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Emergency coronary bypass surgery in patients under the influence of dual antiplatelet therapy: effects of tranexamic acid and desmopressin acetate

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Background/aim: Bleeding in patients undergoing coronary artery bypass grafting (CABG) while using dual antiplatelet therapy (DAPT) is a cause of significant morbidity and mortality. The aim of this study is to examine the perioperative hemostatic effects of tranexamic acid (TnX-A) and desmopressin acetate (Des) in these patients.

Materials and methods: This clinical study was planned in a prospective and randomized manner. Fifty-four patients were enrolled and classified into 4 different groups. They were compared in terms of various bleeding and transfusion parameters.

Results: No significant differences were observed between the groups in pre/intraoperative data apart from closure times. Plasmin/α-2 antiplasmin complex values in the TnX-A and control groups were significantly higher than those in the Des and TnX-A+Des groups at the end of postoperative drug infusion. Mean duration of closure times, first 3-h and total postoperative amounts of drainage, administered volumes of erythrocyte suspension/fresh frozen plasma, cost of blood products, length of intubation, length of stay in the intensive care unit, and time to discharge were also significantly higher in the Des and control groups.

Conclusion: Des had no significant effect on bleeding control and even delayed the hemostatic efficacy of TnX-A. Use of TnX-A infusion alone in these patient groups had a positive effect on hemostasis-related data.

Key words: Clopidogrel, coronary bypass surgery, desmopressin acetate, dual antiplatelet therapy, tranexamic acid

1. Introduction

Approximately 10%–20% of allogeneic blood products worldwide are used in cardiac surgery procedures (1). Bleeding occurring after cardiac surgery generally requires large quantities of blood transfusions and sometimes even reoperation. On the other hand, excessive blood transfusion is also related to increased morbidity, mortality, and transmission of viral diseases (2). According to the statistics, 2% of patients may need reoperation after coronary artery bypass grafting (CABG). This complication often results in increased mortality and prolonged hospitalization (3). Several factors including prolonged cardiopulmonary bypass (CPB), advanced age, number of distal anastomoses, hypothermia, insufficient surgical bleeding control, coagulation disorders, and platelet dysfunction may result in postoperative bleeding (4,5). Platelet dysfunction may occur due to both the effects of CPB on platelet numbers and functions and the antiplatelet therapy administered in the preoperative period (3).

Rates of stent thrombosis, as high as 24% in early coronary artery stent results, have decreased to 2% with advances in antiplatelet treatments today (6). Clopidogrel, a thienopyridine derivative that irreversibly blocks platelet aggregation, has become the standard treatment in the prevention of stent thrombosis in interventional cardiology (7,8). Better results have been observed in both acute and chronic events with the use of clopidogrel both alone or in combination with acetylsalicylic acid (ASA) (9). Studies have shown an increase in the use of clopidogrel in patients requiring CABG, and an increase in the incidence of complications associated with postoperative bleeding has also been noted in these patients (3,7–11). Postoperative bleeding is still a serious concern for cardiac surgeons in patients with acute coronary syndrome (ACS) requiring acute coronary surgery while under the effect of antiaggregant agents.

In addition to surgical trauma, another important cause of postoperative bleeding in cardiac surgery is fibrinolysis triggered by CPB (12). Preoperative antiplatelet therapy

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has also been known as a predisposing factor for excessive blood loss and need for transfusion in the perioperative period due to the platelet dysfunction that it causes. Therefore, there are many pharmacologic agents designed for ameliorating these adverse effects. For example, tranexamic acid (TnX-A), a lysine analog, is a synthetic antifibrinolytic drug. It has positive effect on transfusion requirements both in cardiac surgeries and reoperations due to bleeding (12,13). Desmopressin acetate (Des) is a synthetic arginine vasopressin analog and increases plasma concentrations of von Willebrand factor (vWF) and factor VIII (F8), which are involved in platelet adhesion, by affecting endothelial V2 receptors. Previous clinical studies have reported that Des can reduce bleeding and the need for transfusion in patients undergoing cardiac surgery. It has also been shown to shorten bleeding time in acquired platelet function disorders such as chronic renal insufficiency and ASA use (14,15).

The aim of this study was to observe the effects of TnX-A and/or Des use on clinical and surgical outcomes as well as on blood product use in patients undergoing emergency CABG while receiving dual antiplatelet therapy (DAPT = ASA + clopidogrel).

2. Materials and methods

This clinical study was approved by the Ethics Committee of the Karadeniz Technical University Faculty of Medicine and was in accordance with the Declaration of Helsinki. Informed consent was obtained from every patient in our study. Initially the study was planned to be a prospective and randomized study including 80 adult patients undergoing emergency CABG surgery and receiving DAPT due to ACS. However, we had to prematurely conclude our study due to ethical reasons because there were significantly increased amounts of postoperative drainage in the Des and control groups compared to the groups receiving TnX-A. Due to the priority of the patient's benefit, we planned to stop the study and consulted with the Ethics Committee and the Department of Biostatistics. After consideration, the randomization process was continued in accordance with the suggestions of biostatisticians who suggested that stopping the patient enrollment to the Des and control groups would not affect the power of the study because there were enough patients in each group. Finally, the numbers of patients in each group were defined according to this result.

Our patient group consisted of 54 registered patients undergoing emergency CABG (47 males, 7 females; mean age: 63.9 years, range: 46–84). Patients with chronic renal insufficiency, hepatic dysfunction, hematological disorders, drug addiction that might affect the hematological system, requirements for noncoronary cardiac surgery, or use of intraaortic balloon pumps were excluded from the study. Preoperative data including concomitant diseases such as diabetes mellitus (DM), hypertension (HT), chronic obstructive pulmonary disease (COPD), and carotid artery stenosis (CAS); demographics such as sex, age, height, body mass index (BMI), and EuroSCORE values; and biochemical parameters such as liver and kidney function tests, blood count, international normalized ratio (INR), prothrombin time (PT), partial thromboplastin time (PTT), and bleeding time calculated using the Ivy method were recorded. All patient groups were operated on by the same surgical team with standard anesthesia and surgical techniques. Roller pumps, heparin-uncoated membrane oxygenators, and cannulas were used in CPB. Number of distal anastomoses and durations of cross-clamp, CPB, and closure time (time from heparin neutralization to sternal closure) were recorded in the operating theater.

Patients were divided into four groups. Patients in the TnX-A group (n = 18) were started on TnX-A (Transamine, Fako, 5 mL/250 mg vial) infusions (10 mg/kg of loading dose in 20 min) at the beginning of the surgical incision, and then infusion was continued at 1 mg/kg per hour for 10 h. Patients in the TnX-A+Des group (n = 16) were administered TnX-A as described. Des (Minirin, Ferring, 4 μg/mL vial) was also administered in 20-min infusions at a dose of 0.3 μg/kg following neutralization of heparin with protamine. The Des group (n = 10) only received Des as described. No drug was administered to the control group (n = 10).

In the postoperative period, erythrocyte suspension (ES) was given when hematocrit (Htc) was reduced to 24%, platelet suspension (PLT) was given when platelet count was decreased below $50 \times 10^3/\mu L$, and fresh frozen plasma (FFP) was administered to patients with drainage exceeding 250 mL in the first hour. Postoperatively, hemoglobin values of patients were recorded initially and at the 3rd and 24th hours in the ICU. Amounts of drainage in the first 3 h and total drainage from postoperative thoracic and mediastinal drains, and the amounts as well as costs of the blood products used, were recorded. Patients were closely monitored for development of possible thrombotic complications (acute myocardial infarction, cerebrovascular events, and deep vein thrombosis). Length of intubation and time passed between admission to the ICU and then discharge were recorded. PAP (Imuclone PAP ELISA, American Diagnostica Inc.) and vWF (REAADS, Corgenix Inc.) levels were measured using commercial ELISA kits from blood taken preoperatively (T1), after intraoperative heparin neutralization (T2), at the end of postoperative drug infusion (isotonic fluid infusion for TnX-A and control groups) (T3), and 1 day after the end of postoperative drug infusion (T4).

2.1. Statistical analysis

Numerical data were expressed as mean ± standard deviation and qualitative data as numbers and percentages (SPSS 15.0 for Windows 7). The chi-square test was used for qualitative comparisons, while accordance with normal distribution of measurement parameters was assessed using the Kolmogorov–Smirnov test. Measured data between groups were compared using Kruskal–Wallis analysis of variance following the establishment of parametric conditions. The P-value was set at 0.05. The Mann–Whitney U test was used in post hoc two-way comparisons by lowering error levels. A new P-value was calculated by dividing the 0.05 value by the number of two-way comparisons as 0.05 / 3 = 0.016. The Friedman test was used to assess changes in data in groups over time. The Wilcoxon test was used in post hoc two-way comparisons of these data by lowering error levels. The new P-value was determined as 0.05/6 = 0.008.

3. Results

No significant differences were observed between groups in terms of demographics, preoperative risk factors, or preoperative laboratory tests (Table 1). No significant difference was observed between the TnX-A and TnX-A+Des groups in terms of closure times (33.0 min vs. 32.19 min), nor between the Des and control groups (45.0 min vs. 48.0 min). Closure times in the Des and control groups were significantly longer than those in the TnX-A and TnX-A+Des groups (P = 0.000) (Table 2). Amounts of drainage in the first 3 h and in total (Table 3) were not significantly different, neither between the TnX-A and TnX-A+Des groups (306 mL, 535 mL vs. 353 mL, 574 mL) nor between the Des and control groups (785 mL, 1430 mL vs. 972 mL, 1767 mL). Amounts of drainage in the first 3 h and in total in the Des and control groups were significantly greater than those in the TnX-A and TnX-A+Des groups (P < 0.001).

No significant differences were observed between the TnX-A and TnX-A+Des groups in terms of amounts of ES (125 mL vs. 93 mL) and FFP (22 mL vs. 19 mL) used or blood product costs (66.78 vs. 44.25 Turkish lira, TL). Similarly, no differences were observed between the Des and control groups in terms of amounts of ES (675 mL vs. 900 mL) and FFP used (460 mL vs. 680 mL) or blood product costs (479.60 vs. 842.80 TL). Levels of ES and FFP used and blood product costs were significantly higher in the Des and control groups compared to the TnX-A and TnX-A+Des groups (P < 0.001). Platelet suspension was only used in the control group (120 mL) and this was statistically significant (P = 0.003) (Table 4).

Table 1. Preoperative data (groups n (%) or mean ± standard deviation).

	TnX-A (n = 18)	TnX-A+Des (n = 16)	Des (n = 10)	Control (n = 10)	P-value
Female	3 (16%)	2 (12%)	1 (10%)	1 (10%)	0.94
Age	65.8 ± 6.1	65.6 ± 11.3	66.4 ± 9.3	57.9 ± 14.6	0.45
BMI	28.8 ± 3.6	28.8±5.0	29.3 ± 4.0	28.9 ± 2.9	0.93
Hypertension	11 (61%)	9 (56%)	6 (60%)	6 (60%)	0.99
DM	6 (33%)	5 (31%)	4 (40%)	3 (30%)	0.96
COPD	4 (22%)	6 (37%)	3 (30%)	3 (30%)	0.81
CAS	0 (0%)	1 (6%)	2 (20%)	1 (10%)	0.21
EuroSCORE	3.2 ± 1.5	2.9 ± 1.7	2.5 ± 1.6	2.7 ± 2.0	0.81
Cr (mg/dL)	1.4 ± 1.6	1.0 ± 0.1	0.9 ± 0.2	1.0 ± 0.1	0.41
AST (mg/dL)	27.5 ± 10.4	24.5 ± 11.1	31.6 ± 18.7	27.8 ± 14.2	0.77
ALT (mg/dL)	28.8 ± 13.0	24.6 ± 12.0	26.0 ± 12.9	29.3 ± 8.2	0.72
Hb (g/dL)	14.0 ± 1.8	13.5 ± 1.5	14.3 ± 1.0	13.9 ± 1.4	0.49
Htc (%)	41.1 ± 5.7	40.1 ± 4.2	42.2 ± 2.8	41.4 ± 3.8	0.67
Plt ($\times 10^3$)	222.8 ± 60.6	231.7 ± 99.5	194.7 ± 68.8	230.3 ± 67.7	0.45
PTT (s)	31.3 ± 5.0	30.3 ± 1.7	29.8 ± 2.0	29.9 ± 1.4	0.83
PT (s)	13.2 ± 0.9	13.8 ± 0.7	12.8 ± 1.0	13.2 ± 0.7	0.19
INR	1.1 ± 0.7	1.1 ± 0	1.0 ± 0.1	1.0 ± 0	0.26
Bleeding time	9.9 ± 1.1	9.6 ± 1.2	9.4 ± 1.1	9.4 ± 1.1	0.65

BMI: Body mass index, DM: diabetes mellitus, COPD: chronic obstructive pulmonary disease, CAS: carotid artery stenosis, Cr: creatinine.

Table 2. Operative data (groups n (%) or mean ± standard deviation).

	TnX-A (n = 18)	TnX-A+Des (n = 16)	Des (n = 10)	Control (n = 10)	P-value
Use of LIMA	18 (100%)	16 (100%)	10 (100%)	10 (100%)	>0.99
Distal anastomoses	3.3 ± 0.9	3.1 ± 0.7	2.9 ± 0.7	3.0 ± 0.8	0.44
Aortic CC time (min)	64.1 ± 12.8	64.6 ± 16.1	62.3 ± 18.0	64.4 ± 16.9	0.98
CPB time (min)	121.8 ± 19.4	115.0 ± 23.7	116.5 ± 36.4	116.3 ± 24.9	0.57
Closure time (min)	33.0 ± 5.6	32.1 ± 6.3	45.0 ± 4.0	48.0 ± 7.1	0.00

LIMA: Left internal mammary artery, CC: cross-clamp, CPB: cardiopulmonary bypass.

Table 3. Postoperative drainage volume and hemoglobin values.

	TnX-A (n = 18)	TnX-A+Des (n = 16)	Des (n = 10)	Control (n = 10)	P-value
First 3 hours of drainage (mL)	306.1 ± 57.1	353.7 ± 39.4	785 ± 129.7	972.5 ± 134.6	<0.001
Total blood loss (mL)	535 ± 116.8	574.0 ± 75.5	1430 ± 257.6	1767.5 ± 293.2	<0.001
First Hb (g/dL)	9.1 ± 1.1	9.3 ± 1.4	8 ± 0.3	7.6 ± 0.6	<0.001
3rd hour of Hb (g/dL)	10.1 ± 0.7	10.1 ± 1.2	8.7 ± 0.7	8.7 ± 0.4	<0.001
24th hour of Hb (g/dL)	10.8 ± 0.5	10.8 ± 0.8	10 ± 0.5	10.1 ± 0.4	<0.001

Groups n (%) or mean ± standard deviation.

Table 4. The amount of transfused blood products and cost.

	TnX-A (n = 18)	TnX-A+Des (n = 16)	Des (n = 10)	Control (n = 10)	P-value
FFP (mL)	22.2 ± 64.6	0	460 ± 298.8	680 ± 301.1	<0.001
ES (mL)	125 ± 128.6	93.7 ± 125	675 ± 237.1	900 ± 268.7	<0.001
PS (mL)	0	0	0	120 ± 209.7	<0.001
Cost (TL)	66.7 ± 71.9	44.2 ± 59	479.6 ± 204	842.8 ± 536.5	<0.001

Groups n (%) or mean ± standard deviation. ES: Erythrocyte suspension, FFP: fresh frozen plasma, PS: platelet suspension, TL: Turkish lira.

No significant differences were observed between the TnX-A and TnX-A+Des groups in terms of length of intubation (4.24 h vs. 4.08 h), length of stay in the ICU (41.11 h vs. 42.50 h), and time until discharge (144.1 h vs. 145.3 h). No significant differences were observed between the Des and control groups in terms of length of intubation (6.61 h vs. 6.91 h), length of stay in the ICU (64.20 h vs. 75.90 h), or time until discharge (187.30 vs. 189.60 h). All of these variables were significantly longer in the Des and control groups compared to the TnX-A and TnX-A+Des groups ($P < 0.001$) (Table 5).

No significant difference was observed among the groups in terms of vWF values ($P > 0.05$) (Table 6). No difference was observed between the groups at T1, T2, or T4 in terms of PAP values ($P > 0.05$). No significant difference was observed between the TnX-A and control groups at T3 (191.50 ng/mL vs. 167.38 ng/mL). Similarly, there was no significant difference between the TnX-A+Des and Des groups (101.69 ng/mL vs. 92.23 ng/mL) at T3. Measured PAP levels of the TnX-A and control groups were significantly higher than those of the Des and TnX-A+Des groups ($P < 0.016$) at T3 (Table 7).

Table 5. Postoperative follow-up periods (groups n (%) or mean ± standard deviation).

	TnX-A (n = 18)	TnX-A+Des (n = 16)	Des (n = 10)	Control (n = 10)	P-value
Intubated stay (h)	4.2 ± 0.7	4.0 ± 0.7	6.6 ± 0.5	6.9 ± 0.7	<0.001
ICU stay (h)	41.1 ± 5.8	42.5 ± 7.1	64.2 ± 22.2	75.9 ± 20.6	<0.001
Hospital length of stay (h)	144.1 ± 12.1	145.3 ± 9.2	187.3 ± 21.6	189.6 ± 21.6	<0.001

ICU: Intensive care unit.

Table 6. vWF values (%) (groups n (%) or mean ± standard deviation).

	TnX-A (n = 18)	TnX-A+Des (n = 16)	Des (n = 10)	Control (n = 10)	P-value
T1	168.8 ± 31.9	190.2 ± 19.6	180.4 ± 47.3	168.8 ± 33.9	0.08
T2	173.3 ± 33.8	188.9 ± 21.9	185.3 ± 36.3	186.3 ± 25.5	0.37
T3	169.5 ± 134.2	185.4 ± 122.3	186.1 ± 124.3	164.8 ± 131.5	0.21
T4	176.3 ± 40	162.9 ± 21.7	168 ± 16.6	157.9 ± 29.4	0.50

vWF: Von Willebrand factor (normal value: 47%–197%), T1: preoperative blood collection time, T2: blood collection time after the heparin neutralization, T3: blood collection time after the end of postoperative drug infusion (isotonic fluid infusion for TnX-A and control groups), T4: blood collection time 24 h after the end of drug infusion.

Table 7. PAP values (ng/mL) (groups n (%) or mean ± standard deviation).

	TnX-A (n = 18)	TnX-A+Des (n = 16)	Des (n = 10)	Control (n = 10)	P-value
T1	208.3 ± 87.5	347.9 ± 58.8	233.1 ± 124.1	223.6 ± 22.9	0.53
T2	109.6 ± 44.8	94 ± 48.1	87.5 ± 38.5	114.8 ± 23.4	0.10
T3	191.5 ± 32.6	101.6 ± 40	92.2 ± 50.4	167.3 ± 52.8	0.02
T4	282.2 ± 37.3	204.9 ± 101.9	156.3 ± 96.6	155.2 ± 52.5	0.13

PAP: Plasmin α2 antiplasmin (normal value: 0–514 ng/mL), T1: preoperative blood collection time, T2: blood collection time after the heparin neutralization, T3: blood collection time after the end of postoperative drug infusion (isotonic fluid infusion for TnX-A and control groups), T4: blood collection time 24 h after the end of drug infusion.

During the postoperative period, none of our patients required reoperation due to bleeding or for any other reason, and neither thrombotic complications nor mortality occurred.

4. Discussion

The use of DAPT that includes ASA and clopidogrel is widespread in patients requiring emergency CABG. Studies have shown that the use of clopidogrel reduces the risk of cardiovascular events but increases the risk of major bleeding in patients requiring emergency CABG (6–10). Increased use of blood products, rate of reoperation due to bleeding, and duration of hospitalization have also been reported in these patients (2,3,5–11). Several previous studies have reported the effectiveness of hemostatic agents such as TnX-A and Des on bleeding in elective coronary surgery (12–15). However, the number of studies comparing the efficacy of hemostatic agents in patients undergoing emergency CABG while using DAPT is limited. Shi et al. compared the effect of TnX-A and a placebo in patients using DAPT and receiving the final dose within 7 days before surgery. They reported that TnX-A significantly reduced blood loss, rate of reoperation, and amounts of transfusion (16). We observed that bleeding beginning with skin incision in the form of diffuse tissue leakage delayed graft preparation and sternal closure in patients undergoing CABG while receiving DAPT in our clinic. Delayed sternal closure can result in patient

cooling, arrhythmias, hemodynamic instability, and an increased risk of infection. Our results showed that TnX-A established an approximately 50% decrease in closure time.

In addition, we observed a 3-fold decrease in amounts of first 3-h and total drainage, and approximately 6- to 9-fold decreases in amounts of ES used and 19-fold decreases in blood product costs in the groups administered TnX-A compared to groups not receiving TnX-A. Similarly, postoperative Hb levels were higher in the TnX-A groups in the first hours. TnX-A was also associated with shorter lengths of intubation, ICU stay, and hospitalization. No thrombotic complications related to TnX-A were observed in our patients.

The hemostatic effectiveness of TnX-A in CABG has been shown in previous studies with patient groups undergoing elective surgery (13,14). TnX-A has been reported to reduce blood loss and transfusion requirements without causing thrombotic complications in patients receiving ASA until surgery. Our findings are consistent with the literature and support the idea that TnX-A is an effective hemostatic agent in patients undergoing emergency CABG while receiving DAPT therapy.

Fibrinolysis, which is the one of the main reasons for bleeding in open heart surgery, is triggered by several factors, and especially by CPB. It lasts for 24 h with predominance in the first postoperative hours. Therefore, the idea of initiating antifibrinolytic therapy before CPB has started to be a point of interest (17,18). Brown et al. reported 400 mL less drainage in a group started on TnX-A before CPB than in groups started on it after CPB in a study involving 91 patients scheduled for elective CABG (17). Paramo et al. suggested that antifibrinolytics should be started before CPB (18). Various studies have been performed with the aim of identifying the correct dosage of TnX-A. A bolus dose of 10 mg/kg in 20 min before cutaneous incision followed by infusion at the rate of 1 mg/kg per hour has been suggested as the ideal dosage for bleeding control, and increasing the dosage has been reported as having no additional beneficial effects on bleeding control (19–21). Similar to our study, the highest level of postoperative bleeding was observed in the postoperative first 3 h. We similarly initiated TnX-A infusion with skin incision at the dosage as described.

Des exhibits its hemostatic effect by increasing plasma concentrations of vWF and F8, which are responsible for platelet adhesion. However, Des exhibited no hemostatic effect in the Des group of our study. In addition, increased amount of drainage and use of blood products, low postoperative Hb values, and prolonged intubation, ICU, and hospitalization times were also observed in this group. Measured vWF levels supported this idea by showing no increase in the groups receiving Des. Some previous studies investigated the hemostatic effects of Des in patients undergoing CABG. Salzman et al. and Czer et al. reported that Des reduced blood loss and the need for ES transfusion by significantly increasing vWF and F8 levels (22,23). These studies are not consistent with our findings, mainly because they involved patients who were not under the effects of antiaggregants in elective conditions.

TnX-A exhibits its antifibrinolytic effects by blocking plasminogen binding to fibrin. Levels of PAP complex show that fibrin had formed and the antifibrinolytic system was activated. In other words, it means that plasmin was increased. Therefore, it has been used as a coagulation marker. PAP values at T2 were significantly lower than values at T1 in all groups. This showed that anticoagulation was established with heparin. At the same time, it suggested that coagulation was not sufficient for fibrin formation at biochemical levels during the process in which heparin was neutralized by protamine, although coagulation was started to be observed in the surgical field. The increase in PAP values over time showed that the coagulation system gradually recovered after surgery. Values at T3 significantly increased in the TnX-A and control groups compared to the groups receiving Des. However, no significant differences were observed in values at T3 between the TnX-A and control groups or between the Des and TnX-A+Des groups. These findings indicate that Des also suppressed coagulation in the TnX-A+Des group due to its increasing effect on tissue plasminogen activator (tPA) and delayed the coagulant effect of TnX-A, which exhibits its functions by inhibiting plasmin. PAP values increased significantly at T4 in the groups receiving TnX-A. PAP values were low at T3 and rapidly increased at T4 in the TnX-A+Des group. This suggested that the antifibrinolytic effect of TnX-A was more pronounced once the effect of tPA had diminished. The significant increase over time in PAP values in the patients only receiving TnX-A compared to TnX-A and Des showed that the present plasmin had been activated. Plasmin was unable to inhibit the coagulation system since it could not be used in fibrin breakdown. The significant decrease of bleeding in the early period in patients receiving TnX-A as well as the lack of this decrease in the Des and TnX-A+Des groups support this idea.

In conclusion, on the basis of our findings, Des made no positive contribution to bleeding control in these patient groups and delayed the hemostatic effect of TnX-A. The use of TnX-A infusion alone in these patients had positive effects on data related to hemostasis. Our findings support the idea of the routine use of TnX-A in patients undergoing CABG while using DAPT without significant adverse effects or heavy financial burden. However, further controlled randomized and double-blinded studies with larger patient groups are needed for making definitive conclusions.

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