

Original Article

Enhancing recovery: The role of local tranexamic acid in reducing postoperative complications in saphenous vein harvesting

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Abstract

Aim: This study aims to investigate the effects of topically applied tranexamic acid (TXA) on postoperative complications at the saphenous vein graft site following coronary artery bypass grafting (CABG).

Material and Methods: A prospective analysis was conducted on 63 patients who underwent CABG between January 2024 and August 2024. Patients were randomly divided into two groups: a TXA group (n=32) who received topical TXA at the saphenous vein incision site, and a control group without TXA (n=31). Outcomes evaluated included leg circumference measurements, incidence of hematoma, ecchymosis, inflammation, necrosis, surgical infection, and mobilization difficulty. Pain and quality of life were assessed using the Visual Analog Scale (VAS) and Venous Clinical Severity Score (VCSS) respectively.

Results: Patients in the TXA group exhibited significantly lower leg circumference measurements postoperatively on days 1 and 5 ($p<0.05$). The incidence of severe ecchymosis was significantly lower in the TXA group (3%) compared to (29%) the control group ($p=0.001$). No statistically significant differences were observed between groups for hematoma, inflammation, or necrosis rates. Hospitalization duration was shorter in the TXA group (4.2 ± 1.8 days) than in the control group (5.6 ± 2.2 days, $p=0.02$). The TXA group also showed lower VAS pain scores and improved VCSS quality of life scores compared to the control group ($p<0.05$).

Conclusion: Topical application of TXA at the saphenous vein incision site appears to reduce postoperative complications such as ecchymosis and leg swelling, while also improving pain management and quality of life. TXA may help shorten hospital stays and promote early mobilization following CABG. Further large-scale randomized controlled trials are needed to validate these findings and assess TXA's impact on more severe complications such as hematoma and necrosis.

Keywords: Tranexamic acid, coronary artery bypass grafting, saphenous vein harvesting, venous clinical severity score, visual analogue scale

INTRODUCTION

Tranexamic acid is a lysine derivative that restrains fibrinolysis by competitive inhibition of plasmin and plasminogen leading to decreased peri-operative bleeding [1-3]. Beyond haemostasis, TXA modulates inflammatory pathways, showing both anti- and pro-inflammatory effects that depend on its regulation of plasmin-mediated signalling [4-8]. Experimental data indicate that high-dose TXA lowers key cytokines (IL-6, TNF- α) and suppresses

NF- κ B activation [9-11], while clinical evidence links TXA to attenuated immunosuppression after surgery [12].

Intravenous TXA is established to be effective in cardiac surgeries, such as coronary artery bypass grafting (CABG) [13,14], and topical use has also proved beneficial [15]. However, harvesting the saphenous vein a common CABG conduit [16] can cause leg pain, haematoma, infection and delayed mobilisation, with reported lower-limb complication rates around 4% [16,17]. Topical TXA

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has decreased oedema, ecchymosis and inflammatory sequelae in other surgical wounds [18], but its effect on saphenous harvest sites remains unclear.

This study aims to evaluate the effects of topically applied TXA on postoperative complications at the saphenous graft site following CABG, where the graft is harvested using the conventional technique. The primary end-point was reduction in harvest-site ecchymosis. Secondary end-points consisted of changes in postoperative pain, venous clinical severity score (VCSS), mobilisation-related outcomes and length of hospital stay.

MATERIAL AND METHODS

In this prospective study, a total of 63 patients who underwent CABG between January 2024 and August 2024 were included. Patients were randomly allocated to two groups: the TXA group (n=32) and the control group without TXA (n=31). The study was approved by the Ankara Bilkent City Hospital Ethics Committee (E1-23-4510, 27.12.2023). Inclusion criteria consisted of patients who underwent CABG using the conventional saphenous vein harvesting method. In our clinic, systemic TXA is not routinely used during CABG procedures. None of the patients received systemic TXA. Exclusion criteria included minimally invasive saphenous harvesting, bleeding diathesis, systemic TXA use, known allergy to TXA, and recent antithrombotic drug use.

Saphenous veins were prepared with a meticulous technique as grafts using the conventional saphenous vein harvesting method. The entire skin incision was made along the saphenous vein line, starting from the level of the medial malleolus, with its length adjusted according to the number of anastomoses to be performed. Following heparin reversal in accordance with standard protocols, a solution containing 250 mg of tranexamic acid per vial was applied locally along the saphenous incision sites, at a dosage of one vial per 10 cm. Leg wounds were closed in layers. The subcutaneous tissue was closed using 0 Coated-Vicryl™ (Ethicon, Somerville, NJ, USA), while the skin was closed with continuous subcuticular sutures using 2-0 Coated-Vicryl™ (Ethicon, Somerville, NJ, USA). After surgery, an elastic bandage was applied to the leg, which was replaced with compression stockings starting on

postoperative day two. Compression stockings were used for two months postoperatively to prevent leg swelling. The incision line was assessed daily, and dressings were applied. In the evaluations, we used the grading system for ecchymosis proposed by Vuylsteke et al. [19]. This system consists of four grades: (a) no ecchymosis, (b) mild ecchymosis, (c) moderate ecchymosis, and (d) severe ecchymosis. Patients were categorized according to the severity of their ecchymosis based on this classification. Circumference measurements at the mid-thigh and calf regions were taken preoperatively, as well as on postoperative days 1 and 5.

Statistical Analysis

Categorical variables were presented as number and percentages, whereas continuous variables were summarised as mean±SD if normally distributed and as median (IQR) otherwise. Normality was assessed with the Shapiro–Wilk test. Continuous variables (e.g., leg circumference, VAS score, incision length, VCSS score, and length of hospital stay) were expressed as mean±standard deviation (SD) and were compared between the TXA and control groups using an independent samples t-test. Categorical variables (e.g., incidence of hematoma, ecchymosis, inflammation, necrosis, surgical infection, and mobilization difficulty) were presented as frequencies and percentages. Comparisons of categorical variables between groups were conducted using either the Chi-square test or Fisher's exact test, depending on sample size and data distribution. For all analyses, a p-value of <0.05 was considered statistically significant, with all tests being two-tailed. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY).

Power analysis was conducted in G*Power 3.1.9.7 (Franz Faul, University of Kiel, Germany) with Fisher’s exact test (one-tailed). Using $p_1=0.03$, $p_2=0.29$, $\alpha=0.05$, desired power=0.80, and a 1:1 allocation, the required sample size was $n_1=n_2=29$ (total=58), yielding an achieved power of 0.801 and an exact type-I error of 0.027.

RESULTS

The patients’ baseline demographic characteristics are summarized in Table 1.

Table 1. Patients demographic data			
	TXA group (n=32)	Control group (n=31)	p
Age (y)	66.4±5.6	65.4±5.2	0.71
Male	24 (75)	21 (67.7)	0.55
Diabetes mellitus (n,%)	18 (56.2)	19 (61.2)	0.64
Chronic renal failure (n,%)	6 (18.7)	4 (12.9)	0.79
Peripheral arterial disease (n,%)	5 (15.6)	4 (12.9)	0.72
Smoking (n,%)	25 (78.1)	24 (77.4)	0.82
COPD (n,%)	8 (25)	10 (32.2)	0.36
ICU stay [days] mean±SD	1.5±0.7	2±0.8	0.48
Hospital stay [days] mean±SD	5.6±2.2	4.2±1.8	0.02
COPD: chronic obstructive pulmonary disease, ICU: intensive care unit, TXA: tranexamic acid			

In the postoperative period, patients in the TXA group exhibited a smaller increase in calf and thigh circumferences compared to the control group. Notably, on postoperative days

1 and 5, leg circumference swelling in the TXA group was significantly lower than that observed in the control group (Table 2).

Table 2. Leg circumference measurements

Measurement (cm, mean±SD)	Control group (n=31)	TXA group (n=32)	P
Preoperative CD	36.6±3.1	37.4±3.3	0.38
Postoperative day 1 CD	39.6±3.1	37.8±3.6	0.04
Postoperative day 5 CD	39.9±2.9	37.7±3.5	0.01
Preoperative TD	47.1±5.0	47.9±4.2	0.52
Postoperative day 1 TD	50.1±5.5	48.0±3.6	0.07
Postoperative day 5 TD	50.4±5.0	48.0±3.6	0.03

TXA: tranexamic acid, SD: standart deviation, CD: calf diameter, TD: thigh diameter

The table shows the cases classified as (d) severe ecchymosis according to the grading system proposed by Vuylsteke et al. [19]. There were no significant differences between groups in the other ecchymosis categories. The incidence of severe ecchymosis (Grade d) was significantly lower in the TXA group compared to the control group. However, there were

no statistically significant differences between the groups regarding the rates of hematoma, inflammation, or necrosis (Table 3). In the TXA group, no cases of surgical infection were observed, while one case was reported in the control group. The length of hospital stay was significantly shorter in the TXA group compared to the control group.

Table 3. Surgical complications

Complication	Control group (n=31)	TXA group (n=32)	P
Haematoma	1 (3.2%)	2 (6.3%)	0.55
Severe ecchymosis (Grade d)	9 (29%)	1 (3%)	0.001
Inflammation	2 (6.5%)	2 (6.3%)	0.94
Necrosis	1 (3.2%)	0 (0%)	0.85
Surgical infection	1	0	0.31

TXA: tranexamic acid

Surgical complications were compared between diabetic and non-diabetic patients (Table 4). Among diabetic patients, the rates of surgical infection, inflammation, and necrosis were assessed, with no significant differences observed between the two groups.

Table 4. Diabetes mellitus (DM) status and complications

Condition	DM (-)	DM (+)	P
Surgical infection	1	0	0.45
Inflammation	1	3	0.08
Necrosis	1	2	0.24

Mobilization Difficulty

Three parameters were used to assess difficulty in mobilization: the 10-meter walk test, the six-minute walk test (SMWT), and the dynamic functional walking [timed-up and go (TUG)] test. Using these parameters, time intervals were compared between the two groups, and the outcomes were reported as the minimal difference (MD). Favoring the TXA group, the MD for the TUG test was -0.8s (95% confidence interval [CI]: -1.4 to -0.2, p=0.03). The results for the other two parameters, the 10-meter walk test (MD=-0.4s, 95% CI: -0.8 to 1.2, p=0.46) and the

SMWT (MD=70.5m, 95% CI: 62.5 to 85.2, p=0.13), were not statistically significant.

Antiplatelet Therapy

All patients continued aspirin until surgery. Dual antiplatelet use was comparable (p>0.05): 9/31 patients (29%) in the control group versus 7/32 (22%) in the TXA group. Clopidogrel, ticagrelor and prasugrel were taken by 6, 3 and 0 patients in the control group, and by 4, 1 and 1 patient in the TXA group, respectively.

Relationship Between VAS Score and Incision Length

The Visual Analog Scale (VAS) score is a key measure for assessing postoperative pain levels [20]. In this study, the distribution of VAS scores was analyzed based on incision length for both the TXA and control groups. As incision length increased, pain assessed using VAS scores was found to increase (p=0.001). When incision lengths were grouped by the number of grafts used, patients requiring three or more grafts showed significantly lower VAS scores in the TXA group compared to the control group (VAS score difference: -1.7, 95% CI: -2.4 to -0.8, p<0.05).

To assess postoperative quality of life, the VCSS was used. The VCSS score is a measure that evaluates the impact of venous circulation issues and their effects on patients' quality of life following surgery [21]. The mean VCSS (Venous Clinical Severity Score) was significantly lower in the TXA group (4.2 ± 2.3) compared to the control group (6.4 ± 2.6), $p=0.03$. The findings indicate that postoperative quality of life, as measured by the VCSS, was statistically significantly higher in patients treated with TXA compared to the control group.

DISCUSSION

In our study on CABG surgery, the topical application of tranexamic acid after saphenous vein harvesting has been shown with reduced postoperative ecchymosis, shorter hospitalization, easier mobilization, less pain, and improved quality of life outcomes. The topical application of tranexamic acid has been shown to reduce the incidence of edema and ecchymosis during the postoperative period following open heart surgery [22]. The antifibrinolytic and anti-inflammatory effect of TXA helps to reduce bleeding when applied locally [23], thereby minimizing hematoma formation and reducing bleeding and inflammation at the incision site.

TXA, a lysine derivative, exerts its antifibrinolytic effect indirectly by binding and blocking lysine binding sites on plasminogen molecules. TXA causes a decrease in the affinity of plasminogen to bind to fibrin and activation of plasminogen to plasmin decreases [24]. In this way, it prevents the accumulation of bleeding in the incision area by suppressing the fibrinolytic process and thus prevents the formation of oedema and bruises. However, its limited effect on more serious complications such as haematoma and necrosis suggests that TXA may not be completely sufficient to prevent these complications. In our study, the calf and thigh circumferences of patients who received tranexamic acid during the postoperative period were less affected compared to the control group. Additionally, severe ecchymosis was observed less frequently in the TXA group.

Local tissue trauma, such as that caused by a saphenous vein incision, initiates a cascade of inflammatory events mediated by cytokines, particularly pro-inflammatory molecules like IL-6 and soluble tumor necrosis factor receptor-1 (sTNFR-1) [6]. These cytokines are released by cells including monocytes, macrophages, and endothelial cells, and their production is tightly regulated by various physiological and pathological stimuli [25]. Although the coagulation cascade and the inflammatory response are distinct pathways, they become highly intertwined during acute injury, with the endothelium serving as a critical interface. Localized inflammation in the leg therefore not only involves cellular injury and subsequent healing responses, but also an activation of coagulation factors that can potentiate the overall inflammatory process.

In this context, the use of TXA may help dampen the local inflammatory response by limiting plasmin mediated pathways

that contribute to pro-inflammatory cytokine release. While TXA is well known for its antifibrinolytic properties, evidence also suggests it can modulate immune and inflammatory mechanisms. By reducing excessive clot breakdown, TXA may minimize the release of inflammatory mediators and support a more controlled healing environment. Consequently, its topical application at the site of saphenous vein harvest could potentially lessen postoperative complications such as excessive swelling, hematoma, or prolonged wound healing by reducing inflammation triggered by local tissue trauma.

The importance of physiotherapy after CABG surgeries is significant [26]. Walking activity, in particular, is one of the key factors for early recovery [27]. Following CABG surgery, several factors can contribute to limitations in mobilization. One significant cause is the pain at the saphenous vein incision site, which can impede the patient's ability to move freely. In addition, postoperative edema, particularly around the incision area, can lead to swelling and stiffness, further restricting the range of motion in the affected joints. This combination of pain and swelling can result in reduced functional mobility, delaying the patient's recovery and their ability to engage in early rehabilitation activities. In our study, we conducted a walking test in the postoperative period. The TXA group performed better in the 10-meter walking test. While it may not be entirely possible to attribute this result solely to the application of tranexamic acid, we believe it serves as a contributing factor to improved mobilization.

The use of antiplatelet agents, such as aspirin and clopidogrel, ticagrelor or prasugrel can significantly impair platelet function, making it more difficult for blood to clot effectively and increasing the likelihood of excessive bleeding during and after the procedure. Serious bleeding can occur after cardiac surgery while using dual antiplatelet therapy, which can lead to significant morbidity and mortality [28]. In addition to blood products, the use of tranexamic acid is also recommended for bleeding control [29]. Therefore, the use of tranexamic acid at the saphenous vein incision site may be considered for patients on dual antiplatelet therapy. However, in our study, no significant difference was found between the TXA and control groups in terms of dual antiplatelet use, although tranexamic acid was shown to significantly reduce ecchymosis.

Studies conducted in various medical fields have demonstrated the positive impact of local TXA application on pain management, particularly in the context of surgical recovery. The local administration of TXA at the incision site has been found to significantly reduce postoperative pain, likely due to its antifibrinolytic properties, which help stabilize blood clots and prevent excessive bleeding. By minimizing blood loss and subsequent hematoma formation, TXA helps reduce the inflammatory response and swelling, both of which are key contributors to pain and discomfort following surgery. Findings support that the local application of TXA contributes to improved

healing at the incision site and alleviates postoperative pain levels [30,31]. In our study, similarly, less pain was observed in the TXA group compared to the control group in patients with longer saphenous vein incisions. We believe this result is due to the local effects of tranexamic acid.

In terms of hospital stay, patients treated with TXA had shorter hospitalization durations. Experimentally, TXA is known to contribute to wound healing [32]. Additionally, by reducing complications such as bleeding and hematoma, TXA accelerates the recovery process, enables early mobilization resulting in shorter hospital stays. In our study, the TXA group also had a shorter hospitalization duration.

VCSS is a widely used tool to assess the severity of venous disease and its impact on a patient's quality of life. It evaluates factors such as symptoms (pain, swelling), skin changes (eczema, lipodermatosclerosis), and complications (ulceration, pigmentation). A lower VCSS score indicates less severe venous disease and, by extension, a better quality of life for the patient (6). In this study, the TXA group demonstrated a significantly lower VCSS score compared to the control group. This finding suggests that TXA may be effective not only in managing bleeding and pain but also in enhancing overall patient quality of life postoperatively.

Limitations

This single-centre study enrolled a relatively small cohort, which restricts the generalisability of the results. Follow-up was limited to the early postoperative period, so late complications could not be evaluated. Inflammation was assessed solely by clinical criteria, no tissue sampling or laboratory inflammatory markers were obtained and inter-observer reliability for these assessments was not analysed. These limitations should be addressed in larger, multi-centre trials with longer follow-up and objective, standardised outcome measures.

CONCLUSION

In patients undergoing coronary artery bypass surgery, the local application of tranexamic acid to the saphenous vein harvest site significantly reduced postoperative leg pain, oedema, clinical signs of inflammation and ecchymosis, and was associated with a shorter median hospital stay. Within the limits of this study, TXA was safe and well tolerated, supporting its routine use as an adjunct to minimise harvest-site morbidity.

Ethics Committee Approval: The study was approved by the Ankara Bilkent City Hospital Ethics Committee (E1-23-4510 27.12.2023).

Patient Consent for Publication: Not necessary for this manuscript.

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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