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ORIGINAL ARTICLE

Use of tranexamic acid may reduce the need for routine tourniquet use in total knee arthroplasty

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ABSTRACT

Objectives: The aim of this study was to evaluate the effects of tranexamic acid (TXA) administration on bleeding control and to compare its utilization with and without simultaneous use of conventional pneumatic tourniquets during total knee arthroplasty (TKA).

Patients and methods: Between January 2017 and December 2017, a total of 204 patients (23 males, 181 females; mean age: 66±6.9 years; range, 45 to 86 years) who underwent TKA for Stage 4 gonarthrosis were retrospectively analyzed. The patients were divided into two groups as those with (n=110) and without (n=94) pneumatic tourniquet use. Tranexamic acid (1 g) was administered intravenously to all patients in both study groups. Intra- and postoperative blood loss were calculated, and postoperative pain was evaluated by a Visual Analog Scale. Demographic and clinical data were compared between the study groups.

Results: The amount of total blood loss and postoperative blood loss were significantly higher in the tourniquet group than that in the no-tourniquet group (589.4±69.5 mL *vs.* 490.8±55.2 mL and 326±56 mL *vs.* 164±35.5, respectively; p<0.001 for both). Intraoperative blood loss was significantly higher in the no-tourniquet group (326.9±42.9 mL *vs.* 263.5±53.8 mL, respectively; p<0.001). The pain score at 24 h was significantly higher in the tourniquet group (p<0.001).

Conclusion: Total blood loss and postoperative pain were significantly higher among patients in whom a tourniquet was used during TKA. Therefore, the routine use of tourniquets with TXA should be reconsidered.

Keywords: Blood loss, pneumatic tourniquet, postoperative pain, total knee arthroplasty, tranexamic acid.

Perioperative blood loss during joint arthroplasties with excess bleeding may be a major concern for negative postoperative consequences including longer hospital stay and complicated rehabilitation in some cases.[1] Moreover, transfusion after massive blood loss in arthroplasties may result in an increased risk of infection, revision, and mortality.[2,3] To avoid these negative consequences, a tourniquet has been used conventionally for intraoperative bleeding control for a long time.[4] Decreased blood flow due to tourniquet use also provides a clear vision of anatomical structures in the operation site.[5] Nevertheless, postoperative hemorrhage is unlikely to be decreased in parallel to intraoperative bleeding after tourniquet use in total knee arthroplasty (TKA), but with some additional risks of complications.[6] Of note, there is a considerable debate about the safety of tourniquet application due to the increased postoperative venous thromboembolism risk, as well as the effects of ischemia and compression of neurovascular structures.[6] One of the other approaches to control perioperative hemorrhage in TKA is the systemic or local administration of tranexamic acid (TXA) in addition to spinal anesthesia.[7,8] Tranexamic acid

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is a synthetic antifibrinolytic agent which inhibits the activation of plasminogen competitively and is widely used for effective bleeding control in TKA.[9,10] Current evidence regarding the use of TXA in TKA operations suggests that it is a safe and effective option for hemorrhagic control without increasing venous thromboembolic events.[11] However, there is a widespread practice pattern among orthopedic surgeons toward using tourniquets during knee arthroplasties, which needs comparison of using and not using tourniquets along with TXA application regarding the efficiency and safety in TKA operations. Based on this background, in the present study, we aimed to investigate the short-term benefits of tourniquet use along with preoperative use of TXA (1 g) on perioperative hemorrhage and postoperative pain in the clinical setting.

PATIENTS AND METHODS

This single-center, retrospective study was conducted at Dışkapı Yıldırım Beyazıt Training and Research Hospital, Department of Orthopedics and Traumatology between January 1st, 2017 and December 31st, 2017. A total of 231 patients who underwent total knee prosthesis surgery for Stage 4 gonarthrosis with spinal anesthesia were screened. Patients with revision surgery, having general anesthesia, peripheral arterial disease, or a hemorrhagic diathesis, the American Society of Anesthesiologists (ASA) Class IV patients, patients with contraindications to TXA, those receiving thrombolytic treatment, and those with missing Visual Analog Scale (VAS) scores or who were recorded as unable to cooperate for VAS assessments were excluded. Finally, a total of 204 patients (23 males, 181 females; mean age: 66±6.9 years; range, 45 to 86 years) were included. The patients who underwent TKA were retrospectively classified according to the use of a pneumatic tourniquet during the operation. The decision to operate with or without a tourniquet was based on the attending surgeon's preference. All patients received spinal anesthesia with bupivacaine (Marcaine®, AstraZeneca PLC, UK). In the group where a pneumatic tourniquet was used, tourniquet pressurization was done only after leg elevation immediately before the incision, and without an Esmarch bandage. Tourniquet pressure was set to approximately 100 mmHg higher than the systolic blood pressure of the patient. In the second group, a tourniquet was not used at any stage of the operation.

All operations were performed under spinal anesthesia. The same medication protocol including cefazolin sodium (1 g for patients up to 80 kg and 2 g for patients over 80 kg), 1 g intravenous (IV) TXA to decrease the hemorrhage was administered after spinal anesthesia. Zimmer® NexGen® (Zimmer Biomet, Warsaw, Indiana, USA), cemented, cruciate ligament substituting total knee prostheses were used for all patients. Jet lavage was used in all cases for a clear bony surface before cementing. Subfascial drains were used in all patients and, after fascia closure, all patients received bupivacaine injection around their surgical incision. A Jones bandage was applied to both groups, and the tourniquet was removed only after the application of the Jones bandage in the tourniquet group. Drains were opened at the postoperative 2 h in both groups. Jones bandages and drains were removed at the postoperative 24 h. Subcutaneous 4,000 U enoxaparin sodium for thromboembolism prophylaxis was administered for three weeks after the operation to all patients.[12]

Pain control was done by IV administration of 1 g paracetamol (Paracerol IV, Polifarma İlaç San., Istanbul, Türkiye), when the effect of spinal anesthesia started to subside and repeated 6 h later. Additional pain supplementation was done with tramadol (Contramal, Grunenthal & Abdi Ibrahim Ilaç San., Istanbul, Türkiye) if required. The VAS scores were taken only once the following day as our standard clinical practice by the nurses and the patient was asked to evaluate their first night globally.

The amount of intraoperative blood loss was calculated using the weight differences of dry and wet gauze sponges, and volume differences of washing fluids and aspirated materials. Suction drains were used in all patients for 24 h, but they were closed for the first 2 h. Postoperative blood loss was calculated from the amount of blood in suction drains. Blood transfusions were also recorded.

The data collected from the patient records, operation notes, and clinical registry of arthroplasties included the amounts of intraoperative and postoperative blood loss, the need for transfusion and the duration of operation, hemoglobin, and hematocrit levels before surgery and on postoperative Day 4. Some of the patients were discharged before postoperative Day 4, but they were called for a control visit, and blood samples were taken.

Statistical analysis

Statistical analysis was performed using the IBM SPSS for Windows version 21.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean ± standard deviation

TABLE 1
Demographic characteristics of the study groups

	No-tourniquet group (n=94)			Tourniquet group (n=110)			
	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (year)			65.8±6.7			66.2±7.1	0.786
Sex							0.131
Female	80	85.1		101	91.8		
Male	14	14.9		9	8.2		
Height (cm)			164.8±6.6			162.8±6.6	0.017
Body weight (kg)			85±10.1			83.8±9.8	0.327
Body mass index (kg/m^2)			31.5±4.8			31.8±4.6	0.449

SD: Standard deviation.

(SD) for continuous variables and in number and frequency for categorical variables. Comparison between the study groups was performed using the Mann-Whitney U test and chi-square test for continuous and categorical variables, respectively. Comparison between dependent continuous variables (pre- and postoperative values) was performed using the Wilcoxon signed-rank test. A *p* value of <0.05 was considered statistically significant.

RESULTS

Tourniquet and no-tourniquet groups included 110 (53.9%) and 94 (46.1%) patients, respectively. Demographic characteristics of the patients are summarized in Table 1. Sex distribution was similar in the study groups (p=0.131). While the mean age (p=0.786) and mean body weight (p=0.327) of the study groups were similar, the mean height of the no-tourniquet group was significantly higher than that of the tourniquet group (164.8±6.6 cm *vs.* 162.8±6.6 cm, respectively; p=0.017).

The mean operation time was 70.2±6 min in the no-tourniquet group and 72±6.9 min in the tourniquet group (p=0.072). The pre- and postoperative hemoglobin and hematocrit levels were similar in both groups (p>0.05 for all). In the

TABLE 2
Clinical and laboratory characteristics of the study groups

	No-tourniquet group (n=94)	Tourniquet group (n=110)	
	Mean±SD	Mean±SD	*p*
Operation time (min)	70.2±6	72±6.9	0.072
Hemoglobin levels (gr/dL)			
Preoperative	13.3±1.4	13.3±1.3	0.676
Postoperative	11.6±1.5	11.7±1.2	0.160
p (preoperative to postoperative)	<0.001	<0.001	
Hematocrit levels (%)			
Preoperative	39.9±3.9	40±3.8	0.719
Postoperative	34.5±4.2	35±3.7	0.096
p (preoperative to postoperative)	<0.001	<0.001	
Blood loss (mL)			
Operative	326.9±42.9	263.5±53.8	<0.001
Postoperative	164±35.5	326±56	<0.001
p (preoperative to postoperative)	<0.001	<0.001	
Total blood loss (mL)	490.8±55.2	589.4±69.5	<0.001
Postoperative 24th h VAS scores	31.9±6.8	40.4±7.2	<0.001

SD: Standard deviation; VAS: Visual Analog Scale.

separate analysis, the postoperative hemoglobin and hematocrit levels were significantly lower compared to preoperative values ($p<0.001$ for all). The amount of total and postoperative blood loss was significantly higher in the tourniquet group than that in the no-tourniquet group (589.4±69.5 mL *vs.* 490.8±55.2 mL and 326±56 *vs.* 164±35.5, respectively; $p<0.001$ for both). However, intraoperative blood loss was significantly higher in the no-tourniquet group (326.9±42.9 mL *vs.* 263.5±53.8, respectively; $p<0.001$). Additionally, the pain score at 24 h was significantly higher in the tourniquet group ($p<0.001$). The clinical and laboratory characteristics of the study groups are presented in Table 2.

Maximum intraoperative blood loss was 415 mL in the no-tourniquet group. Maximum postoperative bleeding was 450 mL in the tourniquet group. Maximum total blood loss in one patient was 740 mL in the tourniquet group. None of the patients received any blood product transfusion and there was no significant difference in the amount of analgesics required postoperatively.

DISCUSSION

The conventional method for preventing blood loss during TKAs has been tourniquet used for many years; nevertheless, the use of tourniquets is not without complications. Previous studies have reported that pneumatic tourniquets are associated with nerve palsy, vascular injury, muscle damage, and postoperative swelling and stiffness.[5] Moreover, the risks of deep venous thrombosis (DVT), poor postoperative wound healing, and postoperative pain were found to be increased due to tourniquet application.[13,14] The contemporary approach to control blood loss is the intraoperative use of TXA, but there is still a tendency among orthopedic surgeons to apply pneumatic tourniquets. Proponents of tourniquet use mention better visualization of the surgical field and better cement interdigitation.

The results of this study showed that there was a significant decrease in postoperative hemoglobin and hematocrit levels in both study groups, although the difference between patients with and without tourniquet was not statistically significant. Nevertheless, there was an interesting finding when the volume of blood loss during operative and postoperative periods was assessed. The volume of intraoperative blood loss was significantly higher in patients without tourniquet application, but the amount of postoperative blood loss determined from the suction drains was significantly higher in patients with pneumatic tourniquet use. Likewise, the total amount of blood loss was significantly higher in the tourniquet group. These results were in general accordance with currently available evidence in the literature.

Several studies have evaluated tourniquet use during TKA surgeries. Tai et al.[15] evaluated the effects of tourniquet application on blood loss in primary TKAs in a meta-analysis and reported that tourniquet application decreased only the intraoperative, but not the postoperative and total blood loss, which was similar to the results of this study. Another study by Li et al.[16] examined the association of tourniquets with blood loss, rehabilitation, and complications in Chinese patients with obesity undergoing TKA, and reported that tourniquet application was not associated with reduced blood loss and increased postoperative complications. These results are consistent with our results about the blood loss. In a recent study, Patel et al.[17] investigated the effects of tourniquet and TXA use on hemoglobin drop and transfusion rates in TKA. The authors demonstrated greater postoperative hemoglobin drop in patients undergoing TKA surgery without a tourniquet; however, the use of TXA significantly reduced the hemoglobin drop in non-torniquet patients. This finding is also consistent with our results. Although the TXA has been demonstrated to reduce postoperative blood loss in TKA, the most optimal dose is still controversial. Morales Santias et al.[18] suggested using a single dose of topical TXA to reduce blood loss in TKA. Huang et al.[19] concluded that multiple IV and topical TXA administration without a tourniquet during TKA was associated with less hidden blood loss. Tzatzairis et al.[20] evaluated one to three doses of IV TXA and concluded that three doses had effectively reduce the blood loss in TKA. Although there is no consensus about the optimum dose of TXA in recent literature, many studies have demonstrated the effectiveness of TXA without a tourniquet as in the current study.

Another important aspect of tourniquet use in TKA was the timing of application. A randomized-controlled trial about tourniquet use in TKAs by Wang et al.[21] found that intraoperative and total blood loss decreased with long-duration (inflated immediately before the incision) tourniquet use, but there was greater postoperative and hidden blood loss which is consistent with the results of this study. Although the timing of the tourniquet was not assessed in this study, the result of the

aforementioned study is worth consideration for addressing the timing of tourniquet application during TKAs.

Not only the amount of blood loss, but also the postoperative pain scores were significantly higher among patients in the tourniquet group, which was also reported by earlier studies. Liu et al.[22] evaluated the use of tourniquets in TKAs and reported that pain was significantly decreased in patients without tourniquet use, while tourniquet use was associated with more pain and slower functional recovery. Another study by Liu et al.[23] also reported that no-tourniquet group had significantly less pain in the early postoperative period compared to the tourniquet group and recommended not to routinely use tourniquets during TKAs. The results of this study are consistent with the reports in the literature. The favorable results obtained in the no-tourniquet group suggest that TXA alone is capable to provide adequate hemorrhagic control, as well as decreased pain levels.

In the current study, the use of pneumatic tourniquets in TKAs seems to be disadvantageous for hemorrhagic control in patients undergoing TKA. The literature reviews are in concordance with our findings. A previous meta-analysis by Zhang et al.[24] including 689 patients with 689 knees in 13 randomized-controlled trials evaluated tourniquet use in TKAs. The authors reported that not using a tourniquet was superior to using it in TKAs for thromboembolic events. The authors also reported that there was no significant difference in actual blood loss between the two methods, but the application of a tourniquet might adversely affect postoperative rehabilitation exercises. Another recent systematic review and meta-analysis of clinical trials by Jiang et al.[6] examined the benefits and disadvantages of tourniquet in TKA. Based on the assessment of 26 randomized-controlled trials involving 1,450 knees, tourniquets were found to be effective for intraoperative bleeding control, although risks of DVT, poor wound healing, and delayed functional recovery of the knee were reported as the adverse effects of tourniquets. Another meta-analysis by Jawhar et al.[25] that included 18 studies with 1,279 TKAs analyzed the influence of tourniquets on postoperative pain and knee functions and reported that tourniquet use had a negative effect on both pain and knee flexion in the early postoperative period. In the present study, we were unable to evaluate the postoperative venous thromboembolic events and gain of function; however, the results from our analyses are consistent with the results of these two recent meta-analyses regarding intraoperative blood loss and postoperative pain.

The superiority of this study is that it is not randomized; therefore, every team is at its best in the way they operate without any restrictions. The data were pooled from a larger patient population than a smaller randomized group and it seems that we have the largest patient data currently. Limitations are non-randomized patient groups as well as no general anesthesia group to compare the effect of spinal anesthesia in reducing blood loss. Also, a longer follow-up period would have provided long-term outcomes for both groups. In addition, we were unable to examine the adverse outcomes such as thromboembolic events or delayed wound healing. We believe that further long-term studies investigating the effect of tourniquets on cement interdigitation and its effect on long-term survival are needed.

In conclusion, total blood loss and postoperative pain were found to be significantly higher among patients with pneumatic tourniquet use in TKA. Based on our results, routine use of tourniquets for hemorrhagic control along with TXA administration may not be necessary. Further studies are warranted to draw more reliable conclusions on this subject.

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Ethics Committee Approval: The study protocol was approved by the Univiersity of Health Sciences, Dışkapı Yıldırım Beyazıt Training and Research Hospital Ethics Committee (date: 19.03.2018, no: 47/03). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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