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Body Contouring

Special Topic

Temperance With Tranexamic Acid: Increased Risk of Venous Thromboembolism in Abdominoplasty

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Abstract

Tranexamic acid (TXA) is used widely in surgery to mitigate blood loss by inhibiting the fibrinolytic degradation of clots. The occurrence of venous thromboembolism (VTE) with TXA has not been reported in the plastic surgery literature. In the realm of plastic surgery, abdominoplasty has the highest rate of VTE. The purpose of this study is to report 5 cases of VTE with TXA. A single surgeon reviewed the records of 5 patients who incurred VTE with TXA. TXA was added to the tumescent fluid, 20 mg/kg total. Four of the 5 patients underwent abdominoplasty combined with liposuction and breast surgery, and the fifth, fat transfer to the breast. The abdominoplasty patients had received chemoprophylaxis. Upon presentation of symptoms, the patients were sent to the hospital for anticoagulation and hematology consultation. The 5 patients survived their VTE events; 2 only required oral anticoagulation, 2 required IV heparin then oral, and 1 required tissue plasminogen activator (tPA) then oral. VTE with abdominoplasty occurred in 0 of 399 cases prior to the use of TXA and in 4 of 98 cases after the use of TXA in the tumescent. Although the occurrence of VTE with abdominoplasty increased with the use of TXA for the senior author, this retrospective case study does not prove a causal relationship between TXA and VTE.

Level of Evidence: 4

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Tranexamic acid (TXA) has been highly regarded in plastic surgery as a safe means to decrease blood loss, shorten operative time, decrease ecchymosis, avoid hematoma, and reduce complications of healing. Caution is advised following this first report of a significant increase in venous thromboembolism (VTE) with the use of TXA in tumescence for combined trunk procedures, specifically lipoabdominoplasty.

Plastic surgeons adapted the use of TXA, an antifibrinolytic drug, from high blood loss surgery, trauma, orthopedic, craniofacial, and cardiac surgery.[1,2] Plastic surgery is a low blood loss surgery, but hematomas in potential spaces

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created by abdominoplasty or implant removal could cause hemodynamic instability requiring blood transfusion. Hematomas could lead to a problematic fluid collection, infection, or necrotic wound requiring reoperation. According to 1 study of 7,629,686 procedures in the American Association for Accreditation of Ambulatory Surgery Facilities (AAAASF) database, hematoma is the most common complication with an incidence of 0.20%, and with 6.75% of hematomas requiring hospitalization.[3] Decreasing bleeding also decreases swelling and pain and improves healing and patient experience. Blood loss has been decreased up to 60% as measured in lipoaspirate when TXA was given either IV or in the tumescent.[4]

Abdominoplasty carries a 5.5 times higher risk of VTE than other aesthetic procedures.[3] Studies have demonstrated no increase in VTE risk when concurrent procedures are added to abdominoplasty.[5,6] A retrospective review of 129,007 patients in the Cosmetassure database found 116 (0.09%) confirmed cases of VTE.[7] In that study, VTE occurrence was significantly associated with combined body procedures of the trunk and extremities, BMI, and age. There was no elevation in risk of VTE with outpatient surgery center vs hospital-based abdominoplasty. Another publication on the AAAASF database found 0.07% VTE in abdominoplasty associated with BMI >25 kg/m^2 and age >40.[8] Of the 240 patients who had VTE, 27 died. In this study of 354,391 abdominoplasty cases, the duration of the procedure and the number of concurrent procedures did not increase the risk of VTE. The objective of this study is to report 5 cases of VTE following the use of TXA and combined trunk procedures.

METHODS

A single surgeon performed the abdominoplasties over a 19-year period. The charts of patients diagnosed with pulmonary embolism (PE)/deep vein thrombosis (DVT) were reviewed retrospectively with no violation of the Declaration of Helsinki. No identifying information was included.

TXA was added to the tumescent with a total dose of 20 mg/kg. No additional TXA was given, by IV or topically. Patients received Caprini screening risk assessment, sequential compression devices before induction and throughout surgery, IV anesthesia, early postoperative ambulation (within 60 min), outpatient surgery, incentive spirometer for home, and prescription for 7 days of chemoprophylaxis. Chemoprophylaxis was started at the office, with lovenox 40 mg SC, the morning after surgery. All the patients had a postoperative day (POD) 1 appointment for evaluation, dressing change, and vitals check. All patients were coached on recognizing the signs of DVT and PE as well as the importance of deep breathing and movement at their preoperative appointment by the surgeon. The senior author has patients who stopped taking all oral hormones for 2 weeks prior to surgery, including tamoxifen. In the absence of familial or personal history of clotting disorder or at least 3 miscarriages, testing for clotting disorders is not merited. Once VTE was suspected, the patients went to the emergency department for evaluation and admission to the hospital. All had hematology consultations after VTE.

Case 1

A 52-year-old female developed a DVT POD 3 s/p liposuction of thighs and fat transfer to breasts. She had a BMI of 19 and Caprini Score 4. TXA was added 300 mg/L with 3000 cc tumescent and 2200 cc lipoaspirate. The length of the procedure was 3.5 h. She presented to the emergency department POD 3 with right calf pain. Her DVT resolved with xarelto.

Case 2

A 44-year-old female developed a DVT in the right posterior tibial and peroneal veins POD 4 s/p abdominoplasty, liposuction abdomen, thighs, and fat transfer to breasts. She had a BMI 21 and Caprini Score 4. TXA 300 mg was added per liter with 3000 cc tumescent and lipoaspirate 2000 cc. The length of the procedure was 5 h. She presented to the emergency department with right calf pain. Her DVT resolved with xarelto.

Case 3

A 56-year-old female developed a PE on POD 1 s/p abdominoplasty, liposuction abdomen/flanks, and bilateral breast augmentation. She had a BMI 21 and Caprini Score 4. TXA 300 mg was added per liter tumescent with 2000 cc tumescent and 1400 cc lipoaspirate. The length of the procedure was 4.5 h. She presented to the office POD 1 with a base of neck/upper back pain and pale fingers. On presentation, she was hemodynamically stable with normal pulse oximetry. Her PE resolved with IV heparin then oral xarelto.

Case 4

A 59-year-old female developed a PE POD1 s/p abdominoplasty, liposuction abdomen/flanks, and bilateral breast reduction. She had a BMI 33 and Caprini Score 4. TXA 500 mg was added per liter to the first 4 bags. There was 5000 cc tumescent and 5000 cc lipoaspirate. The length of the surgery was 8 h. She presented on POD 1 as hemodynamically stable and asymptomatic; however, pulse oximetry was in the 80s. Her PE resolved with Heparin IV then oral xarelto.

Table 1. VTE Events s/p Body Contouring With TXA 0.3% to 0.5% (Maximum 20 mg/kg) in Tumescent, All Females

Case	VTE Event	Age	BMI	Caprini Score	Surgery Length	Procedures	Diagnosis Timing	Tumescent/ Lipoaspirate (mL)
1	DVT	52	19	4	3.5	Liposuction, fat transfer to breast	POD 3	3000/2200
2	DVT	44	21	4	5	Abdominoplasty, fat transfer to breasts, liposuction thighs	POD 4	3000/2000
3	PE	56	21	4	4.5	Abdominoplasty, breast augmentation	POD 1	2000/1400
4	PE	59	33	4	8	Abdominoplasty, liposuction back, breast reduction	POD 1	5000/5000
5	PE	53	33	6	6	Abdominoplasty, fat transfer to breasts, liposuction flanks	Week 6	4000/4000

DVT, deep vein thrombosis; POD, postoperative day; PE, pulmonary embolism; TXA, tranexamic acid; VTE, venous thromboembolism.

Case 5

A 53-year-old female with a medical history of breast cancer s/p lumpectomy and radiation developed a PE 6 weeks s/p abdominoplasty, liposuction abdomen/flanks, and fat transfer to left breast. She had a BMI 33 and Caprini Score 6. TXA 500 mg was added per liter with 4000 cc tumescent and 4000 cc aspirate. The length of the procedure was 6 h. She presented on POD 1 with a pulse oximetry of 93%. She was sent to the emergency department for workup, including spiral computed tomography and D-dimer, which was normal, and she continued her week of lovenox already prescribed per protocol. Then, she developed a necrotizing infection requiring debridement and IV antibiotics at 2 weeks. She had received lovenox during admission. She developed shortness of breath at home 6 weeks s/p abdominoplasty and 4 weeks s/p debridement and went to hospital through ambulance. The PE was resolved with tPA, IV heparin, and subsequent oral eliquis.

RESULTS

Over the past 3 years, the senior author performed 98 abdominoplasties using TXA in the tumescent with 4 VTE events, and before this, over the prior 16 years, the senior author performed 399 abdominoplasties without TXA with zero VTE events. The cases of VTE that occurred with abdominoplasty and TXA were compared with their antecedent cohort. A Pearson's χ^2 test with simulated *P*-value (based on 2000 replicates) found a significant difference in cases of VTE before and after the use of TXA ($\chi^2 = 134.31$, df = NA, $P = .0004998$) with an effect size of 0.439.

The 5 patients survived their VTE events; only 2 required oral anticoagulation, 2 required IV heparin then oral, and 1 required TPA then oral. The age range was 44 to 59 years, 1 had a BMI of 19, 2 had 21, and 2 had 33. See Table 1 for further parameter comparisons. None had a history of blood clotting disorders. None of the patients took estrogen, tamoxifen, or other hormones. All patients with VTE underwent hematology evaluation, and none were diagnosed with blood clotting disorders. The hematologists' consultation assessments were VTE events provoked by surgery.

DISCUSSION

The senior author began using TXA in the tumescent in January 2021 to decrease operative blood loss, shorten operative times, and improve outcomes. The rationale for TXA in tumescent was to obtain a more localized effect rather than a centralized systemic effect through IV administration and, hence, a theoretical lower risk of VTE. Drugs delivered subcutaneously bind to tissue delaying systemic absorption. Then, they are partially degraded by half-life and partially removed with the lipoaspirate. There is no standard of care for the use of TXA in tumescent and published concentrations vary widely, from 0.075%[9] to 2%.[1] In a lipotransfer study for breast reconstruction, 3 g in 75 mL saline was infiltrated in 60 patient donor sites after lipo harvest, average BMI was 29, and patients had less bruising and no adverse events compared with 60 historical controls.[10] The senior author used 0.3% to 0.5% TXA in tumescent with a total dose of 20 mg/kg. The minimum tissue concentration for clinical effect is 10 µg/mL.[9] A 2018 meta-analysis of all surgical literature showed the most common systemic dose was 15 mg/kg and doses of 10 to 20 mg/kg IV had no effect on VTE.[11] In the largest retrospective TXA study, on 872,416 total hip or knee arthroplasties, patients received TXA doses ranging from 1 to >3 g with no increase in VTE.[12] The orthopedic cohorts receiving TXA had significantly fewer blood transfusions, VTE, and renal failure. Safe dosing of TXA has been reported up to 1 to 3 g per surgery in plastic surgery.[13] A study of 63 patients who underwent free flaps for breast reconstruction showed no VTE and no

flap thrombosis with TXA doses of 1 to 3 g IV with average BMI 22. These patients were started on low-molecular-weight heparin 12 h before surgery, which may have been protective. Craniosynostosis pediatric patients receiving a 15 mg/kg IV TXA dose had 57% less blood transfusions and no adverse events in a randomized controlled trial (RCT) of 40 patients ($P < .05$).[14] Another RCT of 43 craniosynostosis pediatric patients receiving TXA 50 mg/kg IV had no transfusion in the first 24 h vs 50% in placebo ($P = .008$).[15] Typical TXA plasma clearance of a single IV dose is 55% at 3 h and 90% by 24 h by glomerular filtration[16]; however, tissue levels remain higher longer,[17] perhaps the tumescent delivery and 20 mg/kg dosing translated to a clinically significant and prolonged exposure to TXA.

Topical TXA decreases the first 24 h of sanguineous drainage with less systemic absorption and presumably less risk of VTE. An orthopedic RCT of topical TXA vs placebo found a 100 mL application of 1.5% solution was as effective as 3% and resulted in subtherapeutic plasma levels of only 4.5 and 8.5 µg/mL, respectively, at 1 h.[18] The first 24 h sanguineous drainage was decreased by 20% to 25%. The Society of Cardiovascular Anesthesiologists recommended 1 g of TXA administered topically in saline at the end of cardiothoracic surgery since patients on cardiopulmonary bypass experience consumptive coagulopathy. The recommendation was partially based on reduction of 24 h chest tube drainage with TXA. Similarly, an RCT of 28 breast reduction patients showed 500 mg of topical TXA decreased the first 24 h of drainage, 12.5 vs 20.5 cc ($P = .038$).[19] Conclusions that topical TXA is safe and effective have also been drawn from RCTs with 101 in mastectomy[20] and 200 in adenoidectomy.[21]

TXA can be lifesaving for traumatic or obstetric blood loss and a means to avoid blood transfusion. In the CRASH-2 RCT of 20,211 trauma patients, the all-cause death rate was reduced with TXA, 14.5% vs 16% ($P = .0035$), and death due to bleeding was reduced with TXA, 4.9% vs 5.7% ($P = .0077$).[22] Death due to bleeding was significantly reduced in the TXA cohort in the WOMAN RCT of 20,060 females with postpartum hemorrhage, 1.5% vs 1.9% in the placebo group ($P = .045$).[23] A systematic review of 252 RCTs involving over 25,000 patients demonstrated a 0.61 relative risk reduction in blood transfusion with TXA compared with control.[24] Paradoxically, in this study, blood transfusions were needed in 2 of the 5 patients with VTE owing to tPA and IV heparin given for PE management, the opposite and unwanted outcome.

Within plastic surgery, hematoma is the most common complication of plastic surgery, but no deaths have occurred as the result of hematoma in a database of 7 million outpatient surgeries.[3] Is there a need for antifibrinolytics beyond good surgical hemostasis and less aggressive choice of liposuction cannula to prevent the need for reoperation, blood transfusion, or mortality due to blood loss in aesthetic surgery? Plastic surgeons need to reexamine their reason for using an antifibrinolytic medication, dosage, and delivery, at the least, with abdominoplasty, a high-VTE-risk procedure.

Although most of the literature affirms the safety and fervor of using TXA, a few dissenting articles exist. TXA has been weakly correlated to increased risk of VTE in a meta-analysis of 149 articles, including 76 RCTs.[25] The correlation was considered weak although statistically significant with $P = .045$, and it is worth noting that a similar P-value was found in the WOMAN trial. A retrospective study of a randomized trial of 12,009 gastrointestinal bleeding patients found TXA did not reduce death from gastrointestinal bleeding, and VTE events were higher in the TXA group than the placebo, 0.8% vs 0.4%.[26] A retrospective study of 7331 trauma patients showed 12.5% VTE with 5.6% mortality using TXA vs 4.6% VTE with 1.7% mortality, albeit the group receiving TXA had more severe injuries.[27] A retrospective review of 21,931 Level 1 trauma patients found a 3-fold increase in VTE for 189 well-matched pairs and no benefit of TXA for survival.[28] There have been 5 published case reports of acute cardiothoracic thrombotic events following IV administration of TXA.[29] Prudence with the use of TXA is advised, PE is a potentially fatal risk of abdominoplasty.

After each VTE event, the senior author reviewed the literature and found large and numerous studies with no increased rate of VTE and no complications associated with plastic surgery until November 2023. Flap necrosis was first reported with the use of TXA in tumescent for neck lift[30] which led to the author's cessation of the use of TXA. Over the 16 years of practice prior to using TXA, the senior author experienced zero complications of PE or DVT with abdominoplasty or liposuction. The current case series involves all combined body procedures and patients ages 44 to 59 years. Only 2 of the 5 cases had an elevated BMI.

This is a small-scale case study reporting 5 individual cases of VTE with tumescent infiltration of TXA for body contouring. Although the analysis revealed a significant difference in VTE with abdominoplasty, a complete retrospective review of all 497 abdominoplasty charts would be necessary to definitively determine the relationship of factors such as age, surgery length, or concurrent procedures to VTE in the four abdominoplasty cases. The findings are also limited by the fact that this study represents a single-surgeon retrospective design. We do not recommend randomized controlled designs given the risks of VTE with abdominoplasty, but a larger multisurgeon retrospective study of the use, delivery, and dosage of TXA would be helpful for the knowledge base. Given that abdominoplasty has the highest rate of VTE in the realm of plastic surgery and the senior author experienced a significant increase

in VTE with the use of TXA in the current case studies, the senior author no longer uses TXA for abdominoplasty procedures. The next step will be a retrospective review of the abdominoplasty cases to assess average operative times, lipoaspirate, concurrent cases, BMI, age, Caprini score, comorbidity, occurrence of hematoma, transfusion, and whether or not TXA was given.

CONCLUSIONS

VTE with abdominoplasty and concurrent liposuction and breast surgery occurred in 0 of 399 cases prior to the use of TXA and in 4 of 98 cases with TXA by a single surgeon. Albeit statistically significant, this retrospective case study does not prove a causal relationship between an antifibrinolytic agent and VTE.

Disclosures

The authors affirm that there are no potential conflicts of interest pertaining to the research, authorship, and publication of this article. Dr Mess is on the speaker's bureau for Allergan (North Chicago, IL) and Sciton (Palo Alto, CA). She has consulted for Becton, Dickinson, and Company (Franklin Lakes, New Jersey) once in the past year.

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