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Efficacy of Tranexamic Acid in Total Knee Arthroplasty: Evaluation of Four Blood Management Protocols

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Abstract

BACKGROUND/AIMS: This paper evaluates how tourniquet use and tranexamic acid (TXA) combinations affect blood management in primary total knee arthroplasty (TKA).

MATERIALS AND METHODS: Following ethical approval, a retrospective review was conducted of 96 patients who underwent primary TKA between 2014 and 2017. Patients were divided into four groups: Group 1, no tourniquet with intravenous (IV) TXA 15 mg/kg plus intra-articular (IA) TXA 2 g; Group 2, tourniquet only (control); Group 3, tourniquet with IV TXA; and Group 4, no tourniquet with IA TXA. Demographic data, changes in perioperative hemoglobin (Hb) and hematocrit (Hct), intraoperative blood loss, postoperative drainage volume, and transfusion rates were analyzed using ANOVA and Kruskal-Wallis tests.

RESULTS: The reduction in Hb and Hct was significantly smaller in patients receiving TXA ($p<0.05$). Group 1 demonstrated the least perioperative Hb decrease (1.3±0.8 g/dL) and the lowest transfusion rate (4%), whereas the control group showed the greatest Hb decline (3.5±1.0 g/dL) and highest transfusion requirement (34%) ($p<0.05$). The mean drainage volume was 180±50 mL in Group 1, lower than in other groups ($p<0.05$). No thromboembolic or wound-related complications were observed in any TXA-treated group.

CONCLUSION: Dual-route TXA administered without a tourniquet reduces blood loss and the need for transfusions in TKA without increasing the risk of complications. Tourniquet use alone did not confer any additional hemostatic benefit and may be safely omitted when an optimized TXA protocol is implemented. These findings highlight that pharmacologic antifibrinolytic therapy offers a more effective and safer blood management strategy than mechanical occlusion methods in modern knee arthroplasty practice.

Keywords: Tranexamic acid, tourniquet, total knee arthroplasty, blood loss, transfusion, hemostasis

INTRODUCTION

Total knee arthroplasty (TKA) effectively relieves pain and improves function in patients with advanced knee osteoarthritis.[1] Despite its proven success, TKA is often associated with considerable perioperative blood loss, which may lead to increased morbidity, delayed rehabilitation, and the need for allogeneic blood transfusion.[2] Transfusion, in turn, carries potential risks, including infection, immunologic reactions, and increased healthcare costs. Therefore, minimizing blood loss remains a key component of optimizing perioperative outcomes in TKA.[3-5]

A pneumatic tourniquet is traditionally used to provide a bloodless field and to aid cement fixation during TKA.[6] Prolonged tourniquet use can cause thigh pain, delayed quadriceps recovery, wound issues, and thromboembolic events.[7,8] Consequently, the routine use of tourniquets in knee arthroplasty has become increasingly controversial.

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Tranexamic acid (TXA), an antifibrinolytic that inhibits plasminogen activation, significantly reduces blood loss in orthopedic procedures without increasing thromboembolic risk.[9-12] TXA can be administered intravenously, topically, or in combination, though the optimal route and timing of administration remain subjects of debate.

Given the uncertainty about the efficacy of TXA and tourniquet use for blood conservation, this study compared approaches that combined or omitted these techniques in patients undergoing primary TKA. The effects on perioperative blood loss, changes in hemoglobin (Hb) and hematocrit (Hct), and transfusion requirements were evaluated to determine the most effective and safe strategy for blood management during TKA.

MATERIALS AND METHODS

This retrospective study adhered to the Declaration of Helsinki and was approved by the Dokuz Eylül University Non-Interventional Research Ethics Committee (approval number: 2018/07-47, date: 15.03.2018). We reviewed the medical records of 96 patients who underwent primary TKA and met the inclusion criteria at the Orthopedics and Traumatology Department between 2014 and 2017.

To compare different perioperative blood management strategies, patients were divided into four equal groups (n=24 each) according to tourniquet use and the method of TXA administration. All procedures were performed by a single orthopedic surgeon using the same surgical technique.

Patient Selection

Patients aged 45-80 years with primary knee osteoarthritis were included. Exclusions: secondary gonarthrosis from rheumatologic disorders, bleeding or coagulation issues, previous knee surgery, periarticular implants, hypersensitivity to TXA, or use of anticoagulants or antiplatelet drugs.

Surgical Procedure

All operations were performed by an experienced orthopedic surgeon using a medial parapatellar approach. The Vanguard® Knee System and Vanguard ROCC® prostheses were used in all cases, and no patellar resurfacing was performed. Antibiotic prophylaxis consisted of 2 g of intravenous cefazolin administered preoperatively and continued postoperatively for 24 hours in four divided doses. Patients with a cefazolin allergy received 2 g of clindamycin, following the same regimen.

In the tourniquet groups, inflation pressure was set to 300 mmHg; in the non-tourniquet groups, the cuff remained uninflated for safety purposes only. Following skin preparation and sterile draping, a standard midline incision and medial parapatellar capsulotomy were performed. Appropriate tibial and femoral bone cuts and necessary soft-tissue balancing were completed. Components were implanted using bone cement. In the tourniquet groups, the tourniquet was released after cement polymerization. After fixation, the joint was thoroughly irrigated with saline. A suction drain was inserted before capsule closure, which was performed with the knee flexed. In groups receiving intra-articular (IA) TXA, 2 g of TXA, diluted in 50 mL saline, was injected into the joint cavity via the drain after capsule closure. The study were:

Group 1: No tourniquet; 15 mg/kg intravenous TXA +2 g IA TXA

Group 2: Tourniquet used; no TXA (control group)

Group 3: Tourniquet used; 15 mg/kg intravenous TXA

Group 4: No tourniquet; 2 g IA TXA

At the end of surgery, sterile dressings were applied. Drains were opened 2 hours postoperatively and removed after 24 hours; the total drainage volume was recorded.

Postoperative Management

Hb and Hct levels were measured preoperatively and at 6, 12, 24, and 48 hours postoperatively. The differences between preoperative and postoperative values were documented for each patient.

Allogeneic blood transfusion was administered when the Hb level fell below 8 g/dL. Patients with Hb between 8 and 10 g/dL were evaluated for transfusion based on cardiovascular comorbidities or clinical symptoms, such as tachycardia, dizziness, palpitations, or fatigue. Patients with Hb levels above 10 g/dL did not receive transfusions. All transfusion events were recorded.

For deep vein thrombosis prophylaxis, a single subcutaneous dose of low-molecular-weight heparin was given at the 12th postoperative hour and was continued daily for six weeks.

Statistical Analysis

Statistical analyses were carried out using IBM SPSS Statistics version 22 (IBM Corp., Armonk, NY, USA). Continuous variables are described as mean ± standard deviation when normally distributed, or as median (minimum-maximum) in cases where the data are not normally distributed. Categorical data are presented as counts and percentages. Group means were compared using one-way ANOVA, while medians were compared using the Kruskal-Wallis test. Group 2 served as the control group throughout the analyses. Statistical significance was defined as $p<0.05$. A sensitivity (power) analysis was performed for a one-way ANOVA with four groups, an alpha level of 0.05, and 80% power. With a sample size of 96, the study was sufficiently powered to detect an effect size of approximately Cohen's f=0.34, corresponding to a moderate effect size. Therefore, the sample size was considered adequate for detecting moderate-to-large intergroup differences, although smaller effects may have remained undetected.

RESULTS

The study included 96 patients who received primary TKA. Their average age was 66.8±7.4 years. Most of the patients, 79%, were female. There were no significant differences among the four groups in age, gender, or body mass index ($p>0.05$). The mean body mass index was 28.8±1.6 kg/m², and was similar across all groups. The right knee was operated on in 50 patients (54%), and the left knee was operated on in 42 patients (46%) (Table 1).

The demographic characteristics were similar across the four groups. Most patients were female and overweight. No notable differences were observed in preoperative Hb or packed cell volume levels.

Table 1. Comparison of baseline demographic data and preoperative laboratory parameters among the four study groups

	Group 1	Group 2	Group 3	Group 4	p-value*
Age	68±8.3	69±8.2	69±6	76 ±9.1	0.138
Sex (female/male)	22/1	20/3	21/2	20/3	0.72
BMI	28.9±1.9	28.1±1.1	28.9±1.5	29.3±1.03	0.91
Side (right/left)	13/10	15/8	10/13	12/11	0.93
Preoperative Hb	12.6±1.5	13.1±1.8	13±1.5	12.6±1.5	0.284
Preoperative PCV	38.1±3.4	40±5	39.2±3.8	38±4.6	0.365

*p<0.05.
BMI: Body mass index, Hb: Hemoglobin, PCV: Packed cell volume.

Preoperative Laboratory Parameters

Preoperative Hb was similar across groups: 13.1±1.8 g/dL in Group 1, 13.4±1.6 in Group 2, 13.0±1.5 in Group 3, and 12.6±1.5 in Group 4 (p=0.42).Preoperative Hct values were 38.1±3.4%, 40.0±5.0%, 39.2±3.8%, and 38.0±4.6%, respectively (p>0.05).

Postoperative Hemoglobin and Hematocrit Changes

Postoperative Hb and Hct values decreased in all groups compared with baseline. However, the reduction was significantly smaller in the TXA-administered groups.

At 6 hours postoperatively, mean Hb levels were 12.0±1.4 g/dL in Group 1, 11.3±1.6 g/dL in Group 2, 11.6±1.3 g/dL in Group 3, and 11.4±1.5 g/dL in Group 4 (p=0.021) (Table 2).

At 24 hours, Hb levels decreased to 11.2±1.3, 10.4±1.6, 10.7±1.2, and 10.6±1.4 g/dL, with significant intergroup difference (Kruskal-Wallis, p<0.001). A similar pattern was observed for Hct: Group 1 consistently showed the smallest postoperative decline, while Group 2 (tourniquet only) showed the greatest reduction.

Drain Output and Blood Loss

The total drainage volume in the first 24 hours differed significantly among groups (p<0.001). Mean values were: Group 1: 180±50 mL; Group 2: 250±40 mL; Group 3: 260±35 mL; Group 4: 210±30 mL (Table 2).

The lowest drainage volume was recorded in Group 1, which involved a combination of intravenous and IA TXA without the use of a tourniquet.

Blood Transfusion Requirement

Overall, 14 patients (14.5%) required allogeneic blood transfusion. The highest transfusion rate was observed in the control group (33.3%), followed by Group 4 (12.5%), Group 3 (8.3%), and Group 1 (4.2%) (p=0.018).

Complications

No thromboembolic events, wound healing problems, or allergic reactions related to TXA were observed during hospitalization or the early postoperative follow-up.

DISCUSSION

This study examined how different combinations of tourniquet use and TXA affected perioperative blood loss in TKA patients. According to the results, the group that received both intravenous and IA TXA without a tourniquet showed the smallest decrease in Hb, the least drainage, and the lowest transfusion rate. On the other hand, patients operated on with a tourniquet but without TXA experienced the highest blood loss and the greatest need for transfusion. These findings show that TXA is more effective than a tourniquet in reducing perioperative bleeding, and that using two routes offers additional benefit. Jansen et al.[13] emphasized that TXA was an effective part of blood-saving strategies during arthroplasty. Konig et al.[14] showed that topical TXA administration reduced both blood loss and the need for transfusion in total hip and knee arthroplasties. López-Hualda et al.[15] also demonstrated that local TXA use was safe and effective in minimizing bleeding. Likewise, in another study, the combination of intravenous and IA TXA was superior to a single route of administration.[16] Our study confirms TXA's key role in blood conservation during TKA, regardless of the route of administration. Previous randomized studies have also

Table 2. Comparison of perioperative outcomes among groups

Parameter	Group 1 (no tourniquet, IV + IA TXA)	Group 2 (tourniquet only, control)	Group 3 (tourniquet + IV TXA)	Group 4 (no tourniquet, IA TXA)	1 vs. 2 vs. 3 vs. 4	1 vs. 2	1 vs. 3	1 vs. 4	2 vs. 3	2 vs. 4	3 vs. 4
Maximum Hb change (g/dL)	1.3±0.8	3.5±1.0	3.0±0.9	2.9±1.1	<0.05	<0.05	<0.05	<0.05	0.324	0.143	0.970
Transfusion rate (%)	4	34	13	18	<0.05	<0.05	0.301	0.160	0.870	0.184	0.685
Intraoperative blood loss (mL)	220±30	280±90	210±35	300±25	<0.05	<0.05	0.540	0.020	<0.05	<0.05	<0.05
Drainage volume (mL)	180±50	250±40	260±35	210±30	<0.05	<0.05	<0.05	0.200	0.540	0.310	<0.05

Pairwise p-values indicate significant differences where p<0.05; no boldface highlighting is used.
TXA: Tranexamic acid, IV: Intravenous, IA: Intra-articular, Hb: Hemoglobin.

demonstrated that TXA reduces perioperative blood loss and may be superior to tourniquet-only strategies. However, most studies have evaluated only one or two blood management protocols. In contrast, the present study simultaneously compared four perioperative blood management strategies within the same study population, providing a broader perspective on their relative effectiveness.

Tourniquets are used to reduce bleeding and improve visualization during surgery; however, these benefits were not observed in our series, and recent studies have highlighted potential adverse effects. Extensive literature reports that tourniquet use may cause postoperative thigh pain, delayed recovery, muscle ischemia, and an increased risk of thromboembolic complications.[17,18] Li et al.[19] and Huang et al.[20] further showed that tourniquet use did not reduce the total amount of bleeding; led to an increase in postoperative bleeding in some cases due to reactive hyperemia and fibrinolytic activation after the cuff was released. The study shows that tourniquet use alone offers no benefit and may increase blood loss in the absence of TXA.

The superior results in the group receiving both intravenous and IA TXA can be explained by the complementary mechanisms of the two administration routes. Intravenous TXA provides systemic antifibrinolytic activity, while IA application achieves high local concentrations and acts directly on the surgical field to stabilize clot formation. This combination likely contributed to the significantly lower postoperative Hb drop and drainage output observed in this group. Additionally, avoiding the tourniquet may have reduced tissue hypoxia and subsequent reperfusion-related fibrinolysis, further minimizing bleeding.

Both single-route TXA administrations (intravenous and IA) effectively reduced blood loss compared with the control, but were less effective than the combined approach. Similarly, Adravanti et al.[16] showed that combined use was more successful than either route alone. This supports the idea that TXA use -regardless of the administration route- is a reliable and safe means of reducing bleeding and may decrease the need for tourniquet use during TKA. Importantly, no thromboembolic or wound complications were observed in any of the TXA groups, supporting the safety of its use in this setting.

Study Limitations

The primary limitations of this study are its retrospective design and the relatively small sample size. The follow-up was limited to the early postoperative period, and routine doppler ultrasonography screening for deep vein thrombosis was not performed. Patients were clinically monitored, and doppler evaluation was performed only when clinically indicated; therefore, asymptomatic thromboembolic events may not have been detected. No cost analysis was performed for the different blood management protocols.

CONCLUSION

Our results show that administering both intravenous and IA TXA without a tourniquet is the most effective and safest approach to reduce blood loss during TKA. While tourniquets reduce intraoperative bleeding, they do not improve overall blood conservation. Avoiding tourniquet use may also reduce associated complications, thereby making TXA a safer and more effective strategy for blood management in TKA.

MAIN POINTS

- Combined intravenous and intra-articular administration of tranexamic acid (TXA) resulted in the smallest decrease in hemoglobin, drainage volume, and transfusion rate in primary total knee arthroplasty.
- Tourniquet use alone did not provide superior overall blood conservation compared with TXA-based protocols.
- The Simultaneous comparison of four perioperative blood-management protocols within a single study design is a major strength.
- Although no thromboembolic or wound complications were observed, the retrospective design and limited follow-up require cautious interpretation of safety outcomes.

ETHICS

Ethics Committee Approval: Approved by the Dokuz Eylül University Non-Interventional Research Ethics Committee (approval number: 2018/07-47, date: 15.03.2018).

Informed Consent: Not required due to retrospective study design.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Y.I., M.E., Concept: Y.I., M.E., Design: Y.I., M.E., Data Collection and/or Processing: Y.I., M.Ç., Analysis and/or Interpretation: Y.I., Y.S.K., M.Ç., Literature Search: Y.I., Y.S.K., M.Ç., Writing: Y.I., M.Ç.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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Declaration on the Use of Artificial Intelligence (AI): The authors declare that artificial intelligence (AI) tools were not used, or were used solely for language editing, and had no role in data analysis, interpretation, or the formulation of conclusions. All scientific content, data interpretation, and conclusions are the sole responsibility of the authors. The authors further confirm that AI tools were not used to generate, fabricate, or “hallucinate” references, and that all references have been carefully verified for accuracy.

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