5            | 65.4 ± 11.2               | 0.653 |
| BMI, kg/m²   | 25.4 ± 3.2             | 26.1 ± 2.8                | 0.209 |
| ASA          |                        |                           |     |
| 1–2 (low risk) | 42                     | 40                        | 0.608 |
| ≥3 (high risk) | 18                     | 21                        | 0.594 |
| General anesthesia | 60                     | 61                     | –   |
| Preop ROM knee scores | 86.4 ± 12.1            | 86.1 ± 14.7               | 0.903 |
| Preop VAS    | 8.1 ± 1.6              | 8.2 ± 1.1                 | 0.846 |
| Preop Hb, g/L | 132.7 ± 11.8          | 134.1 ± 9.2               | 0.457 |
| Preop Hct (L) | 38.6 ± 3.2            | 39.4 ± 4.3                | 0.251 |
| Tourniquet time | 40.6 ± 8.2            | 41.4 ± 9.3                | 0.757 |
| Duration of surgery | 69.7 ± 10.9          | 70.2 ± 11.8               | 0.816 |
| The hospital length of stay, days | 5.4 ± 1.3            | 5.2 ± 1.6                 | 0.452 |

### Table 2

| Clinical outcomes | Clamping group (N = 60) | Nonclamping group (N = 61) | P |
|-------------------|-------------------------|-----------------------------|---|
| Hb levels         |                         |                             |    |
| Post day 1        | 106.2 ± 11.5            | 105.4 ± 9.2                | 0.872 |
| Post day 3        | 92.4 ± 7.7              | 90.4 ± 6.6                 | 0.184 |
| Post day 5        | 96.8 ± 8.6              | 94.5 ± 6.5                 | 0.155 |
| Hct levels        |                         |                             |    |
| Post day 1        | 32.3 ± 2.6              | 31.7 ± 2.1                 | 0.163 |
| Post day 3        | 26.4 ± 2.2              | 25.6 ± 1.9                 | 0.119 |
| Post day 5        | 29.3 ± 2.7              | 28.6 ± 2.3                 | 0.135 |
| VAS               | At the time discharge   | 7.6 ± 1.3                  | 0.482 |
|                   | 1 months follow-up      | 3.1 ± 2.4                  | 0.616 |
|                   | 6 months follow-up      | 1.5 ± 0.6                  | 0.294 |
| ROM               | At the time discharge   | 96.3 ± 6.8                 | 97.4 ± 6.1 | 0.351 |
|                   | 1 months follow-up      | 102.6 ± 5.2                | 103.5 ± 4.8 | 0.327 |
|                   | 6 months follow-up      | 107.8 ± 5.4                | 107.2 ± 5.6 | 0.833 |
| Total blood loss  | 980.7 ± 213.8           | 1040.4 ± 208.5             | 0.105 |
| Drainage volume, mL | 148.4 ± 59.9           | 275.8 ± 82.6               | < 0.001 |
| Transfusion requirements | 3.3% (2/60)       | 8.2% (5/61)               | 0.276 |

### Table 3

| Wound-related complications, DVT, and PE at final follow-up. | Clamping group (N = 60) | Nonclamping group (N = 61) | P |
|-----------------------------------------------------------|-------------------------|-----------------------------|---|
| Asymptomatic DVT                                          | 2                       | 0                           | 0.296 |
| PE                                                        | 0                       | 0                           | –   |
| Superficial infection                                     | 2                       | 2                           | 0.993 |
| Deep infection                                            | 0                       | 0                           |     |
| Wound ooze                                               | 4                       | 1                           | 0.207 |
| Hematoma formation                                       | 1                       | 0                           | 0.495 |
| Blistering                                                | 0                       | 2                           | 0.304 |

DVT, PE, superficial infection, deep infection, wound ooze, hematoma formation, and blistering were analyzed by Fisher exact test. DVT = deep vein thrombosis, PE = pulmonary embolism.

### 4. Discussion

TXA, an inhibitor of fibrinolysis, reportedly reduces perioperative blood loss and transfusion requirements in patients undergoing unilateral primary TKA. Moreover, in the recent past, there has been an increasing trend toward MIS-TKA because of its potential benefits. However, previous studies reported that the clamping drainage or not has been discussed controversially in TKA, and the duration of different drainage studies exhibit different methods of clamping and it ranges from 1, 24, and up to 24 hours postoperatively. Shen et al. performed a prospective randomized trial of 89 patients undergoing unilateral un cemented TKA through a midline skin incision and a medial parapatellar capsule incision, studying the benefit of clamping the drainage in the 1st 4 postoperative hours on blood loss. The average bloody drainage was significantly less in the clamped drainage group (514.85 mL) than in the nonclamped drainage group (843.4 mL) without serious wound problems. Raleigh et al. also found a significant reduction in total external blood loss in the clamped drain group (296.67 mL) compared with 796.40 mL in the continuous drainage group, but with no difference in the transfusion requirements between the 2 groups. Unlike most other studies involving temporarily closing drainage were performed prior to MIS TKA and prior to the routine use of TXA, we therefore asked whether 1 intraoperative

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intravenous administration of TXA would reduce postoperative blood loss and blood transfusion requirements after MIS-TKA. To our knowledge, there has been no study investigating the effects of the clamped drain during MIS TKA in patients with TXA.

Because of the increasing interest in applying MIS techniques and TXA to total knee arthroplasty, it is critical for surgeons to assess the specific benefits in the clinical outcomes of these procedures. Although drains are used by many surgeons after TKA, it is still unclear as to whether the drainage should be clamped or not in minimally invasive TKA with TXA. The most important finding of the present study was that clamping the drainage in the 1st 4 postoperative hours could effectively reduce postoperative drainage volume by approximately 127.4mL after MIS-TKA. However, no statistically significant differences were found between the 2 study groups in the postoperative Hb and Hct levels, TBL, and transfusion requirements. Additionally, at the time of discharge and at 1 month and a mean final follow-up of 6 months, there was no significant difference in postoperative ROM, VAS, DVT, PE, and wound-related complications between the 2 groups. Therefore, clamping the drain has no obvious advantages in patients undergoing unilateral MIS-TKA with TXA.

Theoretically, the amount of TBL recorded in TKA is the intraoperative blood loss plus the postoperative drainage. However, we failed to receive the difference in TBL in our study. This phenomenon may have a number of explanations. First, hidden blood loss is an important component of TBL, but it has rarely been quantified until recently. As previously reported, hidden blood loss is derived from blood extravasation into the tissues, residual blood in the joint and loss due to hemolysis. Sehat et al confirmed that the mean hidden blood loss after TKA was 76.5mL, accounting for 49% of the total loss. Thus, TKA includes hidden losses, which are not captured by the routine assessment of intraoperative loss and postoperative drainage. Second, TXA is a synthetic antifibrinolytic drug used to prevent bleeding. Many studies reported the application of intravenous TXA in TKA could effectively and safely reduce blood loss and transfusion rate, with no increased the risks of bleeding complications. However, the statement that clamping or nonclamping drainage is unnecessary in routine during MIS-TKA using TXA is unclear. However, considering the results of the TBL, drainage volume, and transfusion requirements, it was clear that 4 hours of drainage could effectively reduce the drainage volume, but did not reduce the TBL and transfusion requirements. Thus, we do not believe that these limitations would significantly affect the results. Therefore, based on the current findings, clamping drainage is unnecessary in routine during MIS-TKA using TXA.

5. Conclusions
The use of clamping drainage in the 1st 4 postoperative hours in unilateral primary MIS-TKA when using TXA provides no apparent benefits compared with nonclamping drainage. We noted no statistical differences postoperatively in terms of TBL, Hb and Hct levels, transfusion requirements, ROM, VAS, DVT or/and PE, hospital length of stay, and wound-related complications in the postoperative follow-up.

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