ARAŞTIRMA MAKALESİ / *RESEARCH ARTICLE*

Timing of Intraoperative Tranexamic Acid Use in Patients Undergoing Total Knee Arthroplasty: Before or After Tourniquet Application?

Total Diz Artroplastisi Uygulanan Hastalarda İntraoperatif Tranexamik Asit Kullanımının Zamanlaması: Turnike Uygulamasından Önce mi Sonra mı?

Ahmet Volkan Dogan[1], Tuncay Baran[1], Umit Gok[1], Mumin Karahan[2], Erdinc Esen[3]

[1]Department of Orthopedics and Traumatology, Health Science University Kocaeli City Hospital, Kocaeli; [2]Department of Orthopedics and Traumatology, Faculty of Medicine, Kafkas University, Kars; [3]Department of Orthopedics and Traumatology, Faculty of Medicine, Gazi University, Ankara, Türkiye

ABSTRACT

Aim: *Total knee arthroplasty is a good choice for effective treatment of end stage knee diseases. However, there is a considerable blood loss in intraoperative and postoperative periods. The aim of our study is to compare effectiveness of the use of single dose tranexamic acid on blood loss and transfusion need at before tourniquet inflation and after tourniquet deflation.*

Materials and methods: *90 patients who underwent total knee arthroplasty surgery by the same surgical team between April 2023 and July 2025 in the Orthopedics and Traumatology Department of Kocaeli City Hospital were retrospectively evaluated. Patients were divided to three groups; control group which tranexamic acid wasn't administrated (Group 1), before tourniquet group which tranexamic acid (TEA) was administrated before inflation of tourniquet (Group 2) and after tourniquet group which tranexamic acid was administrated after deflation of tourniquet (Group 3). Blood loss at 30th minute and after 24 hours in the hemovac drain, change of hemoglobin (Hb), activated partial thromboplastine time (aPTT), partial thromboplastine time (PTZ) and international normalized ratio (INR) levels, need of transfusion were evaluated.*

Results: *Blood loss, decrease on Hb levels and the need of transfusion at TEA administrated groups were found significantly less than control group. When compared two groups TEA administrated, blood loss was found significantly less in after tourniquet group than in before tourniquet group. It was found that there was not a significant change at aPTT, PTZ and INR levels in TEA administrated groups.*

Conclusion: *Eventually single dose TEA administration after tourniquet lowers blood loss better than administration before tourniquet, but does no significant difference in Hb levels.*

Key words: *tranexamic acid; total knee arthroplasty; hemostasis; complication*

ÖZET

Amaç: *Total diz artroplastisi, son dönem gonartrozun etkili tedavisi için iyi bir seçenektir. Ancak intraoperatif ve postoperatif dönemlerde önemli miktarda kan kaybı meydana gelir. Çalışmamızın amacı, turnike şişirilmeden önce ve indirildikten sonra tek doz traneksamik asit kullanımının kan kaybı ve transfüzyon ihtiyacı üzerine etkinliğini karşılaştırmaktır.*

Gereç ve Yöntem: *Nisan 2023 ile Temmuz 2025 tarihleri arasında Kocaeli Şehir Hastanesi Ortopedi ve Travmatoloji Kliniği'nde aynı cerrahi ekip tarafından total diz artroplastisi ameliyatı geçiren 90 hasta retrospektif olarak değerlendirildi. Hastalar üç gruba ayrıldı; traneksamik asit uygulanmayan kontrol grubu (Grup 1), turnike şişirilmeden önce traneksamik asit (TEA) uygulanan turnike öncesi grubu (Grup 2) ve turnike indirildikten sonra traneksamik asit uygulanan turnike sonrası grubu (Grup 3). Hemovac drende 30. dakika ve 24 saat sonraki kan kaybı, hemoglobin (Hb), aktive parsiyel tromboplastin zamanı (aPTT), parsiyel tromboplastin zamanı (PTZ) ve INR düzeylerindeki değişim ile transfüzyon ihtiyacı değerlendirildi.*

Bulgular: *TEA uygulanan gruplarda kan kaybı, Hb düzeylerindeki düşüş ve transfüzyon ihtiyacı kontrol grubuna göre anlamlı derecede daha az bulundu. Traneksamik asit uygulanan iki grup karşılaştırıldığında, turnike sonrası grupta kan kaybı, turnike öncesi grubuna göre anlamlı derecede daha az bulundu. Traneksamik asit uygulanan gruplarda aPTT, PTZ ve INR düzeylerinde anlamlı bir değişiklik olmadığı bulundu.*

Sonuç: *Turnike sonrası tek doz TEA uygulaması, turnike öncesi uygulamaya göre kan kaybını daha iyi azaltmaktadır, ancak Hb düzeylerinde anlamlı bir fark yaratmamaktadır.*

Anahtar kelimeler: *traneksamik asit; total diz protezi; hemostaz; komplikasyon*

İletişim/Contact: *Ahmet Volkan Doğan, Department of Orthopedics and Traumatology, Health Science University Kocaeli City Hospital, Kocaeli, Türkiye* • ***Tel:*** *0543 353 71 41* • ***E-mail:*** *avolkandogan@gmail.com* • ***Geliş/Received:*** *22.10.2025* • ***Kabul/Accepted:*** *06.03.2026*

ORCID: *Ahmet Volkan Doğan: 0000-0002-8177-5507 • Tuncay Baran: 0000-0002-7052-4171 • Ümit Gök: 0000-0003-2659-7952 • Mümin Karahan: 0000-0002-2137-2634 • Erdinç Esen: 0000-0003-0434-5850*

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Introduction

Total knee arthroplasty (TKA) is a popular surgical procedure for patients with severe gonarthrosis resistant to nonsurgical treatment options and other surgical interventions, including arthroscopic or open debridement, synovectomy, and high tibial osteotomy, when performed properly (1,2). Although perioperative evaluation of patients is made, postoperative morbidities caused by devastating complications like hypovolemic shock secondary to excessive blood loss, venous thromboembolism, and infection are still troublesome for orthopedic surgeons.

Tranexamic acid (TEA) is a synthetic derivative of lysine amino acid, a competitive inhibitor of plasminogen activators and prevents fibrinolysis. Compared with other antifibrinolytic agents such as aprotinin and aminocaproic acid, TEA is more cost-effective. Intravenous administration of TEA has long been used to reduce blood loss and the need for blood transfusions. The method, dose, and time of administration remain controversial issues (3,4).

In this study, we aim to evaluate the effect of tranexamic acid use on blood loss before and after tourniquet inflation and deflation during TKA in patients with severe gonarthrosis.

We hypothesized that a single dose of TEA administered after tourniquet use would reduce blood loss more than a single dose administered before tourniquet use.

Material and Methods

Ethic Approval

This retrospective study was approved by the Kocaeli University Faculty of Medicine Clinical Research Ethics Committee on 25.09.2025 with the protocol code 2025/120.

Study Design

In this study, the records of 90 patients with a diagnosis of gonarthrosis (ICD code M17) who underwent total knee arthroplasty surgery by the same surgical team between April 2023 and July 2025 in the Orthopedics and Traumatology Department of Kocaeli City Hospital were retrospectively evaluated. Patients were divided into three groups: the control group, in which tranexamic acid was not administered (Group 1), the before-tourniquet group, in which tranexamic acid (TEA) was administered before inflation of the tourniquet (Group 2) and the after-tourniquet group, in which tranexamic acid was administered after deflation of the tourniquet (Group 3). Exclusion criteria were neurological diseases, peripheral neuropathy, previous cardiovascular event, severe systemic heart disease, active or previous malignancy, peripheral vascular disease, previous deep venous thrombosis, previous pulmonary embolism and use of anticoagulant treatment because of these conditions. Patients receiving anticoagulant or antiplatelet therapy had their therapy discontinued for an appropriate period prior to surgery in accordance with institutional protocols, and none were still under active effect at the time of surgery.

All surgeries were performed under general anesthesia by the same surgeon, a specialist in TKA. Before the surgery, a tourniquet was placed and inflated to 350 mmHg. A midline skin incision was made. Medial parapatellar approach was used to expose the surgical site of the knee joint. Intra-operative hemostasis was applied in standard fashion. After bone resection of the distal femur and proximal tibia, soft tissue balancing was performed, and the appropriate type and size of knee prosthesis components were cemented, polyethylene liners were inserted, and the patella was resurfaced. Drains were inserted after the wound closed, and tourniquets were removed.

The sex, age, serum hemoglobin levels (preoperative and first postoperative day), and the amount of blood drained through the intra-articularly placed tubes and accumulated in the negative-pressure container were recorded.

All patients also received thromboembolic prophylaxis with 0.4 mL of low-molecular-weight heparin (LMWH). The control group (Group 1) received only LMWH, while Group 2 and Group 3 also received 1 g intravenous (IV) bolus TEA 10 min before tourniquet placement and after tourniquet removal, respectively (5). In all patients, a pneumatic tourniquet was used routinely. The pressure of the tourniquet was 375 mm/Hg.

Thirty minutes and 24 hours after the operation, the amount of blood drained into the negative-pressure container was recorded. Blood samples were gathered from all of the patients 24 hours after the operations to provide complete blood count and evaluate coagulation parameters. At the same time, drainage tubes were removed. All patients started to receive LMWH (daily subcutaneous 0.4 ml enoxaparin sodium) six hours after the operation. When Hb value dropped below 10 g/dl, transfusion of erythrocyte suspension was

performed. Presence of deep venous thrombosis was evaluated clinically in the postoperative period using Doppler ultrasonography.

Statistical Analysis

Statistical analysis of data was done with IBM Statistical Package for Social Sciences (SPSS) program version 18.0 for Windows. Blood collection through the drain and preoperative-postoperative hemoglobin difference was analyzed with one-way ANOVA and Mann-Whitney U tests. Pearson's Chi-square test was used for blood transfusion requirements. When the sample size of categorical data was small, we applied Fisher's exact test. The results were considered significant at P <0.05.

Results

Demographic features of the patients: 82 patients were women (94%), 6 patients were men (%6). Fifty-four operated knees were right (60%), thirty-six knees were left (40%). The range of age was between 60 and 79. The mean age was 68.7±4.1 in the control group, 65.7±9.9 in Group 2, and 67.1±7 in Group 3. The mean age of the groups were statistically similar with Analysis of Variance (Table 1). There was no significant difference in the spread of sex among the groups either.

The mean blood loss three hours postoperatively was 166±35 cc in the control group, 101±40 cc in Group 2, and 63.5±40 cc in Group 3. It was found that the blood loss after 30 minutes from the operation in both Group 2 and Group 3 was significantly less than the control group (Table 2)

When we assessed total blood loss 24 hours postoperatively, it was 640±100 cc in control group, 330±100 cc in Group 2, and 235±47 cc in Group 3. The total blood loss at 24 hours postoperatively in both Group 2 and Group 3 was significantly less than the control group (Table 3).

Table 1. *Demographical and clinical features of cases according to groups*

Variables	Control Group	Before tourniquet	After Tourniquet	p-value
Age	68.7±4.1	63.7±5.4	65.7±9.9	0.285[a]
Sex				
Male	3(%10)	0(%0)	3(%10)	0.429[b]
Female	27(%90)	30(%100)	27(%90)	
Side				
Right	15(%50)	18(%60)	21(%70)	
Left	15(%50)	12(%40)	9(%30)	
Drain 30 min	150(135–250)[d,e]	100(50–200)[d,f]	50(20–150)[e,f]	**<0.001[c]**
Drain Total	600(500–850)[d,e]	350(200–500)[d,f]	250(150–300)[e,f]	**<0.001[c]**
Transfused	18(60%)	0 (0%)	3 (10%)	

[a]: One Way ANOVA; [b]: likelihood ratio test; [c]: Kruskal-Wallis test; [d]: between control group and before tourniquet statistically significant difference (p<0, 001); [e]: between control group and after tourniquet statistically significant difference (p<0, 001); [f]: between before tourniquet group and after tourniquet statistically significant difference (p<0, 05).

Table 2. *Blood loss from drainage tube after 30 minutes postoperatively*

Groups	Count	Mean	Standard deviation	Median	Minimum	Maximum
Group 1	30	166.0	34.6	150.0	135.0	250.0
Group 2	30	101.0	40.9	100.0	50.0	200.0
Group 3	30	63.5	40.4	50.0	20.0	150.0
Total	90	110.1	57.0	100.0	20.0	250.0

Table 3. *Total blood loss from drainage tube for 24 hours postoperatively*

Groups	Count	Mean	Standard deviation	Median	Minimum	Maximum
Group 1	30	640.0	102.1	600.0	500.0	850.0
Group 2	30	333.0	103.2	350.0	200.0	500.0
Group 3	30	235.0	47.4	250.0	150.0	300.0
Total	90	402.6	195.0	350.0	150.0	850.0

Table 4. *Preoperative and postoperative Hb values according to the groups*

	Preop	Postop	p-value[a]	Change	p-value[b]
Haemoglobin					**<0.001**
Group 1	13.0	10.25	<0.001	-2.83	
Group 2	12.9	11.53	<0.001	-1.38	
Group 3	13.8	11.8	<0.001	-1.96	

[a]: comparisons of preoperative and postoperative Hb values between groups, paired t-test; [b]: comparison of preop and postop changes of Hb values between groups, One Way ANOVA.

Table 5. *INR/PTZ/aPTT levels according to the groups*

Variables	Preop	Postop	p-value[a]	Change	p-value[b]
INR					**0.194[e]**
Group 2	1.09	1.23	<0.001[c]	0.14	
Group 3	0.99	1.19	<0.001[c]	0.20	
aPTT					**0.796[f]**
Group 2	19.7	21.0	0.005[d]	1.0	
Group 3	19.5	20.7	0.021[d]	1.0	
PTZ					**0.165[f]**
Group 2	11.5	12.0	0.008[d]	0.5	
Group 3	11.0	12.0	0.008[d]	0.8	

[a]: comparisons of preop and postop values between groups; [b]: comparison of postop changes among the groups according to preop period; [c]: paired t-test, [d]: Wilcoxon signed test; [e]: Student's test; [f]: Mann-Whitney U test.

Erythrocyte suspension transfusion was required postoperatively for eighteen patients (%60) in control group and no ES transfusion was needed in Group 2, while three ES transfusions were needed in Group 3 (10%). Group 2 and 3, with TEA injection, needed significantly less ES transfusion than the control group (Table 1).

In the Group 1, preoperative and postoperative mean Hb values were 13±0.86 g/dl and 10.2±1.1 g/dl, respectively. In Group 2, preoperative and postoperative mean Hb values were 12.9±1.5 g/dl and 11.53±1.1 g/dl, respectively. In Group 3, preoperative and postoperative mean Hb values were 13.8±1.3 g/dl and 11.8±1.6 g/dl, respectively.

The change of Hb values in Group 1, Group 2, and Group 3 were 2.83±0.76 g/dl, 1.38±0.47 g/dl, and 1.96±0.83 g/dl, respectively (Table 4).

Decrease in Hb values of Group 2 and 3 was significantly less than the control group. There was no significant difference between Group 2 and 3 (p=0.93).

Coagulation parameters (INR, aPTT, PT) of the patients which received TEA injection were also assessed. Although there is an increase in INR values, it was not significant statistically. Preoperative and postoperative APTT and PT values of the patients showed no significant increase (Table 5).

Discussion

Total knee arthroplasty is a beneficial and effective treatment modality for late-stage knee osteoarthritis. On the other hand, this surgical procedure can cause severe blood loss, which leads to the need for blood transfusion (6,7).

In our study, before and after tourniquet placement, blood loss in TEA-administered patients at 30 minutes post-operation was significantly lower than in the control group. In some studies, TEA was administered to patients at maximum dose (1 g, IV bolus). In the before-tourniquet group, TEA was administered just before tourniquet inflation. In the after-tourniquet group, TEA was administered after tourniquet deflation. It was shown that a single dose of TEA administration has beneficial effects on blood loss in the before-tourniquet (Group 2) and after-tourniquet (Group 3) groups. Blood loss in Group 3 was less than that in Group 2 for the 30 th-minute blood loss and total blood loss. This result is possibly based on earlier administration of TEA before the tourniquet group, the 3-hour half-life of the drug, and reaching maximum plasma concentration after IV administration in 5–15 minutes and reduction of concentration to its half (8,9).

There are many studies with positive results and a high safety profile supporting TEA use in TKA patients (10,11). However, the optimal TEA treatment protocol remains unknown, and most surgeons have their own usage plans. On the other hand, some studies assert that TEA doesn't reduce blood loss but does decrease the risk of deep vein thrombosis (12). The effective dose and timing are highly controversial. However, in the literature, the most preferred usage is intravenous administration of TEA at 10 mg/kg (maximum 1 g) 10 minutes before tourniquet deflation and again 3 hours later. Maniar et al. investigated the most effective dose and optimal timing of TEA use in a prospective randomized controlled study involving 240 patients. In their study, there is no significant difference between the control group and the single-dose TEA-administered group, though there is less blood loss and drainage (13). A lower dose of single-dose TEA may explain the insignificant results. In our study, we found that the blood loss (in the first 30 minutes and total) in the before-tourniquet and after-tourniquet groups was significantly lower than in the control group.

Decrease in Hb levels in both before tourniquet (Group 2) and after tourniquet (Group 3) groups was less than the control group in this study. However, there was no significant difference between Group 2 and 3. A small patient count and dramatic decreases in Hb levels among some patients in Group 3 are possible reasons for this result. Our results are correlated with the literature (13–17).

When we looked at transfusions, they were correlated with a decrease in Hb and blood loss. Eighteen patients in control group and three patients in Group 3 were transfused. TEA-administered patients required significantly less blood transfusion than the control group in the studies by Ellis et al. and Alveres et al., which are consistent with the current study (13,18). Tranexamic acid inhibits conversion of plasminogen to plasmin, precluding any change in aPTT, INR, and PT values. In this study, there was no significant difference in values. These results are correlated with the literature (14,18–21).

In case series reported in the literature, varying rates of thromboembolism associated with tranexamic acid use have been reported, but in our study, no thromboembolism was observed. Engel et al. reported that two of 12 patients had venous thromboembolism in their study (22). In our study, there were no thromboembolic cases.

Conclusion

In conclusion, single-dose TEA administration after tourniquet removal reduces blood loss compared with before tourniquet placement but does not significantly affect Hb levels. In the future, new studies with more patients will be more informative in solving the problem of excessive blood loss in surgical interventions.

Limitations of the Study

There were some limitations to this study: the sample size (90 patients) was small across groups, and the study design was not a double-blinded, randomized, prospective comparative trial. Venous thromboembolism was not assessed and monitored by ultrasound preoperatively and postoperatively. It was assessed clinically in the postoperative period. However, a positive aspect of this study was that the operations were performed solely by the senior surgeon (EE), and the same intraoperative anesthetic technique was applied by the same anesthesiologist.

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