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Clinical Applications of Tranexamic Acid (TXA) in Plastic and Reconstructive Surgery

Stav Brown MD[1, 2*], Tal Brown BS[2*], Rod J. Rohrich MD[3, 4]

* These authors contributed equally to this manuscript.

1- Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel

2- The Dallas Plastic Surgery Institute, Dallas, TX

3- The Division of Plastic Surgery, Baylor College of Medicine, Dallas, TX

Corresponding author: Rod J. Rohrich MD The Dallas Plastic Surgery Institute Dallas, TX

Rod.Rohrich@dpsi.org

ABSTRACT

Purpose: Tranexamic Acid (TXA) has gained increasing recognition as a valuable pharmacologic agent within plastic surgery. This study reviews the scientific evidence regarding the use of TXA in the full range of plastic and reconstructive surgery to provide clinical recommendations regarding for safe and effective use in various plastic surgical procedures.

Methods: A systematic review and meta-analysis were conducted following the PRISMA guidelines. An established appraisal process was used to rate the quality of articles (Grading of Recommendations Assessment, Development, and Evaluation methodology).

Results: Forty-five studies describing the use of TXA in plastic surgery were included. There is moderate-certainty evidence to support the use of intravenous administration of TXA in craniofacial surgery procedures to reduce blood-loss and transfusion requirements. There is high-certainty evidence to support the use of TXA in cosmetic surgery and intravenous administration in rhinoplasty procedures to reduce blood-loss. Further high-level studies are needed to determine TXA's effects on hematoma rates in facelift surgery and breast-related procedures. There is moderate-certainty evidence to support the use of TXA in burn care. Further studies are required to provide quantitative conclusions on the effects of TXA administration in microsurgery.

Conclusions: This is the largest study to date on the use of TXA in plastic surgery and the first to provide clinical recommendations. The literature highlights TXA's promising role in the fields of craniofacial surgery, cosmetic surgery and burn care. Standardized, objective measurements are required to provide quantitative conclusions regarding TXAs effects on ecchymoses and edema in cosmetic surgery procedures.

INTRODUCTION

The American Society of Plastic Surgeons (ASPS) reports a 131% increase in cosmetic procedures in the past two decades. Similar trends have been reported in reconstructive procedures, with 223% increase in craniomaxillofacial procedures and 75% increase in breast reconstruction procedures since 2000.[1] However, patients undergoing major surgery are often at risk for significant blood-loss, postoperative downtime and prolonged ecchymosis and edema. Mitigating the postoperative sequelae and bleeding-associated side-effects are therefore a main consideration for plastic surgeons.

Tranexamic Acid (TXA) (trans-4-aminomethylcyclohexane-1 fcarboxylic-acid), an antifibrinolytic agent, has gained increasing recognition as a valuable pharmacologic agent in elective surgery.[2-11] A recent meta-analysis of 57 studies in a variety of surgical specialties demonstrated 72% reduced odds of transfusion in surgical patients who received intravenous (IV) TXA preoperatively, with no difference in the incidence of venous thromboembolic events between TXA and control groups.[12] Despite its well-established track record of safety and efficacy in a variety of surgical procedures, the use of TXA has only recently expanded to plastic and reconstructive surgery. In 2017, Rohrich *et al*.[13] reported their experience with TXA in a variety of cosmetic procedures. Since then, TXA has gained increasing recognition as a valuable pharmacologic agent within plastic surgery, and its administration has been described in over fifty original articles in the fields of craniofacial surgery, [14-32] cosmetic surgery, [13,33-47] burn surgery, [48-53] and microsurgery.[54-57] TXAs mechanism of action, indications, contraindications, pharmacodynamics and kinetics are summarized in **Table 1** and illustrated in **Figure 1**.[58]

Despite the accumulation of evidence regarding its safety and efficacy and its promising role in plastic surgery, guidelines for optimum administration of TXA have not been yet established. This study reviews the scientific evidence regarding the use of TXA in the full range of plastic and reconstructive surgery to provide clinical recommendations based on level I data for its safe and effective use in various plastic surgical procedures.

METHODS

Study Selection, Data Collection and Data Analysis

A systematic review and meta-analysis were conducted for publications examining the use of TXA in plastic surgery following the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines (**Figure 2**). The search strategy, including the databases queried, search term, inclusion and exclusion criteria and the data analysis methods are outlined in **Table 2**. Risk of bias for the included studies in included in **Tables 3, 4.**

RESULTS

Forty-five studies describing the use of TXA in plastic surgery from 2003 to 2022 were deemed eligible for inclusion in this systematic review (**Table 5**), comprising a total of 4361 patients, 2249 of them undergoing plastic surgical procedures with intravenous, topical and orally administered TXA. These included studies evaluating the use of TXA in craniofacial surgery (13 studies), cosmetic and breast-related surgeries (24 studies), burn care (6 studies), and microsurgery (2 studies). 19 studies were deemed eligible for inclusion in the meta-analysis.

Craniofacial Surgery

Systemic TXA Administration in Craniofacial Surgery

Intravenous Administration

Four randomized controlled trials (RCTs) and nine retrospective cohort studies describing the use of TXA in craniofacial surgery were identified; all articles discussed the use of intravenously administered TXA. [16-24,27,30-32,59-61] Surgical procedures included cranial vault reconstruction (CVR) and cleft palate operations. Preoperative intravenous loading doses ranged from 10 to 50 mg/kg, with 10 mg/kg being the most used in 50% of the studies reviewed. The infusion rate ranged from 1 to 10 mg/kg/hour, with 5 mg/kg/hour being the most reported (62.5%). Two RCTs and seven retrospective cohort studies reported a statistically significant reduction in transfusion requirements with intravenous TXA administration. [16-19,22,23,27,30,60] A statistically significant reduction in intraoperative blood loss was demonstrated in one RCT and six retrospective cohort studies with intravenous TXA administration. [16-19,23,30,60] An RCT by Goobie *et al*. [23] reported a significant reduction in transfusion requirements by two-thirds compared with placebo in children undergoing CVR. This finding was corroborated by significantly reduced blood loss. TXA was administered in a loading dose of 50 mg/kg, followed by an infusion of 5 mg/kg/hour during surgery. The same regimen has been reported by a different group as well, demonstrating significantly reduced blood loss and transfusion requirements.[19] However, a recent RCT by the same group has demonstrated that a lower TXA bolus dose of 10 mg/kg followed by a similar maintenance infusion of 5 mg/kg/hour is non-inferior to the high-dosage TXA scheme used in their previous study (50 mg/kg) in decreasing intraoperative blood loss and blood transfusion.[24] These findings were later confirmed by Kim et

al.[30], demonstrating significantly reduced blood loss and transfusion requirements, alongside several other outcomes.

Using the same TXA bolus and infusion doses (10 mg/kg, followed by 5 mg/kg/hour), Kurnik *et al*. demonstrated significantly reduced transfusion requirements.[60] Blood loss was also significantly lower in patients receiving TXA. The same group later showed that a 4-hour infusion was as effective as a 24-hour infusion for reducing blood loss in patients undergoing CVR.[31] Transfusion requirements, hemoglobin and hematocrit levels, and estimated blood loss were not significantly different between the groups.

While transfusion reduction was demonstrated in another RCT by Dadure *et al.*[22] using 15 mg/kg TXA followed by continuous infusion of 10 mg/kg/hour, no significant differences in blood loss were reported. A recent retrospective cohort study by Eustache et al.[27] demonstrated a significant reduction in transfusion requirements, drain output and length of stay in 102 patients under a bolus of 15 mg/kg TXA followed by continuous infusion of 10 mg/kg/hour. A bolus of 10 mg/kg TXA followed by continuous infusion of 1 mg/kg/hour has also shown no significant change in intraoperative blood loss in an RCT of children undergoing cleft lip and palate surgery.[20]

Other reported advantages of TXA administration in craniofacial surgery procedures included shorter surgery duration, improved surgical field and surgeon satisfaction, reduced length of stay, reduced drain output, higher postoperative hemoglobin, and lower hemoglobin drop. [14-32] However, the evidence underpinning its effects on these potential outcomes remains inconclusive due to the heterogeneity of outcome measures used in current studies.

With regards to TXA-related complications in craniofacial surgery, the reported incidences of both thromboembolic events and seizures were not significantly different in patients who

received TXA vs. patients who did not. No TXA-related allergic reactions or anaphylaxis events were reported in the current literature.

Oral Administration

No studies reported oral TXA administration in craniofacial surgery.

Local TXA Administration in craniofacial surgery

No studies reported local TXA administration in craniofacial surgery.

TXA in Cosmetic Surgery

Thirteen randomized controlled trials (RCTs), four prospective cohort studies and seven retrospective cohort studies describing the use of TXA in cosmetic surgery were identified. Eight articles discussed the use intravenously administered TXA, two discussed its oral administration, five explored its topical use, seven discussed local infiltration of TXA and two described various combination regimens. [13,33-46] Surgical procedures included facelift, rhinoplasty, blepharoplasty, liposuction, dermatologic surgery and breast-related procedures.

Face lift

Systemic TXA Administration in facelift

Intravenous Administration

One RCT by Cohen et al.[62] explored the use of intravenous TXA administration in 44 patients undergoing facelift surgery. TXA was shown to significantly decrease postoperative collections and surgeon-rated bruising. However, no significant difference was demonstrated in intraoperative blood loss.

Oral Administration

No studies reported oral TXA administration in facelift surgery.

Local TXA Administration

Four studies reported subcutaneous infiltration of TXA in facelift surgery and one discussed its topical use.

Subcutaneous Infiltration

Local infiltration of TXA was first reported in a prospective study of 27 facelift patients, demonstrating decreased intraoperative blood loss, surgery duration and drain output in the TXA group.[63] A larger prospective cohort study of 39 patients by the same group has confirmed these findings.[64] A recent retrospective review of 245 facelift patients, the third published by the same group, further confirmed that locally administered TXA can significantly reduce surgery duration without increase in minor complications.[65]

Topical administration

Topical TXA administration was described by Serrano Reyes et al.[66] who demonstrated non-significant reduction in hematoma rates under topical TXA irrigations.

Rhinoplasty

Systemic TXA Administration in Rhinoplasty

Intravenous Administration

Four RCTs evaluated the use of intravenous TXA administration in patients undergoing rhinoplasty. Ghavimi *et al*.[37] utilized a preoperative 10 mg/kg bolus in an RCT of 50 patients demonstrating a significantly lower blood loss in the TXA group. Beikai et al.[67] reported a significant reduction in blood loss using the same dose regimen in an RCT of 96 patients. However, Avci et al.[47] demonstrated a non-significant difference in total blood loss with IV TXA in 90 patients. TXAs effects on edema and ecchymosis have been explored by several groups,

however, the lack of consistency in outcome measures precludes the development of substantial quantitative conclusions.[34,68]

Oral Administration

Two RCTs explored the use of orally administered TXA. Eftekharian et al.[35] demonstrated statistically significant reduction in blood loss in 50 participants undergoing rhinoplasty after receiving 2 × 500 mg TXA tablets. An RCT by Sakalliogllu et al.[36] administered 1 g oral TXA before surgery and 3 g daily for 5 days in 75 rhinoplasty patients. The TXA group showed significantly less intraoperative bleeding compared with controls as well as decreased periorbital edema and ecchymosis.

Local TXA Administration

No studies reported local TXA administration in rhinoplasty.

Body-contouring

Systemic TXA Administration

Intravenous Administration

Two RCTs explored intravenous administration of TXA in body-contouring. In an RCT by Cansanção et al.[43], patients who received 10 mg/kg TXA before and at the end of surgery showed significantly reduced blood-loss. A more recent RCT by the same group confirmed these findings.[69]

Local TXA Administration

Local infiltration of TXA was shown to significantly reduce the bruise area after liposuction in one retrospective cohort study and one RCT of 33 patients.[70,71]

TXA in Breast-related Procedures

Systemic TXA Administration

Intravenous Administration

One retrospective cohort study of 499 patients undergoing implant-based breast reconstruction evaluated the administration of 1 gr intravenous TXA, resulting in significantly reduced hematoma rates.[72]

Oral Administration

No studies reported oral TXA administration in breast-related surgery.

Combination regimens

Two cohort studies explored the utility of combination regimens of IV TXA followed by local infiltration.[73] Administration regimens and outcomes are summarized in **Table 5**.

Local TXA Administration

Topical administration

One RCT and one retrospective cohort study explored the use of topical TXA administration in breast-related procedures.[44,74] Administration regimens and outcomes are summarized in **Table 5**.

TXA in Blepharoplasty

Systemic TXA Administration

No studies reported systemic TXA administration in blepharoplasty.

Local TXA Administration

One RCT reported the use of local TXA infiltration in blepharoplasty.[75] Study design, administration regimen and outcomes are summarized in **Table 5**.

TXA in Burn Surgery

Systemic TXA Administration

Intravenous Administration

Three randomized controlled trials and three retrospective cohort studies describing 368 total cases were identified in burn surgery.[48-51] Study design, administration regimens and outcomes are summarized in **Table 5**.

TXA in Microsurgery

Systemic TXA Administration

Intravenous Administration

Two retrospective studies reported the use of IV TXA in microsurgery.[55,56] Study design, administration regimens and outcomes are summarized in **Table 5**.

Meta-Analysis Results and Grading of Evidence

Craniofacial Surgery

Blood loss

Ten studies investigating the impact of TXA on total blood-loss (adjusted by weight) in craniofacial surgery were included in this analysis (**Table 6, Supplemental Digital Content**). All 382 patients included received TXA intravenously. A continuous random-effects model was chosen for observational studies and a fixed effects model was chosen for RCTs. TXA administration was associated with reduced perioperative blood-loss in craniofacial surgery with a mean difference of -13.71 (95% CI -19.42, -8.00; low-certainty evidence) for observational studies and a mean difference of -15.68 (95% CI -28.79, -2.56; moderate-certainty evidence) for RCTs.

Transfusion requirements

A reduction in transfusion was also demonstrated in the TXA group with a mean difference of -10.25 (95% CI –16.34, -4.17; low-certainty evidence) for observational studies and -10.72 (95% CI -17.41, -4.03; moderate-certainty evidence) for RCTs. (**Table 6, Supplemental Digital Content**).

Cosmetic Surgery

Blood Loss

Six RCTs investigating the impact of TXA on total blood loss (adjusted by weight) were included in this meta-analysis (**Table 6, Supplemental Digital Content**). 132 patients received TXA intravenously and 50 patients orally. A continuous random-effects model was chosen for observational studies and a fixed effects model was chosen for RCTs. Intravenous administration of TXA was associated with a mean difference of -17.42 (95% CI -21.49, -13.35; high-certainty evidence) in rhinoplasty while oral administration demonstrated a higher mean difference of -61.70 (95% CI -83.02, -40.39; moderate-certainty evidence).

Hematoma Rates

A total of nine studies investigating the impact of TXA on hematoma rates in facelifts, breast-related procedures and liposuction were included in this meta-analysis (**Table 6, Supplemental Digital Content**). A dichotomous fixed-effects and random-effects models were used to calculate effects sizes for RCTs and non-RCTs, respectively. A significant association between TXA and reduced hematoma rates was demonstrated in cosmetic surgery, with an odds ratio (OR) of 0.36 (95% CI 0.16 to 0.79; low-certainty evidence) for observational studies and OR 0.13 (95% CI 0.01 to 2.14; high-certainty evidence) for RCTs. An OR of 0.42 (95% CI 0.17 to 1.06; very low certainty evidence) was demonstrated for observational studies looking at

breast-related procedures and OR 0.21 (95% CI 0.04 to 1.09; very low certainty evidence) for observational studies looking at facelift procedures.

Burn Care

Blood Loss

A total of three studies (two RCTs) investigating the impact of TXA on blood loss in burn surgery were included in this meta-analysis (**Table 6, Supplemental Digital Content**). A continuous fixed-effects model was used to calculate effects sizes for RCTs. A mean difference of 196.73 (95% CI 290.93 to 102.53; moderate-certainty evidence) was demonstrated in burn surgery.

DISCUSSION

This article summarizes the current knowledge regarding the safety and efficacy of TXA administration in plastic surgery. While the analysis and grading were performed for both RCTs and non-RCTs, clinical recommendations were made based on the grading of level I evidence only (RCTs) when available (**Table 7**).

The Role of TXA in Craniofacial Surgery

The role of TXA in craniofacial surgery has been well studied, compared to other areas of plastic surgery. [14-32] All current studies on TXA in craniofacial surgery discuss Intravenous administration, with a bolus of 10 mg/kg TXA followed by continuous infusion of 5 mg/kg/hour being the most utilized TXA administration regimen. A recent meta-analysis has demonstrated a significant reduction in blood-loss and need for transfusion compared to placebo/no intervention in children undergoing surgical correction of craniosynostosis, without TXA-related adverse effects. Based on both qualitative and quantitative analysis, the authors recommended the implementation of TXA in surgery protocols.[25] These findings were supported by another meta-

analysis, further demonstrating elevation of postoperative hemoglobin and hematocrit levels, and reduction of operation duration in the TXA group.[26] These findings have led the authors to recommend the routine administration of intraoperative TXA in craniosynostosis repair surgery in all centers that practice these procedures.[27] Further studies are recommended to determine the need and ideal time frame for continuous TXA infusion postoperatively.

The Role of TXA in Cosmetic Surgery

This study provides evidence of high certainty for significant associations between TXA administration and reduced hematoma rates and blood loss in cosmetic procedures. While evidence of high certainty was demonstrated for the use of IV TXA in rhinoplasty, oral administration has shown moderate certainty. While the most common administration mode described in the literature is intravenous administration, current studies demonstrate heterogeneity in the ideal TXA dosage and administration mode for aesthetic procedures, and reported protocols include oral, topical and IV dosing. Therefore, further studies are indicated to compare the different administration techniques in various cosmetic procedures.

A recent meta-analysis [42] concluded that TXA had the ability to significantly reduce intraoperative blood-loss and postoperative edema and ecchymosis among patients undergoing primary elective rhinoplasty. Another recent meta-analysis [41] reported significant differences in blood-loss, surgical field quality, edema rating of upper and lower eyelid, and ecchymosis rating of upper and lower eyelid following TXA administration. In addition to its antifibrinolytic properties, TXA's promising role in aesthetic procedures can be attributed to its anti-inflammatory effects achieved by blocking the activation of plasminogen into plasmin, a pro-inflammatory cell activator.[76,77] Minimizing edema and ecchymosis may be significantly beneficial in such procedures, where postoperative edema may mask results and influence patient

and surgeon perception of surgical outcome for several months postoperatively. [38,39] Therefore, standardized, objective measurements are required to provide quantitative conclusions regarding TXAs effects on ecchymoses and edema in plastic surgery procedures.

The Role of TXA in other Plastic Surgery Procedures

While TXA is increasingly utilized in aesthetic and craniofacial surgery, the current literature demonstrates limited use of TXA in microsurgery. The paucity of large trials published in this field limits the quantitative conclusions that can be drawn in the aggregate. Our study provided moderate-certainty evidence that TXA administration in burn care procedures is associated with reduced blood loss. However, further studies are needed to determine the ideal TXA administration regimen in burn care.

While seizures, thrombotic events, and wound healing complications have been described as potential complications of TXA, none of the articles attributed complications to TXA administration nor demonstrated higher complication rate with TXA use.[78-85] Despite TXAs favorable safety profile, knowledge of the risk factors and clinical manifestations of potential adverse events is imperative for safe administration of TXA.

CONCLUSION

This article summarizes the clinical applications of TXA in the full range of plastic surgery and is the first to provide clinical recommendations. There is moderate-certainty evidence to support the use of intravenous administration of TXA in craniofacial surgery procedures to reduce blood-loss and transfusion requirements. There is high-certainty evidence to support the use of TXA in cosmetic surgery and intravenous administration in rhinoplasty procedures to reduce blood-loss. However, standardized, objective measurements are required to provide quantitative conclusions regarding TXAs effects on ecchymoses and edema in cosmetic

surgery procedures. Further high-level studies are needed to determine TXA's effects on hematoma rates in facelift surgery and breast-related procedures (very low-certainty evidence). While intravenous administration is most studied in cosmetic surgery, topical formulations and local infiltration, are increasingly utilized to achieve localized effects minimizing systemic levels. With regards to burn care, there is moderate-certainty evidence to support the use of TXA to reduce reduced blood loss. However, further studies are needed to determine the ideal TXA administration regimen. Further studies are required to provide quantitative conclusions on the effects of TXA administration in microsurgery.

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Figure Legends

Tables

Figures

	Table 1. Mechanism and pharmacodynamics of the antifibrinolytics tranexamic acid (TXA)
Mechanism of action	Reversibly inhibiting the activation of plasminogen to plasmin Preventing the enzymatic breakdown of fibrin clot and improving its stability Preserving platelets for late clot formation by improving platelet function Inhibiting plasmin-induced activation at high concentrations
Available formulations	Intravenous, oral
Bioavailability (oral)	**Oral:** 45%
Time to peak	**Oral** (single dose): 2.5 hours (range: 1 to 5 hours)
Terminal half-life	**Intravenous:** 2 hours **Oral:** 10 hours
Elimination	95% renal excretion
Clinical FDA-approved indications	**Intravenous:** hemophilia (short term use of 2-8 days), reduce or prevent hemorrhage and reduce the need for replacement therapy during or following tooth extraction. **Oral:** cyclic heavy menstrual bleeding in females of reproductive potential
Contraindications	**Intravenous:** Subarachnoid hemorrhage Active intravascular clotting Hypersensitivity to TXA **Oral:** Concomitant use of combined hormonal contraceptives Active thromboembolic disease or a history or intrinsic risk of thrombosis or thromboembolism Hypersensitivity to TXA
Known drug interactions	**Anti-inhibitor Coagulant Complex (Human)**: Antifibrinolytic Agents may enhance the thrombogenic effect of Anti-inhibitor Coagulant Complex (Human). Risk X: Avoid combination. **Estrogen Derivatives:** May enhance the thrombogenic effect of TXA. Risk X: Avoid combination. **Factor IX Complex (Human) [(Factors II, IX, X)]**: Antifibrinolytic Agents may enhance the adverse/toxic effect of Factor IX Complex (Human) [(Factors II, IX, X)]. Specifically, the risk for thrombosis may be increased.

	Risk X: Avoid combination. **Hormonal Contraceptives:** May enhance the thrombogenic effect of TXA. Risk X: Avoid combination. **Prothrombin Complex Concentrate (Human) [(Factors II, VII, IX, X), Protein C, and Protein S]**: Antifibrinolytic Agents may enhance the adverse/toxic effect of Prothrombin Complex Concentrate (Human) [(Factors II, VII, IX, X), Protein C, and Protein S]. Specifically, the risk for thrombosis may be increased. Risk X: Avoid combination. **Thrombolytic Agents:** Tranexamic Acid may diminish the therapeutic effect of Thrombolytic Agents. Thrombolytic Agents may diminish the therapeutic effect of TXA. Risk X: Avoid combination. **Tretinoin (Systemic):** May enhance the thrombogenic effect of Antifibrinolytic Agents. Management: Concomitant use of antifibrinolytics and tretinoin is not recommended. If combined, monitor patients closely for any signs of thrombotic complications. Risk D: Consider therapy modification
Main adverse effects	Thrombosis with concomitant use of several agents (see below under "drug interactions"), seizures, hypersensitivity, visual or ocular adverse effects, dizziness, headache, sinus and nasal symptoms, back pain, abdominal pain, muskoloskeletal pain, joint pain, muscle cramps, migraine, anemia and fatigue.
Recommended dosages	**IV** Normal renal function: 10 mg/kg 2 to 8 days, 3 to 4 times daily. Cr 1.36 to 2.83 mg/dL: 10mg/kg twice daily Cr 2.83 to 5.66 mg/dL: 10 mg/kg once daily Cr >5.66 mg/dL: 10 mg/kg every 48 hours or 5 mg/kg every 24 hours **Oral** **Normal renal function:** 1,300 mg three times a day (3,900 mg/day) for a maximum of 5 days during monthly menstruation **Renal impairment:** Lower dosage is needed (for a maximum of 5 days during menstruation) if serum creatinine concentration (Cr) is higher than 1.4 mg/dL Cr above 1.4 mg/dL and ≤ 2.8 mg/dL: 1,300 mg two times a day (2,600 mg/day)

	Cr above 2.8 mg/dL and ≤ 5.7 mg/dL: 1,300 mg once a day (1,300 mg/day) Cr above 5.7 mg/dL: 650 mg once a day (650 mg/day)

Abbreviations: *Cr*, serum creatinine

Table 2: Data Collection and Analysis Methods

Systematic review	***Literature Search Strategy*** Two independent investigators conducted a literature search of the PubMed, Cochrane, and Google Scholar databases since their inception for relevant clinical studies. All databases were queried using the following keyword terms: "TXA," "tranexamic acid," "antifibrinolytics," "antifibrinolytic agents," "plastic surgery," "craniofacial surgery,", "cosmetic surgery", "aesthetic surgery,", "breast surgery", "breast reduction", "reduction mammoplasty", "breast augmentation", "breast reconstruction", "burns,", "burn care", "burn surgery", "microsurgery," and "reconstructive surgery." **Study Selection** Inclusion criteria included the following: randomized and nonrandomized controlled trials and prospective and retrospective cohort studies of the use of the TXA in plastic surgery in the fields of craniofacial surgery, cosmetic surgery, breast surgery, burn care, and reconstructive microsurgery. Titles and abstracts were reviewed for the following exclusion criteria: (1) absence of discussion of TXA in plastic surgery/non TXA-administration focus; (2) absence of index plastic surgery procedures; (3) animal studies; (4) studies not written in English; and (5) case reports/series. Titles and abstracts were screened by two independent reviewers. Full texts of included abstracts were then fully reviewed by the two reviewers, and discrepancies were identified and resolved through discussion. The date of the last search was April 24, 2023. **Data Collection** Study design, Procedure types, dosing regimen, time and mode of administration, outcomes and complications for each study were recorded. Outcome data collected in the meta-analysis included blood loss, transfusion requirements and hematoma rates.
Meta-analysis	**Data analysis** Data analysis was performed using Review Manager (RevMan) Version 5.4 (The Nordic Cochrane Center, The Cochrane Collaboration). Mean differences (MD) with corresponding 95% Confidence Intervals (CIs) were calculated for continuous variables and odds ratios with 95% CIs were calculated for dichotomous variables. A p value lower than 0.05 indicated a statistically significant effect. Both random effects and fixed effects models were considered and implemented for each outcome, considering study heterogeneity. Statistical heterogeneity was tested using the I^2 statistic, considering values lower than 50% low heterogeneity and values greater than 50% high heterogeneity. (Higgins et al., 2019) Sub-group analysis was done by study type and procedure type.
Grading of Clinical Recommendations	An established appraisal process was used to rate the quality of relevant scientific research using the Grading of Recommendations Assessment, Development, and Evaluation methodology (GRADE). GRADE considers multiple factors, including study design, risk of bias, inconsistency, indirectness,

	imprecision, as well as risk of publication bias. (Guyatt et al., 2008). Important directions for future research were also identified.

Table 3. Summary of Risk of Bias among Non-randomized Trials (ROBINS-I tool)

Study, Year	D1	D2	D3	D4	D5	D6	D7	Overall
Varidel et al., 2022	Low	Moderate	Low	Low	Low	Moderate	Low	Low
Eustache et al., 2021	Low	Moderate	Low	Low	Low	Moderate	Low	Low
Kim et al., 2018	Low	Moderate	Low	Low	Low	Moderate	Low	Low
Kurnik et al., 2017	Low	Moderate	Low	Low	Low	Moderate	Low	Low
Hansen et al., 2017	Low	Moderate	Low	Low	Low	Moderate	Low	Low
Martin et al., 2016	Low	Moderate	Low	Low	Low	Moderate	Low	Low
Crantford et al., 2015	Low	Moderate	Low	Low	Low	Moderate	Low	Low
Engel et al., 2015	Low	Moderate	Low	Low	Low	Moderate	Low	Low
Maugans et al., 2011	Low	Moderate	Low	Low	Low	Moderate	Low	Low
Tapking et al., 2022	Moderate	Low	Low	Low	Low	Moderate	Low	Low
Domínguez et al., 2017	Moderate	Moderate	Low	Low	Low	Moderate	Low	Low-Moderate
Coombs et al., 2022	Moderate	Moderate	Low	Low	Low	Low	Moderate	Low-Moderate
Cristel et al., 2021	Low	Low	Low	Low	Low	Moderate	Moderate	Low
Weissler et al., 2021 (liposuction)	Low	Moderate	Low	Low	Low	Moderate	Low	Low
Weissler et al., 2021 (reduction mammoplasty)	Low	Moderate	Moderate	Low	Low	Moderate	Moderate	Moderate

Weissler et al., 2020 (breast reconstruction)	Low	Low	Low	Low	Low	Moderate	Moderate	Low
Couto et al., 2020	Low	Low	Low	Low	Low	Moderate	Moderate	Low
Serrano Reyes et al., 2020	Low	Moderate	Low	Low	Low	Low	Moderate	Low
Schroeder et al., 2020	Moderate	Low	Low	Low	Low	Moderate	Low	Low
Lardi et al., 2018	Serious	Moderate	Serious	Moderate	Moderate	Moderate	Moderate	Moderate
Valerio et al., 2015	Serious	Serious	Serious	Moderate	Moderate	Moderate	Moderate	Serious-Moderate

D1: Bias due to confounding
D2: Bias due to selection of participants
D3: Bias in classification of interventions
D4: Bias due to deviations from intended interventions
D5: Bias due to missing data
D6: Bias in measurement of outcomes
D7: Bias in selection of the reported result

Table 4. Summary of Risk of Bias among Randomized (ROB2 tool)

Study, Year	D1	D2	D3	D4	D5	Overall
Arantes et al., 2017	Low	Moderate	Low	Moderate	Moderate	Moderate
Durga et al., 2015	Low	Low	Low	Moderate	Moderate	Low
Dadure et al., 2011	Low	Low	Low	Moderate	Low	Low
Goobie et al., 2011	Low	Low	Low	Moderate	Low	Low
Ajai et al., 2021	Low	Low	Low	Moderate	Low	Low
Jennes et al., 2003	Low	Moderate	Low	Moderate	Moderate	Moderate
Abboud et al., 2021	Low	Low	Low	Moderate	Moderate	Low-Moderate
Cohen et al., 2021	Low	Low	Low	Moderate	Moderate	Low-Moderate
Kochuba et al., 2021	Low	Low	Low	Low	Moderate	Low
Fayman et al, 2020	Low	Low	Low	Moderate	Moderate	Low-Moderate
Zilinsky et al., 2019	Low	Low	Low	Moderate	Moderate	Low-Moderate
Sagiv et al., 2018	Low	Moderate	Low	Moderate	Moderate	Moderate
Mehdizadeh et al., 2018	Moderate	Moderate	Low	Moderate	Moderate	Moderate
Cansanção et al., 2018	Low	Low	Low	Moderate	Moderate	Low-Moderate
Ghavimi et al., 2017	Moderate	Moderate	Low	Moderate	Moderate	Moderate
Eftekharian et al., 2016	Moderate	Moderate	Low	Moderate	Moderate	Moderate
Cansanção et al., 2015	Low	Low	Low	Moderate	Moderate	Low-Moderate

Beikai et al., 2015	Low	Moderate	Low	Moderate	Moderate	Moderate
Sakalliogllu et al., 2015	Low	Moderate	Low	Moderate	Moderate	Moderate
Ausen et al., 2015	Low	Low	Low	Low	Moderate	Low

D1: Bias arising from the randomization process
D2: Bias due to deviations from intended intervention
D3: Bias due to missing outcome data
D4: Bias in measurement of the outcome
D5: Bias in selection of the reported result

Table 5. Tranexamic Acid (TXA) in Plastic Surgery

Subspecialty	Study, Year	Study Design	Study group (Total sample size)	Surgery Type	TXA Administration Mode, Time, Dosage	Outcomes (TXA group)	TXA-related Complications
Craniofacial Surgery	Varidel et al., 2022	RCS	128 (206)	CVR	IV LD: 15 mg/kg for 15 min IR: 5 mg/kg/h throughout surgery	Significant reduction in IOB and TTR.	None
	Eustache et al., 2021	RCS	70 (102)	CVR	IV, inoperative + postoperative LD: 10 mg/kg IR: 10 mg/kg/h until skin closure.	Significant reduction in TTR, PTR, DO and LOS.	None
	Kim et al., 2018	RCS	23 (48)	CVR	IV LD: 10 mg/kg for 15 min IR: 5 mg/kg/h throughout surgery	Significantly reduced IOB, TR, clotting time during the postoperative period and D-dimer levels, higher clot strength, lower duration of mechanical ventilation, and number of postoperative respiratory-related complications	None
	Kurnik et al., 2017	RCS	35 (114)	CVR	IV, inoperative + postoperative LD: 10 mg/kg IR: 5 mg/kg/h for 24 hours	Significantly reduced TTR, ITR, PTR and IOB. No significant difference in postop Hb, Hct, LOS, and SD	None
	Hansen et al., 2017	RCS	16 (25)	CVR	IV, inoperative LD: 10 mg/kg IR: 5 mg/kg*h	Significantly higher postop ERCV, Hb, reduced Hb drop and DO (24h) No significant difference in TR	None
	Arantes et al., 2017	RCT	66 (136)	CP	IV, inoperative LD: 10 mg/kg IR: 1 mg/kg/h	No significant change in IOB	None

Abbreviations: RCS- retrospective cohort study, CVR- cranial vault reconstruction, IV- intravenous, LD- loading dose, IR- infusion rate, TTR- total transfusion requirements, ITR- intraoperative transfusion requirements, PTR- postoperative transfusion requirements IQR-interquartile range, pRBC- packed

	Martin et al., 2016	RCS	69 (187)	CVR	IV, inoperative LD: 50 mg/kg IR: 5 mg/kg*h	Significantly reduced IOB, TR, LOS and DO No significant difference in postop Hct	None
	Crantford et al., 2015	RCS	17 (37)	CVR	IV, inoperative LD: 20 mg/kg IR: 10 mg/kg/h	Significantly reduced TR and IOB No significant difference in HCT drop and SD.	None
	Durga et al., 2015	RCT	33 (65)	CP	IV, preoperative 10 mg/kg	Significantly improved surgical field and surgeon satisfaction.	None
	Engel et al., 2015	RCS	17 (33)	CVR	IV, inoperative LD: 10 mg/kg IR: 5 mg/kg/h	Significantly reduced IOB, TR No significant difference in SD	None
	Dadure et al., 2011	RCT	19 (39)	CVR	IV, inoperative LD: 15 mg/kg IR: 10 mg/kg*h	Significantly reduced ITR and TTR No significant difference in IOB and surgeon satisfaction	None
	Goobie et al., 2011	RCT	23 (43)	CVR	IV, inoperative LD: 50 mg/kg IR: 5 mg/kg*h	Significantly reduced TBL, IOB, POB and TR.	None

	Maugans et al., 2011	RCS	26 (56)	CVR	IV, inoperative LD: 50 mg/kg IR: 5 mg/kg*h	Significantly reduced IOB and TR.	None
Burn care	Tapking et al., 2022	RCS	26 (78)	Wound excision and grafting	IV, preoperative, perioperative LD: 10 mg/kg 30 min just prior to surgery. IR: 1 mg/kg*h during the further perioperative period.	Significantly reduced TTR, ITR No significant difference in LOS or mortality	None
	Ajai et al., 2022	RCT	15 (30)	Tangential excision in pts with deep dermal thermal burns <30%	IV, preoperative 15 mg/kg	Significantly reduced average blood loss per square centimeter burn area excised no significant difference in TBL, TR, postoperative hemoglobin, LOS and graft-take.	None
	Mohan et al., 2021	RCS	38(76)	Burns excision and skin grafting	Topical, 0.5% TXA to 1 in 200,000 adrenalin solution	Significantly reduces blood loss without increasing the risk of side-effects or complications.	None
	Bhatia et al., 2017	RCT	25(50)	Adult patients having >20% total body surface area of burn wounds, scheduled for wound debridement/eschar removal ± skin grafting after 10 days of burn injury	IV, preoperative 15 mg/kg diluted to 25 ml with isotonic saline over 10 mins	Significantly reduces blood loss without increasing the risk of side-effects or complications.	None
	Domínguez et al., 2017	RCS	52 (107)	Burns	IV, inoperative	Significantly reduced TR	None

	Jennes et al., 2003	RCT	14 (27)	Tangential burns excision	IV, preoperative 20 mg/kg	Non-Significant difference in IOB	None
Cosmetic Surgery	Coombs et al., 2022	RCS	72 (245)	Facelift surgery alone or in combination with fat transfer and perioral chemical peel.	Subcutaneous infiltration of 0.5% lidocaine/1:200:000 epinephrine with or without 1-2mg/mL TXA.	Significantly reduced SD Non-Significant difference in minor complications	None
	Cristel et al., 2021	PCS	50 (50)	Rhinoplasty	intravenous and intraoperative injections	No significant difference in ecchymoses rate	None
	Weissler et al., 2021	RCS	257 (385)	Reduction mammaplasty	Intravenous + topical	No significant difference in seroma, hematoma and drain duration.	None
	Weissler et al., 2021	RCS	60 (120)	Liposuction	75 mL of TXA (3 g in NaCl 0.9%) infiltrated into the liposuction donor sites	Significantly reduced bruising No significant difference in complications	None
	Abboud et al., 2021	PCT	36 (36)	breast reduction by liposuction and resection (PALM)	5 mL IV of 0.5 g/5 mL TXA on induction + 1 L normal saline: one with 5 mL of 0.5 g/5 mL TXA associated with epinephrine 1:100,000	Significantly reduced ratio of decanted to lipoaspirated volume, decreased dermal bleeding and postoperative ecchymosis.	None
	Cohen et al., 2021	RCT	44 (44)	Facelift	Intravenous: 1 g IV × 2 doses (15 min before skin incision and 4 hr later)	Significantly decreases surgeon-rated postoperative bruising and postoperative collections. No significant difference in IOB	None
	Kochuba et al., 2021	PCT	39 (39)	facelift	Local infiltration: 1 or 2 mg of TXA	Decreased IOB, SD, and DO.	None

					per 1 mL of 0.5% lidocaine with 1:200,000 epinephrine		
	Avci et al., 2020	RCT	60(90)	Rhinoplasty	Group 1: preoperative 1 g IV TXA + 1 g IV TXA at the end of the operation. Group 2: preoperative 1 g IV TXA Group 3: Normal saline	Non-significant difference in total blood loss	None
	Weissler et al., 2020	RCS	208 (364)	Implant-based breast reconstruction	75 ml of TXA (3 g in NaCl 0.9%), applied topically into the breast pocket before closure.	Significantly reduced seroma rate, time to drain removal No significant difference in hematoma rate	None
	Weissler et al., 2020	RCS	116 (499)	Implant-based breast reconstruction	IV 1 gr before mastectomy incision and IV 1 gr at the conclusion of the procedure.	Significantly reduced hematoma rate.	None
	Couto et al., 2020	RCS	27 (27)	Facelift	Local infiltration: 1 mg of TXA/1 mL of tumescent (0.5% lidocaine 1:200,000 epinephrine)	Decreased IOB, SD, and postoperative DO.	N/A
	Fayman et al, 2020	RCT	33 (33)	Liposuction	tumescent infiltration: saline, bupivacaine lignocaine and	Significantly reduced bruising on days one and seven postoperatively.	N/A

					adrenalin mixed with 0.1% TXA.		
	Serrano Reyes et al., 2020	PCS	30 (60)	Facelift	2.5% topical TXA irrigation	Significantly reduced drain output in the first 24 h Non-significant reduction in postoperative complications and hematoma	None
	Schroeder et al., 2020	RCS	44 (76)	Facelift	Local infiltration final concentration: 9.1 mg TXA/1 mL of local and tumescent	Significantly reduced POD1 drain output, days to drain removal, percentage drains removed POD1, percentage POD1 drain output <25 cc and intraoperative estimated blood loss (EBL). Non-significant reduction in minor hematoma, major hematoma, Nitro-bid use, and thromboembolic events.	N/A
	Zilinsky et al., 2019	RCT	127 (127)	Dermatologic surgery	Local infiltration, preoperative lidocaine 2% diluted 1:1 with TXA 100 mg/1 mL	Significantly reduced bleeding, and improved subjective hemostasis.	N/A
	Sagiv et al., 2018	RCT	17 (34)	Upper blepharoplasty	Lidocaine 20 mg/ml diluted 1:1 with 100 mg/ml TXA	No difference in blood weight in pads or cautery time No significant difference in ecchymoses	None
	Mehdizadeh et al., 2018	RCT	30 (60)	Rhinoplasty	intravenously (IV) 1 h before and three doses every 8 h postoperatively. Group D (n = 15) received 8 mg dexamethasone, group T (n = 15) received 10 mg/kg tranexamic	Significantly reduced periorbital edema and ecchymosis in the TXA groups compared to control No significant difference in periorbital edema and ecchymosis between the TXA and dexamethasone groups.	None

					acid, group DT (n = 15) received both 8 mg dexamethasone and 10 mg/kg tranexamic acid, and group P (n = 15) received neither medication and served as the placebo control group		
	Cansanção et al., 2018	RCT	10 (20)	Liposuction	IV 10 mg/kg TXA in the preoperative and postoperative periods.	Significantly reduced volume of blood loss for every liter of lipoaspirate, Hct levels at day 7 postoperatively.	None
	Ghavimi et al., 2017	RCT	24 (50)	Rhinoplasty	IV, preoperative 10 mg/kg	Significantly reduced IOB, pre and postoperative Hct, eyelid edema, periorbital ecchymosis and improved surgeon satisfaction Non-Significant change in pre and postoperative Hb	None
	Eftekharian et al., 2016	RCT	25 (50)	Rhinoplasty	Oral, preoperative 2 × 500 mg	Significantly reduced TBL and SD and improved SF satisfaction	None
	Cansanção et al., 2015	RCT	10 (20)	Liposuction	IV, preoperative+ Postoperative LD (30 mins preop):10 mg/kg+10 mg/kg at the end of surgery	HCT reduction Significantly reduced blood volume in the aspirate Volume of blood per liter of aspirate	None
	Beikai et al., 2015	RCT	48 (96)	Rhinoplasty	IV LD: 10 mg/kg	Significant reduction in blood loss	None

	Sakallioglu et al., 2015	RCT	25 (50)	Open septo-rhinoplasty	Oral, preoperative+ postoperative 1 gr (2h preop), 1 gr every 8 hours x 5d	Significantly reduced IOB, postop peri-orbital edema and postop ecchymosis	None
	Ausen et al., 2015	RCT	28 (56)	B/L reduction mammoplasty	Topical, inoperative, 20 ml (25mg/ml)	Significantly reduced DO No significant difference in pain scores	None
Microsurgery	Lardi et al., 2018	RCS	98	Free tissue transfers for breast reconstruction	IV, up to 3 g TXA	Significantly reduced IOB and hematoma rate No significant difference in flap thrombosis	None
	Valerio et al., 2015	RCS	19 (173)	73 pedicles, 100 free flaps	IV, preoperative, Dose N/A	Non-Significant difference in flap failure rate, flap complications or VTE rate	None

red blood cells, IOB- intraoperative bleeding, Hb- hemoglobin, Hct- hematocrit, LOS- length of stay, SD- surgery duration, NS- non-significant, ERCV- estimated red cells volume, DO- drain output, DVT- deep vein thrombosis, RCT- randomized controlled trial, CP- cleft palate, HCT- hematocrit, SF- surgical field, TBL- total blood loss, POB- postoperative bleeding, N/A- not available

Table 6. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) Evidence

Certainty assessment							№ of patients		Effect		Certainty	
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	[TXA]	[control]	Relative (95% CI)	Absolute (95% CI)		
Craniofacial surgery: IV TXA's effects on blood loss - non-RCTs												
8	observational studies	serious[a]	serious[b]	not serious	not serious[c]	strong association dose response gradient	340	376	-	MD **13.71 lower** (19.42 lower to 8 lower)	⨁⨁◯◯ Low	
Craniofacial surgery: IV TXA's effects on blood loss - RCTs												
2	randomised trials	not serious	serious[d]	not serious	serious[e,f]	dose response gradient	42	40	-	MD **15.68 lower** (28.79 lower to 2.56 lower)	⨁⨁⨁◯ Moderate	
Craniofacial surgery: IV TXA's effects on transfusion requirements - non-RCTs												
8	observational studies	serious[a]	serious[b]	not serious	not serious[c]	dose response gradient	340	376	-	MD **10.25 lower** (16.34 lower to 4.17 lower)	⨁⨁◯◯ Low	
Craniofacial surgery: IV TXA's effects on transfusion requirements - RCTs												
2	randomised trials	not serious	serious[d]	not serious	serious[e,f]	dose response gradient	42	40	-	MD **10.72 lower** (17.41 lower to 4.03 lower)	⨁⨁⨁◯ Moderate	
Cosmetic surgery - TXA's effects on hematoma rates - RCTs												
2	randomised trials	not serious	not serious	not serious	serious[e,f]	dose response gradient	0/55 (0.0%)	2/45 (4.4%)	**OR 0.13** (0.01 to 2.14)	**38 fewer per 1,000** (from 44 fewer to 46 more)	⨁⨁⨁⨁ High	
Cosmetic surgery: TXA's effects on hematoma rates - non-RCTs												
7	observational studies	serious[a]	not serious	not serious	not serious[c]	dose response gradient	10/772 (1.3%)	35/847 (4.1%)	**OR 0.36** (0.16 to 0.79)	**26 fewer per 1,000** (from 34 fewer to 8 fewer)	⨁⨁◯◯ Low	
Cosmetic surgery: TXA's effects on hematoma rates - breast, non-RCTs												
3	observational studies	serious[a]	not serious	not serious	serious[f]	dose response gradient	8/581 (1.4%)	27/667 (4.0%)	**OR 0.42** (0.17 to 1.06)	**23 fewer per 1,000** (from 33 fewer to 2 more)	⨁◯◯◯ Very low	
Cosmetic surgery: TXAs effects on hematoma rates - facelift, non-RCTs												

Certainty assessment							№ of patients		Effect		Certainty	
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	[TXA]	[control]	Relative (95% CI)	Absolute (95% CI)		
3	observational studies	serious[a]	not serious	not serious	serious[f]	dose response gradient	2/131 (1.5%)	8/120 (6.7%)	**OR 0.21** (0.04 to 1.09)	**52 fewer per 1,000** (from 64 fewer to 6 more)	⊕◯◯◯ Very low	
Cosmetic surgery: TXA's effects on blood loss - rhinoplasty, RCTs												
6	randomised trials	not serious	serious[b]	not serious	not serious[c]	dose response gradient	182	184	-	MD **18.97 lower** (22.97 lower to 14.38 lower)	⊕⊕⊕⊕ High	
Cosmetic surgery: oral TXA's effects on blood loss - rhinoplasty, RCTs												
2	randomised trials	not serious	serious[d]	not serious	serious[e,f]	dose response gradient	50	50	-	MD **61.7 lower** (83.02 lower to 40.39 lower)	⊕⊕⊕◯ Moderate	
Cosmetic surgery: IV TXA's effects on blood loss - rhinoplasty, RCTs												
4	randomised trials	not serious	not serious	not serious	serious[e,f]	dose response gradient	132	134	-	MD **17.42 lower** (21.49 lower to 13.35 lower)	⊕⊕⊕⊕ High	
Burn care: TXA's effects on blood loss - RCTs												
2	randomised trials	not serious	serious[b,d]	not serious	serious[e,f]	dose response gradient	40	40	-	MD **196.73 lower** (290.93 lower to 102.53 lower)	⊕⊕⊕◯ Moderate	

CI: confidence interval; **MD:** mean difference; **OR:** odds ratio

Explanations

a. observational methodology
b. Heterogeneity > 50%
c. large number of studies, relatively large sample size
d. Wide confidence interval
e. Small sample size
f. Small number of studies

Table 7. Clinical Recommendations for TXA Administration in Plastic and Reconstructive Surgery

Surgery type	**Most commonly utilized administration regimen**	**Main benefits of TXA administration**	**Certainty evidence**	**Further research directions**
Craniofacial surgery	a bolus of 10 mg/kg TXA followed by continuous infusion of 5 mg/kg/hour	Blood loss reduction Transfusion requirements reduction	Moderate Moderate	Further studies are recommended to determine the ideal time frame for postoperative continuous infusion.
Cosmetic surgery	Variable Variable	Blood loss reduction Hematoma rates	High High	Further studies are recommended to define the ideal administration regimen for each cosmetic procedure.
Rhinoplasty	Preoperative bolus of 10 mg/kg or 1 g TXA 500 mg*2 tablets preoperatively	Blood loss reduction	High Moderate	Further studies are needed to determine the ideal regimen postoperatively for oral administration
facelift	intravenous administration and local infiltration.	Hematoma rates	Very Low	Randomized controlled trials are recommended to determine the utility and ideal TXA administration regimen in facelifts.
Breast-related procedures	intravenous administration and local infiltration.	Hematoma rates	Very Low	Randomized controlled trials are recommended to determine the utility and ideal TXA administration regimen in facelifts.
Burn care	Variable	Blood loss	Moderate	Further studies is needed to determine the ideal TXA administration regimen in burn care.

Figure 1

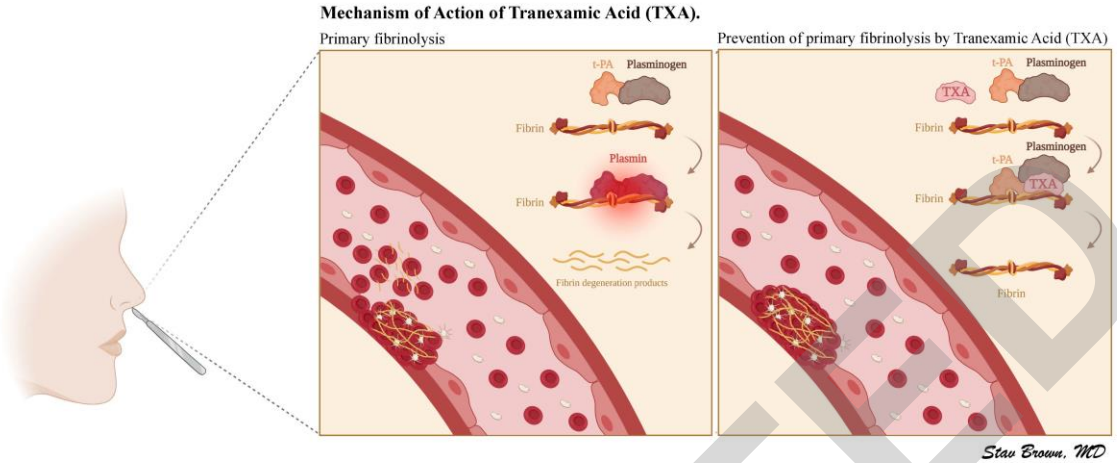
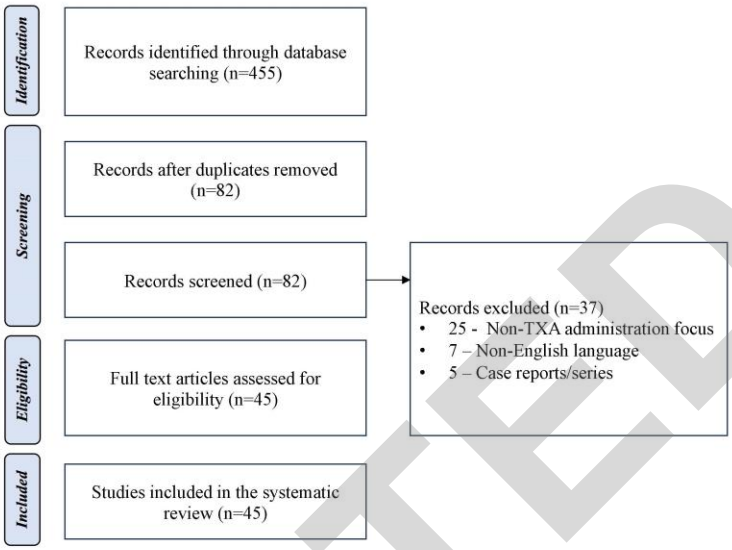
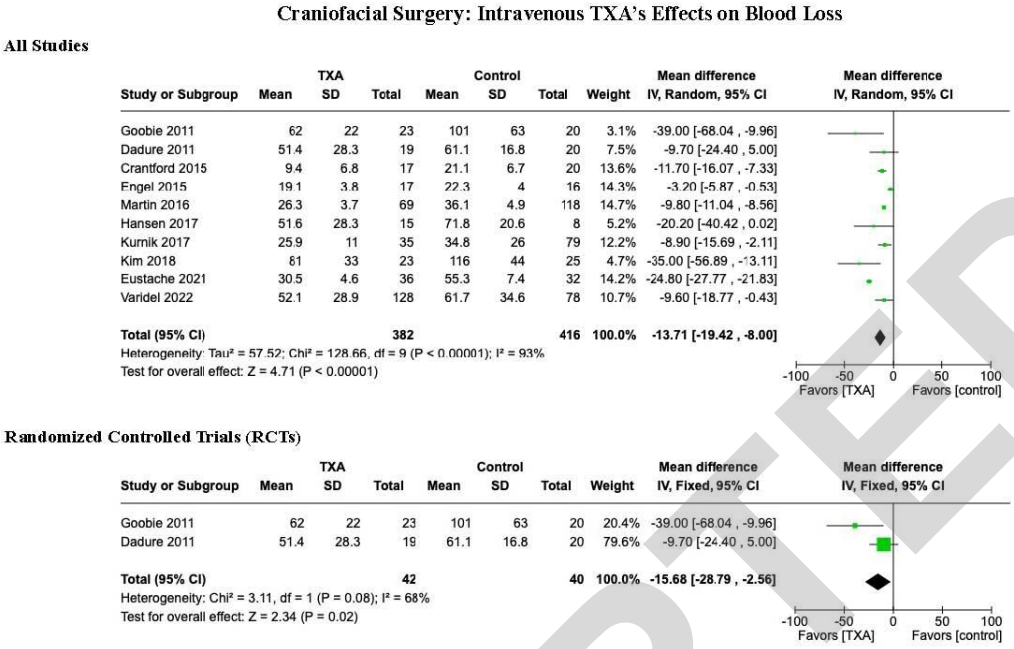


Figure 2. PRISMA Flow Diagram of the Process of Article Selection for the Systematic Review



SDC Figure 1

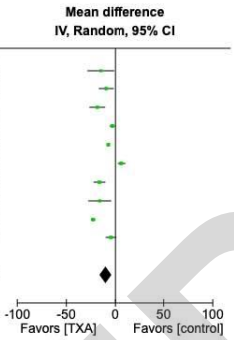


Craniofacial Surgery: Intravenous TXA's Effects on Transfusion Requirements

All Studies

Study or Subgroup	TXA Mean	TXA SD	TXA Total	Control Mean	Control SD	Control Total	Weight	Mean difference IV, Random, 95% CI
Goobie 2011	33	13	23	48	29	20	7.2%	-15.00 [-28.78 , -1.22]
Dadure 2011	7.2	10.8	19	16.6	13.5	20	9.7%	-9.40 [-17.05 , -1.75]
Crantford 2015	12.8	11.7	17	31.3	13.4	20	9.5%	-18.50 [-26.59 , -10.41]
Engel 2015	19.1	3.8	17	22.3	4	16	11.2%	-3.20 [-5.87 , -0.53]
Martin 2016	31.5	5.3	69	38.8	4.3	118	11.4%	-7.30 [-8.77 , -5.83]
Hansen 2017	22.9	3.8	16	16.2	6.1	9	10.8%	6.70 [2.30 , 11.10]
Kurnik 2017	28	11	35	44.3	22	79	10.3%	-16.30 [-22.37 , -10.23]
Kim 2018	49	17	23	65	24	25	8.1%	-16.00 [-27.70 , -4.30]
Eustache 2021	20	3.1	36	42.8	6.1	32	11.3%	-22.80 [-25.14 , -20.46]
Varidel 2022	20.3	17.7	128	25	20.1	78	10.5%	-4.70 [-10.11 , 0.71]
Total (95% CI)			**383**			**417**	**100.0%**	**-10.25 [-16.34 , -4.17]**

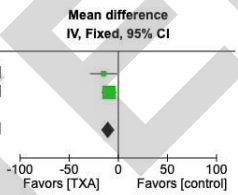
Heterogeneity: Tau² = 84.01; Chi² = 220.24, df = 9 (P < 0.00001); I² = 96%
Test for overall effect: Z = 3.30 (P = 0.0010)



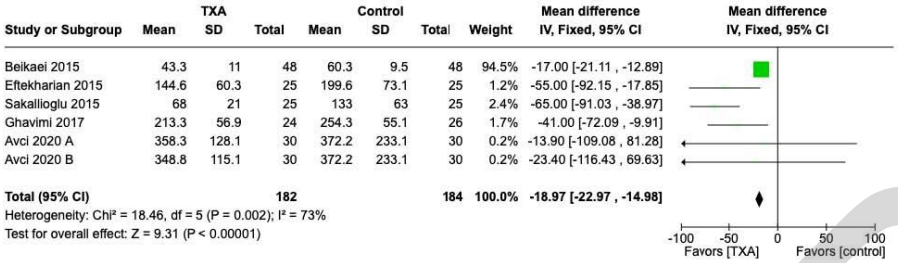
Randomized Controlled Trials (RCTs)

Study or Subgroup	TXA Mean	TXA SD	TXA Total	Control Mean	Control SD	Control Total	Weight	Mean difference IV, Fixed, 95% CI
Goobie 2011	33	13	23	48	29	20	23.6%	-15.00 [-28.78 , -1.22]
Dadure 2011	7.2	10.8	19	16.6	13.5	20	76.4%	-9.40 [-17.05 , -1.75]
Total (95% CI)			**42**			**40**	**100.0%**	**-10.72 [-17.41 , -4.03]**

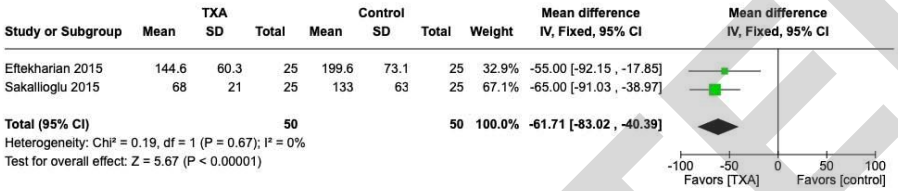
Heterogeneity: Chi² = 0.49, df = 1 (P = 0.49); I² = 0%
Test for overall effect: Z = 3.14 (P = 0.002)



Rhinoplasty: Randomized Controlled Trials (RCTs)

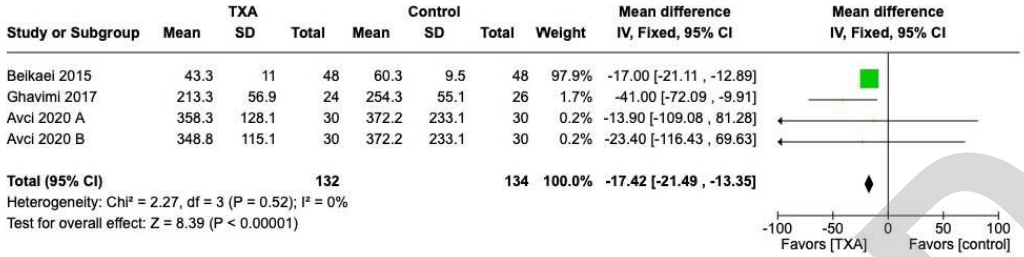


Rhinoplasty: Randomized Controlled Trials (RCTs), Oral TXA



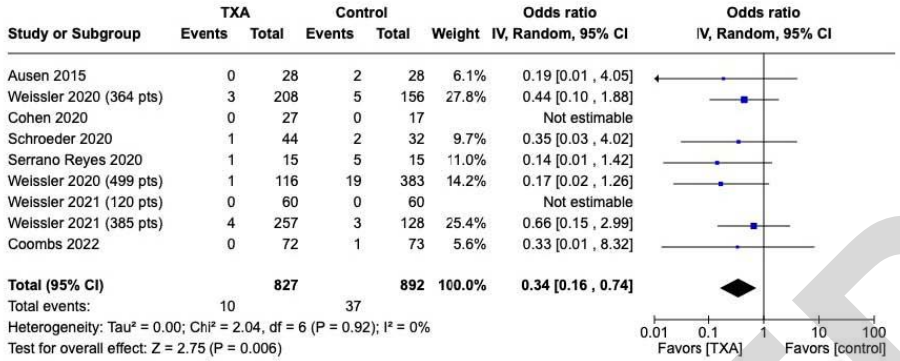
Cosmetic Surgery: TXA's Effects on Blood Loss

Rhinoplasty: Randomized Controlled Trials (RCTs), Intravenous TXA



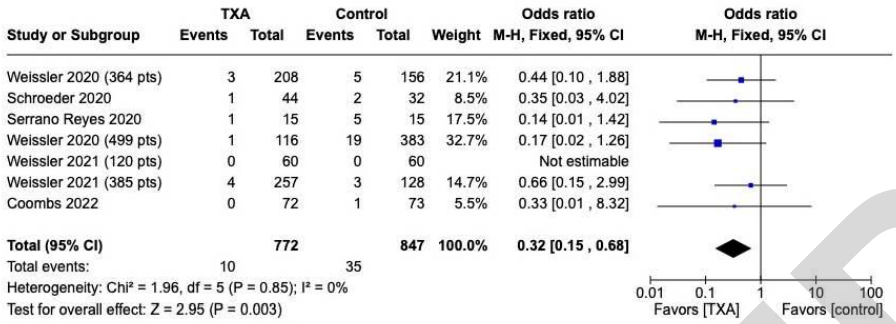
All Studies

Cosmetic Surgery: TXA's Effects on Hematoma Rates



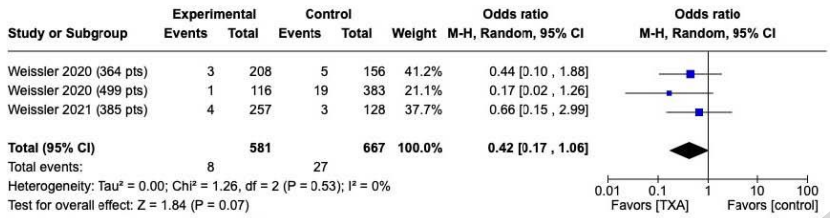
Cosmetic Surgery: TXA's Effects on Hematoma Rates

Randomized Controlled Trials (RCTs)

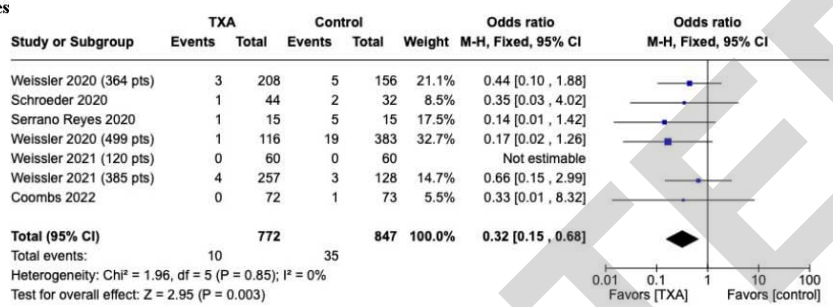


Cosmetic Surgery: TXA's Effects on Hematoma Rates

Facelift

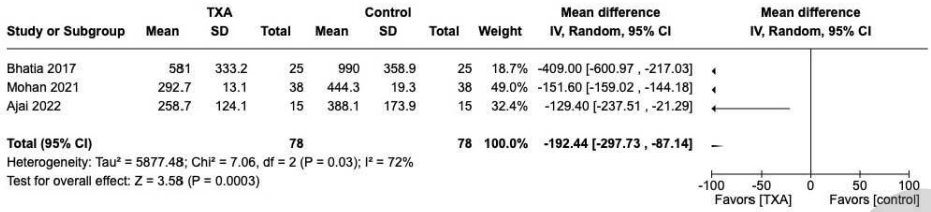


Breast Procedures



Burn Surgery: TXA's Effects on Blood Loss

All Studies



Randomized Controlled Trials (RCTs)