Optimal Release Timing of Temporary Drain Clamping to Reduce Postoperative Bleeding After Total Knee Arthroplasty With an Intraarticular Injection of Tranexamic Acid

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Abstract

Background: Intraarticular injection of tranexamic acid (IA-TXA) plus drain-clamping is a preferred method of reducing bleeding after total knee arthroplasty (TKA). However, no consensus had been reached regarding the timing of clamping. The purpose of this study was to determine the optimum duration of drain-clamping after TKA with IA-TXA.

Methods: We retrospectively reviewed 151 patients that underwent unilateral TKA with IA-TXA plus drain-clamping for 30 minutes (Group A, 60 patients), 2 hours (Group B, 42 patients), or 3 hours (Group C, 49 patients). Total drained volumes, hematocrit (Hct) reductions, estimated blood losses (EBLs), transfusion rates, and wound complications were reviewed.

Results: Mean total drained volume, Hct reduction, EBL, and transfusion rate were significantly less in group C than in groups A or B ($p < 0.01$). No significant intergroup difference was found for wound-related complications. No surgical site infection or deep vein thrombosis was observed.

Conclusion: IA-TXA plus drain-clamping for 3 hours is optimal for reducing blood loss with minimal complications after TKA.

Background

Total knee arthroplasty (TKA) is a major orthopedic surgical procedure used to treat end-stage osteoarthritic knees and has good clinical and functional outcomes. However, TKA is associated with significant blood loss and 18–67% of patients require blood transfusion postoperatively.^{1–3} For these reasons, various methods such as tourniquet application, drain clamping, epinephrine or tranexamic acid (TXA), and fibrin sealant have been proposed to reduce blood loss.^{4–8}

TXA is a hemostatic substance that inhibits fibrinolysis, and thus, provides a pharmacological option to reduce blood losses. Previous studies have reported intraarticular TXA (IA-TXA) combined with drain clamping is a more effective means of preventing blood losses than drain clamping alone.^{9–13} Liao et al. conducted a meta-analysis of the results of 7 different studies and confirmed the efficacy of IA-TXA plus drain-clamping.¹³ However, in this meta-analysis little data was available for clamping times between 1 and 4 hours.¹³ To the best of our knowledge, no study has compared blood losses with respect to drain-clamping time after TKA with IA-TXA.

Accordingly, the present study was performed to determine an optimum drain-clamping time after TKA with IA-TXA by comparing blood losses and complication rates for different drain-clamping times.

Materials And Methods

This study had been approved by our Institutional Review Board (IRB No. INHAUH 2020-03-035). The requirement for informed consent was waived due to the retrospective nature of the study. The medical and surgical records of 151 patients that underwent TKA surgery at our hospital from January 2017 to December 2019 were retrospectively reviewed. According to our database, 328 patients underwent TKA surgery after being diagnosed with knee osteoarthritis. However, 177 patients were excluded after applying the following exclusion criteria: simultaneous bilateral TKA; concomitant operation; TKA with lateral retinacular release; TKA with patella

resurfacing; use of an extended stem; a diagnosis of secondary osteoarthritis; a neurologic disorder; and the receipt of medications, such as antiplatelet or anticoagulant medications, likely to interfere with findings.

The 151 study subjects were allocated to 3 groups according to clamping time, that is Group A (n = 60) clamping time 30 minutes, Group B (n = 42) clamping time 2 hours, and Group C (n = 49) clamping time 3 hours. A schematic of patient selection is presented in Fig. 1.

Operation Procedures

All patients underwent TKA by a single senior surgeon (MKK) and were provided the same procedures and post-operative managements, except clamping time. Under spinal anesthesia in the supine position, a standard mid-line skin incision was made using a medial parapatellar approach after applying a pneumatic tourniquet at 350 mmHg. The same implant system (Persona - Zimmer Biomet, Warsaw, Indiana, USA) with cement fixation (Optipac 80, Biomet Orthopaedics GmbH, Switzerland) was applied to all patients, and a 3.2 mm drainage tube and a BAROVAC (400mL, Sewoon Medical, negative pressure 90mmHg) comprised the drainage system. Intraarticular tranexamic acid (3g/30cc + normal saline 70cc) was administered immediately after joint capsule closure.^{14,15} 1 – 0 Vicryl simple interrupted sutures were used for joint capsules and tendons, and 3 – 0 Vicryl simple running sutures were used for synovium. After subcutaneous and skin closures with 2 – 0 Vicryl and skin staples respectively, we confirmed no leakage. An aseptic compression dressing was applied using elastic bandage. Drains were clamped off in a timely manner.

Postoperative management

Anti-embolism stockings and intermittent pneumatic compression were applied in all cases to prevent deep vein thrombosis (DVT) or pulmonary thromboembolism (PTE). In addition, anticoagulant (rivaroxaban, Xarelto®, 10mg) was given from postoperative day (POD) 3 to 14. Drainage amounts were recorded at 24 and 48 hr postoperatively, and all drains were removed at 48 hr postoperatively. Patients with a hemoglobin level of < 7g/dL or that maintained a hemoglobin level between 7 and 9g/dL received a postoperative blood transfusion.¹⁶ All patients performed weight-bearing exercise (using a walker), active thigh lifting exercise, and passive range of motion (ROM) exercise daily from POD 1.

Perioperative laboratory factors and hemodynamic factors

Because of massive irrigation during TKA, blood loss under anesthesia cannot be measured appropriately. We used Nadler's formula adjusted for height and body weight using Mercuriali's formula to calculate blood volumes from preoperative and POD5 hematocrit values.^{17,18} Mercuriali's and Nadler's formulae are as follows.

$$\text{Estimated blood loss} =$$

$$\text{Blood volume} \times (Hct_{preop} - Hct_{5dayspostoperative}) + \text{volume of transfused RBCs}$$

$$\text{Blood volume in men (L)} =$$

$$\text{Height}(m)^3 \times 0.367 + \text{Body weight}(kg) \times 0.032 + 0.604$$

$$\text{Blood volume in women (L)} =$$

$$\text{Height}(m)^3 \times 0.356 + \text{Body weight}(kg) \times 0.033 + 0.183$$

Complications

Complications such as DVT and PTE were evaluated closely because they can occur during clamping. From POD 2, surgical wounds were monitored to evaluate superficial infections and wound complications such as major bruises, oozing, hemarthrosis, subcutaneous hematoma, and blisters. Wounds were assessed up to POD12 to evaluate possible superficial or deep wound infections. Major bruises were defined as bruises that extended > 5 cm around wounds. Oozing was defined when three or more gauzes were soaked with blood.

Statistical Analysis

Results are presented as means $\pm$ standard deviations for continuous variables and as numbers and relative frequencies for categorical variables. Groups were compared using one-way analysis of variance (ANOVA) for quantitative data or Pearson's chi-squared test for qualitative data. Post hoc testing was used to assess the significances of intergroup differences. The analysis was performed using IBM SPSS Statistics for Windows version 25.0 (IBM Corp., Armonk, N.Y., USA), and statistical significance was accepted for P values < 0.05.

Results

Patient Demographics

Age, gender, surgery side, height, weight, blood volume, anesthesia method, and preoperative Hct level before surgery are presented in Table 1. No significant difference was found between these variables in the three groups (all P > 0.05).

Table 1
The patients' preoperative characteristics data.

Characteristics	Time of Clamp Release			P Value
	30 min (n = 60)	1 hour (n = 42)	2 hours (n = 49)	
Age at surgery (year) ^a	70.9 ± 6.8	71.8 ± 7.9	69.9 ± 7.5	0.517
Gender ^b				0.805
Female	47 (78.3%)	31 (73.8%)	36 (73.5%)	
Male	13 (21.7%)	11 (26.2%)	13 (26.5%)	
Side ^b				
Right	33 (55.0%)	18 (42.9%)	26 (53.1%)	0.453
Left	27 (45.0%)	24 (57.1%)	23 (46.9%)	
Height (cm) ^a	160.7 ± 4.7	161.6 ± 5.5	159.4 ± 8.2	0.429
Weight (kg) ^a	62.2 ± 5.6	60.9 ± 7.8	60.5 ± 8.1	0.614
Blood volume (L) ^a	3.78 ± 0.38	3.81 ± 0.54	3.74 ± 0.62	0.947
Anesthesia ^b				0.666
General anesthesia	5 (8.3%)	3 (7.1%)	2 (4.1%)	
Spinal anesthesia	55 (91.7%)	39 (92.9%)	47 (95.9%)	
Preoperative Hct level (%) ^a	37.3 ± 3.7	37.6 ± 3.0	38.5 ± 3.5	0.425
^a Data presented as mean ± standard deviation.				
^b Data presented as number of patients having that condition (percentage of this group)				
Hct: Hematocrit				

Drainage Amount

Mean total drainage amounts at 48 hours postoperatively in groups A, B, and C were 332.3 ± 100.2, 286.4 ± 127.9, 255.8 ± 84.5 mL, respectively (P = 0.001). Group C had a significantly lower amount than group A (P = 0.001), but no significant difference was observed between groups A and B (P = 0.09) or groups B and C (P = 0.495) (Table 2). The proportions of patients in the three groups with a drainage amount < 300 ml were, 36.6%, 59.6%, and 79.6%, respectively. Notably, as clamping time increased, the percentage of patients with a drainage amount of < 300 mL also increased (Fig. 2).

Table 2
Blood loss and blood transfusion outcome in three groups.

Variable	Time of Clamp Release			P-Value			
	30 min (n = 60)	2 hour (n = 42)	3 hours (n = 49)	Over-All significance	30 min vs. 2 hour	30 min vs. 3 hour	2 hour vs. 3 hour
Drain amount (mL) ^a							
24 hours	240.2 ± 92.6	183.8 ± 96.9	143.2 ± 82.5	0.001	0.236	< 0.001	0.185
48 hours	130.1 ± 65.5	103.2 ± 65.5	81.3 ± 53.8	0.010	0.046	0.021	> 0.999
Total	332.3 ± 100.2	286.4 ± 127.9	255.8 ± 84.5	0.001	0.09	0.001	0.495
Decreasing Hct (%) ^a	10.8 ± 2.3	8.7 ± 2.0	6.6 ± 2.2	< 0.001	< 0.001	< 0.001	< 0.001
Estimated blood loss (mL) ^a	513.6 ± 276.3	396.7 ± 212.5	280.6 ± 182.0	< 0.001	0.085	< 0.001	0.112
Transfusion							
Transfusion volume (mL)	106.7 ± 253.7	66.7 ± 174.8	32.7 ± 137.5	0.146			
Transfusion rate ^b	9 (16.7%)	4 (9.5%)	2 (4.1%)	0.165			
Hct: Hematocrit							
^a Data presented as mean ± standard deviation.							
^b Data presented as number of patients having that condition (percentage of this group)							
Statistical significance was determined by one-way ANOVA followed by Scheffe's post hoc analysis							

Total Blood Loss

Mean EBL calculated using Mercuriali's and Nadler's formulae was higher in Group A than in the other groups (P = < 0.001) (Table 2). Mean EBL showed a decreasing tendency as clamping time increased.

Need for Transfusion

Regarding the need for transfusion, results showed a tendency similar to EBL and drainage amounts. Mean transfusion volume was highest in group A and tended to decrease with clamping time. Transfusion rates showed

a similar tendency and were 16.7, 9.5, and 4.0% in groups A, B, and C, respectively.

Complications

No deep vein thrombosis or superficial infection occurred. Wound complications were categorized as major bruises, hemarthrosis, subcutaneous hematomas, and blisters, but no significant intergroup difference was observed (Table 3).

Table 3
Complications

Variable	Time of Clamp Release			P value
	30 min (n = 60)	2 hour (n = 42)	3 hours (n = 49)	
Deep vein thrombosis	0 (0%)	0 (0%)	0 (0%)	0.999
Superficial infection	0 (0%)	0 (0%)	0 (0%)	0.999
Wound complications ^a	6 (10.0%)	4 (9.5%)	5 (10.2%)	0.994
Major bruise	1 (1.7%)	2 (4.8%)	1 (2.0%)	0.600
Hemarthrosis	3 (5.0%)	2 (4.8%)	3 (6.1%)	0.951
Subcutaneous hematoma	1 (1.7%)	0 (0%)	1 (2.0%)	0.667
Blisters	1 (1.7%)	0 (0%)	1 (2.0%)	0.667
^a Data presented as number of patients having that condition (percentage of this group)				
Data presented as number (%). Statistical significance was determined by Pearson's chi-squared test.				
Postoperative complications				
Adverse events in three groups				

Discussion

In the present study, TKA with IA-TXA plus drain clamping for 3 hours resulted in a significant blood loss reduction as compared with clamping for 2 hours or 30 minutes. No significant intergroup difference was observed for complication rates.

Blood loss is an important postoperative consideration that must be considered after TKA. Bleeding into soft tissues surrounding the knee increases pain, stiffness, and length of recovery following surgery.¹⁹ TXA application has recently become one of the most popular methods for reducing blood loss and transfusion requirements. TXA (tranexamic acid) is an antifibrinolytic agent and was discovered in 1962. It prevents the formation of plasmin, and thus inhibits the breakdown of fibrin clots and decreases bleeding. Although TXA has been administered intramuscularly, intravenously, and intraarticularly, it is being increasingly administered locally due to theoretically lower rates of systemic effects, including those related to thromboembolic disease. However, due to safety concerns regarding PTE, interest is growing in the use of TXA as an IA agent in TKR. In the present study, we decided to use IA-tranexamic acid to reduce blood loss after TKA.

IA-TXA with drain-clamping reduces blood loss in TKA as compared with IA-TXA without clamping. This method is considered effective for reducing bleeding by forming a tamponade before opening. Prior studies have examined many methods, such as the intermittent method and specific timed drain clamping after surgery to reduce blood loss postoperatively. However, no study has determined the optimum timing of drain clamp release after TKA with TXA. Liao et al.¹³ conducted a systematic review and meta-analysis on the efficacy of TXA plus drain-clamping in TKA and concluded that this technique reduced blood loss and the need for transfusion. However, the seven clinical studies^{8,20-25} included in their meta-analysis¹³ were conducted using different clamping times (from 1 to 3 hours) and TXA dosages (range 250 to 1000 mg). We tried to define an effective clamping time by injecting TXA at 3 g/30 cc + 70 cc of normal saline and found EBLs decreased and the percentage of patients with a drainage amount of < 300 mL increased as clamping time increased.

When clamping is released early, effective bleeding control cannot be achieved, that is, longer clamping times are required to form effective tamponades. Since the half-life of tranexamic acid is 3 hours, we examined the effects of clamping times up to 3 hours.²⁶ Furthermore, it should be noted that complications such as hematoma can occur when clamping times are excessive (ca. > 4 hrs), as accumulations of blood in knee joints can lead to swelling, delayed wound healing, and increased risk of infection.¹¹ We found no significant difference between the three groups in terms of complications such as DVT, superficial infections, and wound complications.

The cytotoxic effect of IA-TXA on cartilage should be considered when the surgical intention is to preserve native cartilage tissues; its cytotoxicity may not affect total joint arthroplasties involving removal of entire articular cartilage. Effective dosing for topical TXA ranges from 15 to 100 mg/ml. Increased exposure time to TXA at high concentrations is cytotoxic to cartilage. Because patients included in this study did not undergo patella resurfacing, we needed to minimize TXA exposure time and concentration on the articular surface, and thus, decided to use TXA at a concentration of 30 mg/ml and to limit the maximum exposure time to 3 hours.

The study has several limitations. First, a relatively small number of cases were included in each group because all operations were performed by one surgeon in a single center. Second, postoperative blood loss was low in some patients when the surgeon was able to well identify and cauterize bleeding vessels, though vessel bleeding was carefully cauterized in all cases. Third, individual bleeding tendencies differ, and numerous factors that influence blood loss should have been considered. However, given the size of our cohort, we included factors considered important and excluded factors that may have confounded results, such as a history of anticoagulant/antiplatelet medication, abnormal coagulation factors, and cases involving soft tissue release. Fourth, as blood loss could not be accurately measured, EBLs were calculated using Mercuriali's and Nadler's formulae. However, Nadler's formula calculates blood volume based on weight and height, and thus, fluid-induced body changes preop to 5 days postop may have introduced errors. Despite these limitations, we believe our findings are meaningful as they provide evidence of the optimal duration of drain-clamp application after TKA with IA-TXA and provide a rationale how to minimize bleeding after TKA.

Conclusions

Temporary drain clamping after TKA with an intraarticular injection of tranexamic acid can effectively reduce EBL and transfusion requirements. Clamping IA-TXA for 3 hours proved to be more effective than clamping for ≤ 2 hours in terms of blood loss. We conclude, drain clamping for 3 hours after TKA with IA-TXA is optimal for reducing postoperative blood loss.

Abbreviations

TKA: total knee arthroplasty; IA-TXA: Intraarticular injection of tranexamic acid; Hct: hematocrit; EBL: estimated blood losses; ANOVA: analysis of variance; DVT: deep vein thrombosis; PTE: pulmonary thromboembolism

Declarations

Acknowledgements

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Authors' contributions

Myung Ku Kim, Dong Jin Ryu, and Yoon Sang Jeon designed the study. Sang Hyun Ko and Yoon Cheol Nam performed the data collection and participated in manuscript. Won Hwan Kwon performed the statistical analysis. Myung Ku Kim performed the surgeries. All authors have read and approved the final manuscript.

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Availability of data and materials

The data used and analyzed during the this study is available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The design and protocol of this study were reviewed and approved by the institutional review board of Inha university hospital (IRB No. INHAUH 2020-03-035). An exemption from informed consent was obtained from institutional review board of Inha university hospital due to its retrospective nature. All the experiments were performed in accordance with the relevant guidelines and regulations.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

Figure 1

Flowchart of patient selection for this study

Figure 2

Percentages of patients with drainage volumes of < 300 ml Percentages of patients with a drainage volume of < 300 ml increased with drainage time.