

# Efficacy of topical tranexamic acid in bilateral cementless total knee arthroplasty

Topical tranexamic acid in cementless knee arthroplasty

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## Abstract

**Aim:** Tranexamic acid (TXA) can be used to reduce local and systemic blood transfusion in the total knee prosthesis. In this study, the amount of bleeding in simultaneous cementless bilateral total knee prosthesis (SCBTKP) surgery has been analyzed in groups of patients who used/did not use intra-articular TXA, while considering the patients' age, gender and additional diseases.

**Material and Methods:** This retrospective study was carried out by analyzing the data obtained from 227 patients who had SCBTKP operation. TXA was used in 158 patients, whereas TXA was not used in the other 69 patients. Evaluation was carried out considering various factors such as duration of operation, levels of hemoglobin and hematocrit, blood transfusion ratio, levels and types of anesthesia, age, additional diseases, antiaggregant usage history.

**Results:** The amount of total blood loss was significantly higher in the group, which did not use TXA and in relation to this fact, the amount of blood given to patients was significantly higher in the group, which used TXA. The length of hospital stay was significantly shorter for patients who used TXA. There were no differences in the rates of cases of venous thromboembolism in post-operative patients. For both groups, there were no differences in complications.

**Discussion:** One of the important complications of the total knee prosthesis is blood loss. TXA is one of the methods used to reduce surgical bleeding or reduce traumatic bleeding. This study reveals that for patients who used TXA, blood loss and Hemovac drainage volumes were significantly low.

## Keywords

Tranexamic Acid, Simultaneous Bilateral Cementless Total Knee Prosthesis, Bleeding, Venous Thromboembolism

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## Introduction

Osteoarthritis is one of the factors leading to a decrease in the quality of life of old patients. Pain causes structural changes in the joints. As a result, joint movements are limited. In the US, the percentage of patients over 60 years old with symptomatic knee arthritis is reported as 12%. If conservative treatment is insufficient, surgical treatment is performed. One of the surgical treatment options is total knee arthroplasty [1]. Future projections predict that up to 2050, 1.5 million operations will be performed annually. This will further increase the cost [2]. Part of this cost is blood transfusion cost.

The total knee prosthesis is an orthopedic surgical procedure used worldwide. It is most commonly used with cement but it can also be performed cementless, with successful results in recent years [3]. Lately, simultaneous bilateral knee prosthesis can be performed in accordance with the patient and the surgeon's choice [4]. While there are disadvantages of simultaneous bilateral knee prosthesis such as pulmonary embolism, increased need for blood transfusion, deep vein thrombosis, cardiac side effects, wound complications, which are still being discussed [5]. It has some advantages like short recovery time and low cost [6].

Approximately 50% of the patients need blood after total knee prosthesis operation and this need can be as much as 2-3 units per one-sided arthroplasty [7]. It has been reported that the amount of blood needed is higher in one-staged bilateral knee prosthesis [8]. Various drugs and mechanical precautions are used to reduce blood loss including non-pharmacological precautions such as various types of anesthesia, the use of tourniquet, drains, and some types of prosthesis [9,10]. Also, pharmacological agents, such as epinephrine, norepinephrine, tranexamic acid, epsilon aminocaproic acid can be used. Among these agents, tranexamic acid is commonly used [11].

TXA is a synthetic lysine analog [12]. TXA prevents the plasminogen from becoming plasmin, and this prevents the fragmentation of factor V, factor VIII, fibrin clot and fibrinogens [10]. There are oral, intravenous, intraarticular and periarticular applications of TXA [12]. In recent years, studies about TXA applications have reported a reduction in blood loss [13]. As far as we know, there are no studies in the literature investigating blood loss after SCBTKP operation and the efficiency of TXA. Our main goal in this study is to investigate the effect of post-SCBTKP intraarticular TXA usage on bleeding. The secondary goal is to evaluate the side effects of TXA regarding additional diseases of patients and the type of anesthesia.

## Material and Methods

This study has been carried out with patients with an advanced degree of bilateral knee osteoarthritis who had SCBTKP operation between 2013 – 2021. The ages of patients were between 45 and 84 years. In total, 227 patients were included in the study. Patients with one-sided total knee prosthesis, infection-induced arthritis, advanced bleeding and thrombotic disorder, revision patients, and patients with chronic anemia were excluded. Patients who used anticoagulants stopped taking them 1 week before the study. In case of necessity, low molecular weight heparin was given. The study was approved by the Trabzon Kanuni Training and Research Hospital Ethics

Committee.

In this study, which included 227 patients, patients were divided into 2 groups: Group A: SCBTKP surgery with local TXA application; Group B: SCBTKP surgery without local TXA. Two nurses recorded postoperative bleeding volumes on the files through visual inspection of drains. Anesthetic data, additional diseases of patients and bleeding records were also recorded in the files.

**Surgical Method:** All the surgeries were carried out by the same experienced surgical team using various anesthesia methods. The body part, on which the operation was to begin was chosen by the surgeon, and the preference for the part varied in accordance with the conditions of the case. After the necessary preparations, tourniquet pressure was increased up to 250 mm/hg, provided that the overall condition and blood pressure of the patient were appropriate. The knee joint was opened using the medial parapatellar approach. Cementless total knee prosthesis was used in all the cases. After the prosthesis application, 2mg of Traxamine capsules were applied intra-articularly. Additional cauterization was not performed. After the operation, at the end of the first day, drainage was removed and physical exercises started. On the second day, flexion and extension exercises, started and patients who could tolerate them were engaged in walking exercises.

**Collection of results:** Total blood loss: Hb and htc were recorded pre-operatively. They were recorded after 2 hours and 1 day after the surgery. The days of the record varied in accordance with the need for blood transfusion by the patient. Special attention was paid to keep the hemoglobin levels of the patients at 10 g/dl at the time of their discharge, which was between 5-7 days.

**Patient information:** Age, gender, body mass index, duration of operation, other diseases, history of antiaggregant use before the surgery,

**Blood transfusion ratio:** Blood transfusion to the patients was planned when the patients had symptomatic anemia (mild headache, fatigue, shortness of breath, palpitation) or when the Hb level was detected below 10.

**Complications:** In this group of evaluation, problems that occurred after the surgery were analyzed, such as deep vein thrombosis, myocardial infarction and wound problems.

## Statistical analysis

Descriptive statistics were used to summarize patient characteristics. The change in baseline hemoglobin and hematocrit values over time and the difference between groups were analyzed by repeated measure two-way ANOVA test. The Chi-square test for categorical variables and Independent Samples T-test were processed to compare groups. A p-value of less than 0.05 was considered to be statistically significant between the variables. Statistics were performed with IBM SPSS Statistics for Windows, version 26 (IBM Corp., Armonk, N.Y., USA).

## Ethical Approval

Ethics Committee approval for the study was obtained.

## Results

This study was conducted with 227 patients who had SCBTKP surgery between 2014 – 2020. The ages of the patients varied

between 45 and 84. The average age was 65.5 + 8 years; 207 of the patients (90.3%) were females. The average BMI of the patients was 33.7 ± 4.9 and the dominant blood groups were A Rh+ (42.3%) and O Rh+ (30.4); 112 patients (49.3%) had hypertension, 37 (16.3%) had diabetes, 16 (7%) had hyperthyroid and 6 (2.6%) had coronary artery disease.

The local transamine was used for 158 (68.6%) patients, however, it was not used for 69 (31.4%) patients. The ages of the patients varied between 45-84, and the average age was 65.5 ± 8; 207 (90.3%) patients were women. Hb, htc, age, ASA, BMI, gender, additional diseases, type of anesthesia used in the surgery, operation duration, hospital stays, erythrocyte replacements are given in Table 1.

**Total blood loss:** Total blood loss was higher in the group, which did not use TXA. It was ensured that post operation hemoglobin levels of the patients did not drop below 10 gr/dL because of blood loss and symptomatic anemia. In time-related change of these levels, no statistical difference was observed between the groups, which used TXA and the group, which did not.

**Erythrocyte replacement:** Throughout the follow-up time, erythrocyte replacement was applied to 115 patients among the TXA applied group (72.8%); 98 of these patients (62%) had 1-2 units of erythrocyte suspension (ES) replanted, and 17 of them (10,8%) had 3 units of ES replanted. All patients of the group, in which TXA was not applied, had ES replacement and, this ES replacement was at least 3 units or more for 59 (85.5%) patients. This value referred to a statistically significant finding. With the ES replacement given to the patients in the follow-up time, patients' hemoglobin levels were stable at approximately 10 when they left the hospital.

**Previous diseases:** Previous diseases and chronic diseases of the patients were considered before the surgery.

As is shown in the table above, the effects of past diseases

on the patients were evaluated and their effects on blood transfusion were also evaluated regarding TXA usage and need. The results revealed that the relevance level between the patients' use of anticoagulants, their hypertension and diabetes history, being obese and gender were not significant. It was found out that the relevance level regarding the ages of patients was significant.

**Age:** Erythrocyte suspension was not applied to 28.4% of the patients younger than 65, while for patients older than 65, this rate was 12.1 %. A minimum of 3 erythrocyte suspensions were applied to 22.1% of the patients younger than 65, while a minimum of 3 erythrocyte suspensions were replaced for 41.7% of the patients older than 65 (p<0.001).

**Complications:** Among all patients, 2 patients had infection, and revisions were made for 4 patients. There was no statistically significant difference between the ones who used transamine and who did not use (p=0.516, p=0.317, respectively).

**Venous thromboembolism:** 2 venous thromboembolism cases were observed during the follow-up of both groups. There was no statistically significant difference (p=0,516).

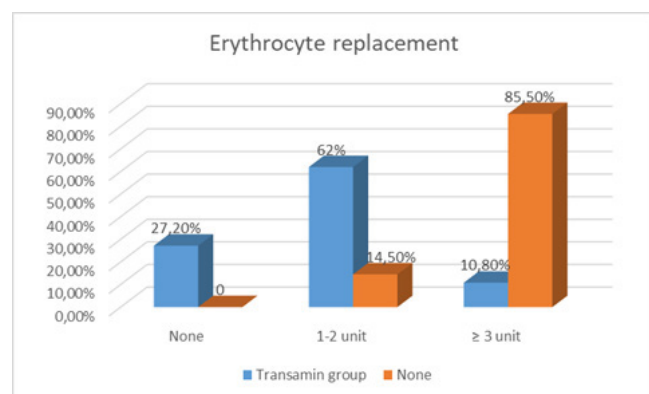
**Table 1.** Basic clinical and demographical features of patients.

	Transamine group (n=158)	None (n=69)	P
Gender, woman	145 (91.8%)	60 (87%)	0.259
Age (≥ 65 years)	81 (51.3%)	51 (73.9%)	0.001
Type of anesthesia	General	8 (11.6%)	0.001
	Spinal	44 (27.8%)	
	Spinal + epidural	90 (57%)	
BMI (≥ 35 kg/m <sup>2</sup> )	61 (38.6%)	18 (26.1%)	0.069
Time in surgery, min	66.1 ± 11.6	77.5 ± 14.1	
Length of hospital stays, days	11.5 ± 3.6	14.5 ± 3.4	<0.001
Pre-op Hb (gr/dL)	13,4+1,6	13,2+1,2	0.408
Pre-op Htc (%)	40,1+3,5	40,2+3,6	0.927

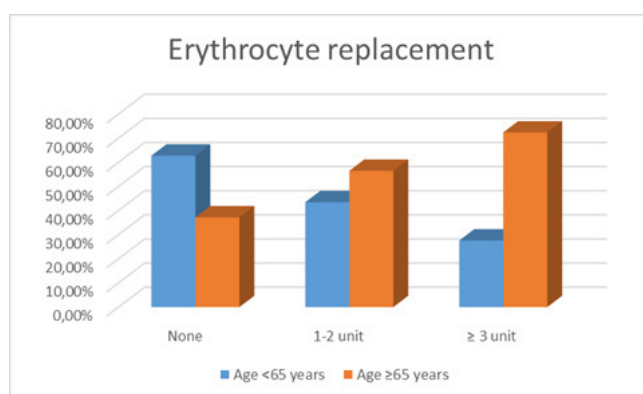
**Table 2.** Amount of blood loss and erythrocyte transfusion for patient groups.

Variable	Transamine group		None		P value	
	Initial	Output	Initial	Output	Time	Group
Hb(gr/dL)	13.4 ± 1.6	10.2 ± 0.7	13.2 ± 1.3	10.2 ± 0.7	<0.001	0.452
Hct	40.1 ± 3.5	30.6 ± 2.7	40.2 ± 3.6	30.8 ± 2.5	<0.001	0.712
Erythrocyte replacement						
0	43 (27.2%)		0			
1-2 unit	98 (62%)		10 (14.5%)			<0.001
≥ 3 unit	17 (10.8%)		59 (85.5%)			

(p-value is significant at .05 level)



**Figure 1.** TXA usage of groups.



**Figure 2.** Erythrocyte requirement by age.

**Table 3.** Evaluation of patients' clinical history.

		Transamine group (n=158)	None (n=69)	P-value
Gender, woman		145 (91.8%)	60 (87%)	0.259
Age ( $\geq 65$ years)		81 (51.3%)	51 (73.9%)	0.001
Operation type	General	24 (15.2%)	8 (11.6%)	0.001
	Spinal	44 (27.8%)	5 (7.2%)	
	Spinal + epidural	90 (57%)	56 (81.2%)	
BMI ( $\geq 35$ kg/m <sup>2</sup> )		61 (38.6%)	18 (26.1%)	0.069
ASA	1	23 (14.6%)	6 (8.7%)	0.458
	2	99 (62.7%)	45 (65.2%)	
	3	36 (22.8%)	18 (26.1%)	
Anticoagulant usage		8 (5.1%)	4 (5.8%)	0.758
Comorbid disease, any		104 (65.8%)	40 (58%)	0.259
HT		77 (48.7%)	35 (50.7%)	0.783
DM		30 (19%)	7 (10.1%)	0.097
Time in surgery, min		66.1 $\pm$ 11.6	77.5 $\pm$ 14.1	
Length of hospital stays, day		11.5 $\pm$ 3.6	14.5 $\pm$ 3.4	<0.001
Erythrocyte replacement	None	43 (27.2%)	0	<0.001
	1-2 unit	98 (62%)	10 (14.5%)	
	$\geq 3$ unit	17 (10.8%)	59 (85.5%)	

(p-value is significant at .05 level)

## Discussion

One of the important complications of total knee prosthesis is blood loss [14]. Various methods are used to reduce blood loss. In this study, the effect of local TXA usage in patients, undergoing SCBTKP surgery on blood loss has been investigated. Secondly, the effect of the drugs used by the patients and the reasons of additional diseases of the patients on blood loss have been investigated. The results of the study revealed that, independent of the extra factors, blood need was reduced in patients who used TXA locally, and very few complications occurred.

TXA inhibits the conversion of plasminogen to plasmin. In this way, it is used to reduce surgical bleeding or to reduce traumatic bleeding [15]. Chambers et al. investigated the use of local TXA in cemented and hybrid prostheses in their study with 139 unilateral knee prostheses. The authors reported that topical TXA was as effective as cement fixation in hybrid fixation. This study is important in terms of reporting that TXA reduces bleeding, although there is no cement at the bone-implant interface that does not prevent blood loss [16]. In their study, Santias M et al looked at the reduction of bleeding by TXA without the use of a tourniquet. In a study conducted with 268 patients, 2 g of topical TXA was given in 50 ml of saline after the surgery and the amount of bleeding was found to be 1094 ml in patients who did not use TXA, while the average amount of bleeding was found to be 620 ml in patients using TXA, and no blood transfusion was performed in any patient using TXA [17]. In this study, a significant reduction in blood loss in bilateral knee prosthesis without cement was compatible with the hypothesis of the study. It was determined that the need for 2gr of local TXA blood per knee was significantly reduced. Thus, 17% of the patients who received TXA had 3 or more erythrocyte replacements, while 85.5% of the patients who did not receive local TXA had at least 3 erythrocyte replacements. TXA can be used orally, intraventricularly or topically. Intravenous administration of TXA can significantly reduce blood loss

[18]. While dose-dependent oral TXA usage is reported to be linked with venous thromboembolism [19], in comprehensive meta-analyses, it is reported that it was not the cause of thromboembolic problems. Similarly, oral and iv TXA usage reduces the blood loss and there are hardly any complications due to reduced TXA usage, however, it is reported to increase DVT ratio [20,21]. Digas et al. reported that in-joint use of TXA reduces blood loss more than other methods, but they did not mention venous thromboembolic problems in their study [22]. In addition, 2 mg TXA usage in each knee has significantly reduced the amount of bleeding and the fact that there were limited complications gives us an idea about the effective dose, usage timing and method. There are many studies about TXA usage and method, however, timing or dose of usage has not been standardized in these studies [23]. Thus, it would be more meaningful to conduct this study in a wide series of bilateral cementless simultaneous cases, as no studies on this issue have been found in the literature.

As known, prosthesis surgeries are usually performed on old patients with risk factors. Studies report that age, gender, multi-comorbidity can increase the amount of bleeding [24]. In this study, medical histories of patients were recorded in detail and included in the study. This study reveals that the additional comorbidities of patients did not affect the amount of bleeding, and the amount of blood needed is higher in old patients. Various types of complications can occur after knee prosthesis surgeries, such as bleeding, wound problems, thromboembolic problems, neurovascular injuries, ligament injuries, swelling, deep periprosthetic infection and fractures [25]. Among these complications, venous thromboembolism is reported by some authors to be affected by transamine usage [21]. In the literature, other possible complications are not linked to TXA usage. In this study, venous thromboembolism was observed in 2 patients, and this rate of incidence is smaller than the rate reported in the literature. In addition, while not being

statistically important, 2 patients had infection and 4 patients had their one-sided prosthesis revised due to loosening. Patients who took part in this study did not have any thromboembolic problems up to their last controls.

This study reveals that for patients who used TXA, blood loss and Hemovac drainage volumes were significantly low, hospital stays were shortened and complication ratios were relatively low. As a result, 2 g topical TXA application for each knee in patients undergoing SCBTKP surgery significantly reduced blood loss, did not increase additional risks and its use was beneficial during the operation.

#### Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

#### Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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#### Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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