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Efficacy and Safety Profile of Tranexamic Acid in Traumatic Thoracolumbar Fracture Management: A Systematic Review and Meta-Analysis

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ABSTRACT

Objective: In this article, the authors systematically evaluated the efficacy and safety of tranexamic acid (TXA) in surgeries for spinal trauma.

Methods: Potentially relevant academic articles were identified from the Cochrane Library, MEDLINE, PubMed, and Google Scholar. Secondary sources were identified from the references of the included literature. RevMan software was used to analyze the pooled data.

Results: A total of 7 randomized controlled trials (RCTs) and 2 non-RCTs were included in the review. There were significant differences in total blood loss (standard mean difference [SMD] = −2.54 [95% CI, −3.72, −1.37], $P = 0.0001$), intraoperative blood loss (SMD = −0.96 [95% CI, −1.28, −0.64], $P < 0.00001$), postoperative blood loss (SMD = −1.42 [95% CI, −1.72, −1.11], $P < 0.00001$), and length of hospital stay (SMD = −3.73 [95% CI, −4.41, −3.06], $P = 0.00001$). No significant differences were found regarding transfusion requirement, operative duration, deep vein thrombosis, and pulmonary embolism between the 2 groups.

Conclusions: The present meta-analysis indicates that the use of TXA in spinal surgery decreases blood loss and duration of hospital stay while not increasing the risk of side effects such as deep vein thrombosis and pulmonary embolism.

Clinical Relevance: The study aims to provide clinicians who operate on spine trauma with information on the use of tranexamic acid to decrease blood loss and related complications.

Level of Evidence: 1.

Other and Special Categories

Keywords: tranexamic acid, spine, blood loss, transfusion, spine trauma, meta-analysis

INTRODUCTION

Multilevel spine surgery is known to involve blood loss, although the exact definition of significant loss is unclear.[1] Bleeding in spine trauma surgery can occur from the dissected paraspinal muscles, fractures, bone surfaces that have been stripped of periosteum, as well as epidural bleeding following laminectomy.[2] The consequences of this blood loss remain uncertain, although the complications of consequent blood and blood product transfusions are well known. These can include transfusion-related acute lung injury, coagulopathy, immune system depression, and even increased infection rates.[1,2]

Multiple strategies to reduce blood product–related complications in spine surgery have been used, including autologous blood predonation, preoperative erythropoietin use, antifibrinolytics, and intraoperative cell saver technology.[1]

Antifibrinolytics have been used in spine surgery to minimize blood loss.[3] Aprotinin and epsilon aminocaproic acid were noted to be less effective compared with tranexamic acid (TXA) in terms of total blood loss (TBL) and transfusion rates.[4] TXA is a synthetic antifibrinolytic and competitively blocks the lysine-binding sites of plasmin, tissue plasminogen activator, and plasminogen. This retards fibrinolysis and hence clot degradation, thereby decreasing blood loss.[5] It has been used to reduce the need for blood transfusions for more than a decade, and its safety and efficacy in trauma patients have been established.[6–8]

In patients with normal renal function, the half-life of TXA is 80 minutes, with recommendations of a broad range of doses in published literature.[5,9] It is predominantly excreted unchanged in the urine, and dose modification should be considered in renal impairment.[10,11] TXA in spine surgery is administered via topical, oral, and intravenous routes, although optimum doses are

still uncertain.[5,12] Intravenous tranexamic acid (iTXA) is the most commonly used route for administration with a recommended dose of 10 to 20 mg/kg bolus followed by a 1 mg/kg/h infusion, although multiple other regimens are also used in clinical practice.[5,9,11] The dose of topical tranexamic acid (tTXA) is more variable and likely represents the heterogeneous surgical wounds across orthopedic and neurosurgical specialties, ranging between 1 and 3 g dissolved in saline. This is typically placed in the wound before wound closure.[9,13]

The most feared complication of iTXA is an increased risk of thrombotic events. Although there is a general apprehension that TXA may increase thrombogenicity, the literature does not reveal a significant increase in thrombotic events, such as deep vein thrombosis (DVT) and pulmonary embolism (PE), with most events being anecdotal and sparse.[3,5,7,9,11,14] Seizures are another complication that is thought to arise from the blood-brain barrier penetration of TXA and may be due to glycine and GABA receptor inhibition, as well as possible cortical ischemia.[10,15] Seizures are mainly reported to occur with high doses and have an incidence of 2.7%.[9,10,16] The other complications of TXA include gastrointestinal manifestations, dermatitis, and visual disturbances.[10]

tTXA is theoretically poised to avoid these complications due to a lesser systemic penetration.[17] However, a very real possibility in spine trauma patients is the inadvertent entry of TXA into the intrathecal space during topical application. A recent review of 21 cases of accidental intrathecal administration of TXA revealed seizure activity in all patients along with cardiac events leading to a mortality of almost 50%.[15] Cardiac events such as arrhythmia may be secondary to massive sympathetic discharge during seizure activity.[15] Whether TXA penetrates through intact dura mater is an interesting question. A study on TXA-soaked gelatin sponges placed epidurally postlumbar laminectomy did not show any increase in TXA-related complications, perhaps indicating poor penetration through intact dura, although further studies are needed to establish this beyond doubt.[18]

The use of TXA is established in spine deformity surgery and spine malignancies.[9] Studies have shown its cost-effectiveness, making it a useful tool in the spine surgeon's armamentarium.[19,20] However, there is a paucity of literature involving the use of TXA in the operative management of spine fractures. This systematic review with meta-analysis was designed to understand the efficacy and safety of both intravenous as well as tTXA in the reduction of blood loss during surgery for traumatic fractures of the thoracolumbar spine.

METHODS

Search Strategy

A systematic search for published studies was performed on MEDLINE, the Cochrane Library, PubMed, and Google Scholar up to 15 December, 2020. Currently registered trials were searched on the following platforms: ClinicalTrials.gov (US National Institutes of Health), International Standard Randomized Controlled Trial Number, Chinese Clinical Trial Register, and EU Clinical Trials Register. MEDLINE, PubMed, and the Cochrane Library were searched using the MeSH terms "tranexamic acid" and "spinal fractures." The search terms "tranexamic acid" (including TXA, tTXA, iTXA, topical TXA, and intravenous TXA), "thoracolumbar fractures," and "spine fractures" or "spinal fractures" were also used in various combinations along with their synonyms and the Boolean operators AND and OR. Study selection was restricted to studies on humans and those published in the English language. Reference lists were also examined manually to identify any initially omitted articles.

Inclusion and Exclusion Criteria

Inclusion criteria were used to identify studies that (1) focused on adult patients undergoing surgery of any type for thoracolumbar spine trauma, (2) assessed TXA as an independent variable in the achievement of hemostasis of spine trauma surgeries, and (3) provided outcome measures to assess perioperative blood loss or blood transfusions. In studies on pediatric patients, only nontrauma diagnoses as well as case reports and case series with less than 10 participants were excluded. The study was designed based on the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines.

Data Extraction

Three independent reviewers manually performed data extraction (S.T., K.P., and L.R.) and analysis of published studies as well as current registered clinical trials. Any disagreement was solved by discussion or decision by the senior author (S.R.). The following data were extracted:

1. Demographic data: first author, country, published year, sample size, mean age, gender, and study design

2. Surgical/intervention data: surgical approach, dose and route of TXA administration
3. Surgical outcomes including TBL, postoperative blood loss (PBL), hidden blood loss (HBL), intraoperative blood loss (IBL), operation duration, transfusion rates, and postoperative complications. Other relevant data were also extracted from individual literature when necessary.

From the protocols of registered clinical trials, data were extracted according to the PICOS framework as well as inclusion and exclusion criteria.

Quality Assessment

Quality assessment was performed by 2 authors (S.T. and K.P.) using the RoB-2 tool for randomized studies as per the Cochrane Handbook for Systematic Review of Interventions and the methodological index for non-randomized studies tool for nonrandomized trials.[21,22] Publication bias was assessed using a funnel plot.

Data Analysis and Statistical Methods

Data analysis was performed using RevMan (Review Manager, version 5.4; The Cochrane Collaboration, 2020). Statistical heterogeneity was assessed using the I^2 statistic as well as the standard χ^2 statistic. $I^2 > 50\%$, $P < 0.1$ was considered to imply significant heterogeneity, and the random effects model was used for analysis.[23] A sensitivity analysis was conducted where necessary. Dichotomous outcomes were expressed the risk difference (RD) with 95% CIs while, for continuous outcomes, the weighted mean differences or mean differences (MD) and 95% CIs were calculated. Statistical significance was defined as $P < 0.05$.

RESULTS

Search Results

A total of 856 literature sources were reviewed. Of those articles, 314 were rejected due to duplication. After scanning titles, abstracts, and full texts as necessary, an additional 533 articles were rejected based on relevance to the topic as well as inclusion/exclusion criteria. Nine articles were included for the systematic review, and all but a single article were included for the meta-analysis due to lack of clarity in reported outcomes.[24] Of these, 7 were prospective randomized trials, 1 was a retrospective cohort study, and 1 prospective observational study.[24–32] Combined, the total participant strength was 828 patients. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram is shown in Figure 1. The demographic characteristics and details are presented in Table 1. Of the 155 registered clinical trials matching our search criteria, only 2 RCTs were identified and are represented in Table 1.[33,34]

Risk of Bias Assessment

Two of the studies did not provide clear inclusion and exclusion criteria. Risk of bias analysis was performed for the randomized as well as nonrandomized studies and is displayed in Figure 2. Of the randomized studies, randomization was performed using random number generation in 2 studies, block randomization in 2 studies, and not mentioned in the others. Sealed envelope allocation concealment was reported in 3 studies, and 1 study reported only single blinding. Only 1 study reported assessor blinding. All studies reported complete outcome data. Methodological index for nonrandomized studies scores for the nonrandomized studies were 14 and 15 (Table 2).[29,30] Publication bias for IBL was assessed using a funnel plot and is displayed in Figure 3.

Study Characteristics

Completed Studies

The demographics, intervention, and study designs of the included studies are mentioned in Table 1. The surgeries performed included open pedicle screw fixation (PSF) in 5 studies, paraspinal Wiltse approach and PSF in 1 study, open PSF with interbody fusion in 1 study, percutaneous PSF in 1 study, and 1 study did not mention the type of surgery.

The study published by Garg et al was published as an abstract employing a prospective randomized trial on 52 participants and looked at the effect of a bolus dose of iTXA on blood loss.[24] However, as their blood loss statistics lacked SDs and transfusion statistics were not clear, the study was not included in the meta-analysis. Hamdi et al also published an abstract detailing their prospective randomized study on the effect of TXA on patients undergoing surgeries for spine trauma.[25]

The study by Wang et al[29] involved a comparison of different doses of iTXA to placebo. Therefore, the 2 different doses were used as 2 different studies: Feng (A) comparing intra- and postoperative iTXA to placebo and Feng (B) comparing intraoperative iTXA alone to placebo. They noted that iTXA decreases
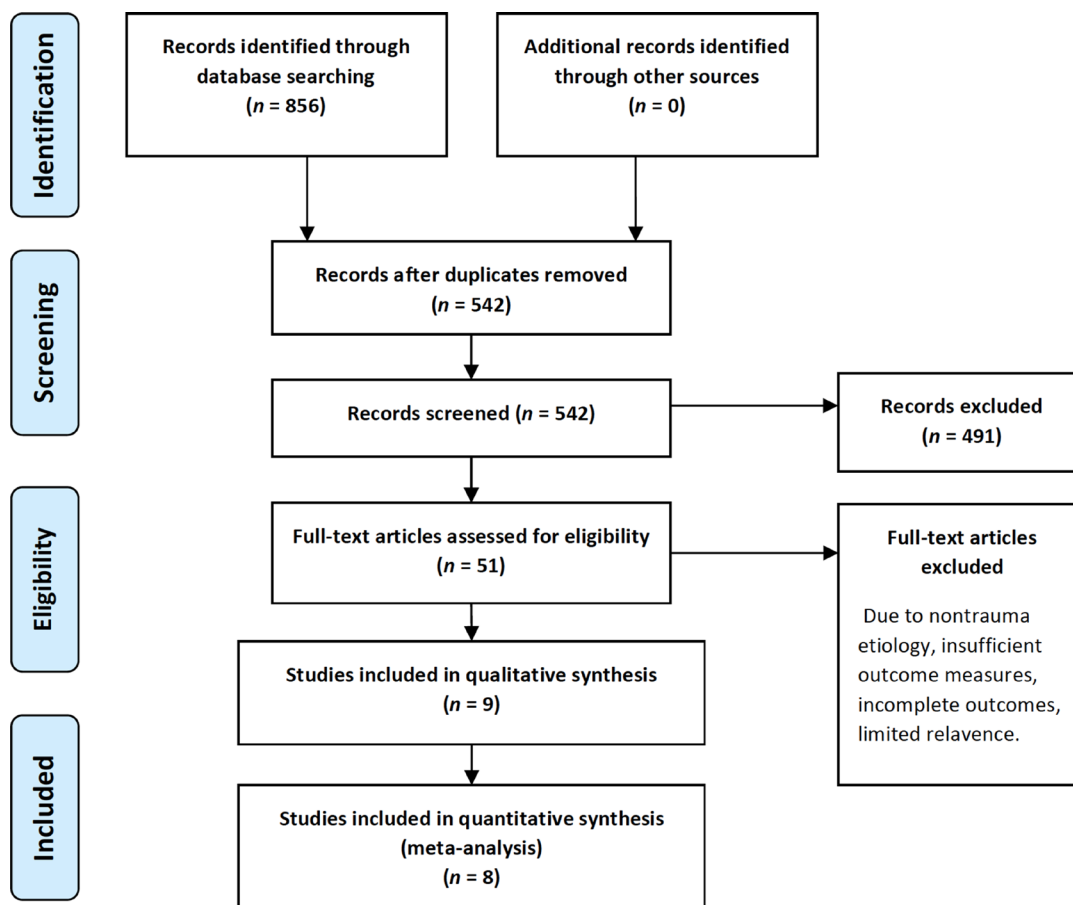
Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram.

blood loss, with multiple doses further reducing the blood loss.[29]

Wang et al[27] published a study comparing intravenous, topical, and combined iTXA and tTXA and their effects on blood loss. Although the study did not compare values to placebo, statistics were extracted and compared with either the topical or intravenous group as a control for the operative duration and HBL. They eventually concluded that while iTXA effectively decreases blood loss, tTXA does not.[27]

Registered Trials

The details of the 2 selected trials are represented in Table 1. Lehman et al have described their study looking into the effect of tTXA on blood loss and focus on important secondary outcome measures such as wound infection rates, cost analysis, and impact on quality of life.[34] Sheng et al detailed in their protocol a randomized single-blinded study comparing the effect of iTXA and tTXA to placebo in patients undergoing open PSF surgeries.[33]

Outcomes for Meta-Analysis

Total Blood Loss

TBL was reported in 3 studies with a total of 4 groups.[28,29,31] A random effects model was used due to significant heterogeneity ($I^2 = 96\%$, $P < 0.00001$). A significant effect was noted in terms of TBL (standard mean difference [SMD] = −2.54 [95% CI, −3.72, −1.37], $P = 0.0001$) (Figure 1). No significant difference was noted on performing leave-one-out sensitivity analysis (Figure 4).

Intraoperative Blood Loss

IBL was reported in 6 studies with a total of 481 patients.[25,26,28–31] Two studies used tTXA, and 4 studies used iTXA. As heterogeneity was significant ($I^2 = 81\%$, $P < 0.0001$), random effects model was used. Overall analysis showed a significant positive impact of TXA over placebo (SMD = −0.96 [95% CI, −1.28, −0.64], $P < 0.00001$) (Figure 5A). However, these results must be interpreted with caution as one of the studies used TXA at the end of the intraoperative period and may not have

Table 1. Studies included in the qualitative and quantitative synthesis.

Study	Country	Study Type	Surgical Method	Groups	Age, y, Mean ± SD	Gender M:F	TXA Dosing	Inclusion Criteria	Exclusion Criteria	Outcome Measures
Garg 2012[24]	India	Prospective, randomized	Open posterior instrumentation	Intervention, Control	Not mentioned	Not mentioned	15 mg/kg bolus IV, 15 min before incision	Not mentioned	Not mentioned	IBL, PBL, number of blood transfusions, DVT incidence, and D-D
Hamdi 2016[25]	Tunisia	Prospective, randomized	Not mentioned	Intervention, Control	48.4 ± 16.2, 54.4 ± 13.7	17:8, 15:10	10 mg/kg bolus IV, 1 mg/kg/h IV intra- and postoperatively	Not mentioned	Not mentioned	IBL, PBL, number of blood transfusions, DVT incidence, and D-D
Weera 2019[26]	Thailand	Prospective, randomized	Open long-segment PSF without decompression	Intervention, Control	52 (33.5, 55.5), 51.5 (33.5, 58)	20:9, 15:13	1 g in 20 mL saline topical application via drain, clamped for 2 h	Adults with thoracolumbar fractures undergoing posterior fixation surgery, no neurological deficits, ASA I, II, III	History of thromboembolic/cardiac disease, coagulation disorder displaced laminar fractures	Transfusion rates, PBL, drain removal time, duration of hospitalization
Xiji 2019[27]	China	Prospective, randomized, single blinded	Percutaneous pedicle screw fixation	Intervention A, Intervention B, Intervention C	45.43 ± 8.18, 45.72 ± 9.96, 45.47 ± 11.24	34:27, 37:24, 33:26	Group A: 15 mg/kg bolus IV, 30 min before incision, Group B: topical 3 g in saline before wound closure, Group C: combined IV + topical as above	Adults with single-level thoracolumbar fractures with no neurological deficits undergoing surgery within 2 wk of injury	History of DVT, intake of antiplatelet/anticoagulant medications, multiple injuries	Pre- and postoperative: Hct, D-D; DVT in lower limbs, transfusion rate, complications, operative duration, IBL, TBL, HBL
Wentao 2019[28]	China	Prospective, randomized, double blinded	Open PSF with transforaminal interbody fusion	Intervention, Control	41.2 ± 10.3, 42.5 ± 9.5	25:18, 18:19	10 mg/kg bolus IV, 15 min before incision, 1 mg/kg/h infusion during surgery	Adult patients with fracture dislocation at the thoracolumbar junction undergoing surgery within 24 h for	Involved segments above T11 or below L2, on anticoagulation, any contraindication to TXA use, severe injuries, CSF leakage	Operative duration, TBL, IBL, Hb, transfusion rate, DVT incidence, levels of pre- and postoperative GMP 140, FIB, FDP, and D-D
Feng 2020[29]	China	Retrospective cohort	PSF using Wiltse approach	Intervention A, Intervention B, Control	42.14 ± 9.86, 40.34 ± 10.28, 41.06 ± 10.26	60:24, 57:30, 63:30	Group A: 20 mg/kg TXA at 5 min before skin incision and 16 h after first dose; Group B received 20 mg/kg TXA at 5 min before skin incision	2-level involvement Adults with single segment fractures without neurological deficits who underwent surgery using the Wiltse approach and other conservatively managed fractures	Pelvic and femoral fractures, cardiac/CNS disease, intake of medication that alter hemostasis	Pre- and postoperative: Hb, FDP, D-D, FIB, Hct, PT-INR, APTT, CRP, IL-6; DVT in lower limbs, transfusion rate, complications, operative duration, IBL, TBL, HBL
Pradhan 2015[30]	Nepal	Prospective, observational	Open PSF	Intervention, Control	39.47 ± 13.52, 32.19 ± 10.71	Not mentioned	10 mg/kg bolus IV, 30 min before incision and 3 h postoperatively + oral medication	Adults undergoing single-level PSF	2-Level surgeries, fracture level screw fixation, iliac crest graft	Pre- and postoperative Hb, PT-INR, transfusion rates, operative duration, IBL, PBL, complications

Table 1. Continued.

Study	Country	Study Type	Surgical Method	Age, y, Mean ± SD	Gender M:F	TXA Dosing	Inclusion Criteria	Exclusion Criteria	Outcome Measures
Jieliang 2020[31]	China	Prospective, randomized, double blinded	Open PSF	38.85 ± 4.17, 39.41 ± 6.51	25:14, 22:15	1 g in 100 mL saline topical application in the wound postmuscle dissection, kept for 5 min	Adults with single-level thoracolumbar fractures with/without neurological deficits undergoing surgery within 24 h of injury without osteoporosis	Multiple comorbidities, multiple fractures, coagulopathies, CSF leakage, pathological fractures	TBL, HBL, IBL, PBL, HB, Hct, transfusion rate, length of hospital stay, operative duration
Abdel 2020[32]	Egypt	Prospective, randomized, double blinded	Open PSF	52 (33.5, 55.5), 51.5 (33.5, 58)	7:8, 4:11	1 g in 50 mL saline topical application via drain, clamped for 2 h	Adults with thoracolumbar fractures without neurological deficits	Renal insufficiency, history of thromboembolism, history of cardiovascular diseases, coagulopathies, allergy to TXA, history of aspirin or NSAID intake 1 wk before randomization	Pre- and postoperative Hb, PBL
Lehman et al[34]	United States	Prospective, randomized, double blinded				3 g TXA in 70 mL saline topical solution left in wound for 5 min vs saline placebo	Adult thoracolumbar spine trauma with/ without deficits undergoing surgery within 21 d; adult patients undergoing long-segment fusions (>5 fusion levels)	Coagulopathies or history of thromboembolic events; therapeutic anticoagulation requirement; use of intravenous TXA during prestudy period; trauma penetrating spinal cord or dural tears; history of seizure; traumatic brain injury	Primary outcome: maximal postoperative Hb drop, secondry outcomes: Health related quality of life, complications, cost analysis, surgical site infection, systemic absorption
Sheng et al[33]	China	Randomized controlled trial, single blinded				Group 1: intravenous TXA 10 mg/kg before incision; Group 2 topical TXA 10 mg/kg wash before wound closure; Group 3: saline placebo	Adult thoracolumbar spine trauma with no coagulopathy undergoing surgery within 2 wk	Low Hb or platelet counts or preoperative coagulopathy; has received antiplatelet/ coagulant therapy; hypercoagulable states or history of thromboembolism	Primary outcome: IBL; secondary outcome: blood transfusion, PBL, Hb, PT-INR, D-D, and APTT

Abbreviations: APTT, activated prothrombin time; CSF, cerebrospinal fluid; D-D, D-dimer; DVT, deep vein thrombosis; FDP, fibrinogrn degeneration products; FIB, fibrinogrn intermediate products; Hb, hemoglobin; HBL, hidden blood loss; Hct, hematocrit; IBL, intraoperative blood loss; IV, intravenous; NSAID, non-steroidal anti-inflammatory drugs; PBL, postoperative blood loss; PE, pulmonary embolism; PSF, pedicle screw fixation; PT-INR, prothrombin time-international normalized ratio; TBL, total blood loss; TXA, tranexamic acid.

substantially affected the IBL; thus leave-one-out analysis was performed.[26] Heterogeneity was reduced to I^2 = 70% (P = 0.009) when the study by Weera et al was left out (Figure 5B). Subgroup analysis revealed significant heterogeneity was contributed predominantly by the tTXA group (I^2 = 95%, P < 0.00001). There was no significant heterogeneity in the iTXA group (I^2 = 43%, P = 0.15), whereas the tTXA group showed significant heterogeneity (I^2 = 95%, P = 0.00001).

Postoperative Blood Loss

PBL was reported by 6 studies with a total of 331 patients[25, 26,28,30–32] Random effects model was used (I^2 = 34%, P = 0.18). The overall effect of TXA on PBL was significant (SMD = −1.42 [95% CI, −1.72, −1.11], P < 0.00001) (Figure 6).

Hidden Blood Loss

HBL was reported by 5 groups in 4 studies.[27–29,31] The random effects model was used due to significant heterogeneity (I^2 = 91%, P < 0.00001), which showed a significant positive effect (SMD = −1.11 [95% CI, -1.70,–0.51], P = 0.0003) (Figure 7).

Hemoglobin Levels

Hemoglobin levels were reported by 4 studies.[26,30–32] The random effects model was used, which showed a significant difference in postoperative hemoglobin (mean difference [MD] = 1.03 [95% CI, 0.77, 1.29], P = 0.00001) (Figure 8).

Operative Duration

Operative Duration With Use of tTXA

Operative duration was reported by 3 studies.[26,27,31] Random effects model was used due to significant heterogeneity (I^2 = 96%, P < 0.00001). Pooled analysis showed a nonsignificant effect on operative duration overall (SMD = −0.54 [95% CI, −1.85, 0.77], P = 0.42). However, leave-one-out sensitivity revealed that excluding Jieliang 2020 from the analysis reduced the heterogeneity (I^2 = 43%, P = 0.18), although the effect remained nonsignificant (SMD = 0.15 [95% CI, −0.26, 0.56], P = 0.48) (Figure 9A and B).

Operative Duration with Use of iTXA

Operative duration was reported in 4 studies.[27–30] Heterogeneity was noted to be significant, hence random effects model was used (I^2 = 88%, P < 0.001). There was no significant change in operative duration (SMD = −0.29 [95% CI, −0.90, 0.32], P = 0.35). Leave-one-out sensitivity analysis revealed that excluding Wentao 2018 reduced the heterogeneity to I^2 = 59%, P = 0.09 with the overall effect still being nonsignificant (SMD = −0.01 [95% CI, −0.38, 0.35], P = 0.95) (Figure 10A and B).

Transfusion Rate

Although 1 study reported transfusion rates, 2 different sets of values were reported and due to a lack of clarity, its results were not included in the meta-analysis.[24] A total of 5 groups were included from 4 studies with a total of 528 patients.[26,29–31] The random effects model was used as there was significant heterogeneity (I^2 = 62%, P = 0.03). There was no significant difference in the number of patients requiring transfusion (risk difference [RD] = −0.05 [95% CI, −0.11, 0.02], P = 0.17) (Figure 11).

Length of Hospital Stay

Only 2 studies reported hospital stay, and both studies used tTXA.[26,31] The random effects model was used (I^2 = 0%, P = 0.66), revealing a significant difference in length of hospital stay (MD = −3.73 [95% CI, −4.41, −3.06] P = 0.00001) (Figure 12).

Incidence of DVT

Incidence of DVT was reported in 6 studies.[25,26,28–31] Random effects model was used (I^2 = 0%, P = 1.00). The effect of TXA on the incidence was not noted to be significant (RD = −0.01 [95% CI, −0.03, 0.02], P = 0.60) (Figure 13).

Incidence of PE

The incidence of PE was reported in 4 studies.[26,28–30] Random effects model was used (I^2 = 0%, P = 1.00). The effect of TXA on the incidence was not noted to be significant (RD = −0.00 [95% CI, −0.01, 0.01], P = 0.99) (Figure 14).

DISCUSSION

Overall Assessment

To our knowledge, this is the first meta-analysis looking into the efficacy and safety of the use of TXA in traumatic spine injuries, specifically thoracolumbar fractures. The CRASH trials have established that TXA can be used in the setting of trauma without a significant increase in prothrombotic events.[7,8] TXA may have a positive effect on decreasing blood loss, although its
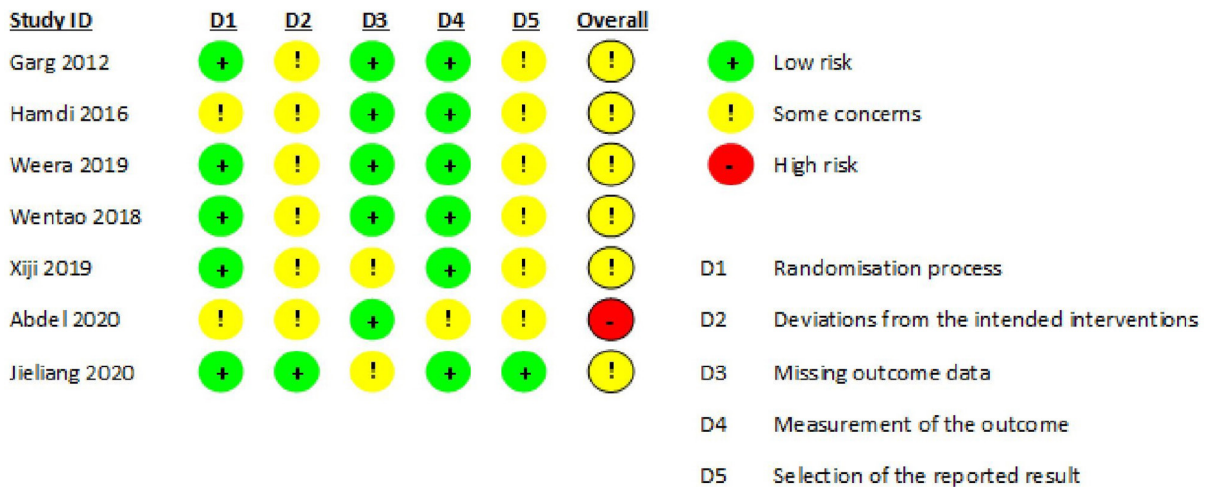
Figure 2. Risk of bias table generated using the RoB-2 tool.

effects on rates of blood transfusion are uncertain. Its use is not associated with an increased risk of specific adverse effects.

Dosing of iTXA and tTXA is a controversial issue, with variable recommendations in different studies.[5] Although the commonly used intravenous dosage is 10 mg/kg bolus followed by 1 mg/kg/h during the study, multiple studies only use bolus doses while tTXA dosage suffers from an even higher variability.[9] Only 2 studies included in our meta-analysis used a continuous infusion of TXA, while others used bolus doses. Wang et al compared 2 different dosing regimens and concluded that higher/multiple bolus dosing may lead to decreased overall blood loss, although transfusion rates did not appear to be significantly altered.[29] Further,

well-designed studies on the effect of timing and different doses of TXA are required.

The variability in the surgical method used in the individual studies itself leads to some bias in this analysis as they have different rates of blood loss. Xiji et al have tried to understand the effect of TXA on percutaneous PSF and concluded that iTXA can reduce IBL and TBL even though none of their patients required a transfusion.[27] However, the importance of blood loss in percutaneous PSF is not clear, and more studies are needed to corroborate this finding and its clinical significance.

Blood Loss

In our review, the pooled analysis revealed that TXA makes a significant difference in blood loss in terms of TBL, IBL, PBL, and HBL. This is in keeping with

Table 2. Nonrandomized studies evaluated for bias using the MINORS criteria.

	MINORS Criteria	Pradhan 2015	Feng 2020
1	Clearly stated aim	2	2
2	Inclusion of consecutive patients	0	0
3	Prospective collection of data	2	0
4	Endpoints appropriate to aim of study	2	2
5	Unbiased assessment of the study endpoint	0	2
6	Follow-up period appropriate to the aim of the study	1	1
7	Loss to follow-up less than 5%	0	0
8	Prospective calculation of study size	0	0
9	An adequate control group	2	2
10	Contemporary groups	2	2
11	Baseline equivalence of groups	2	2
12	Adequate statistical analysis	1	2
	Total	14	15

Abbreviation: MINORS, methodological index for nonrandomized studies.
Note: The items are scored 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate). The global ideal score is 16 for non-comparative studies and 24 for comparative studies
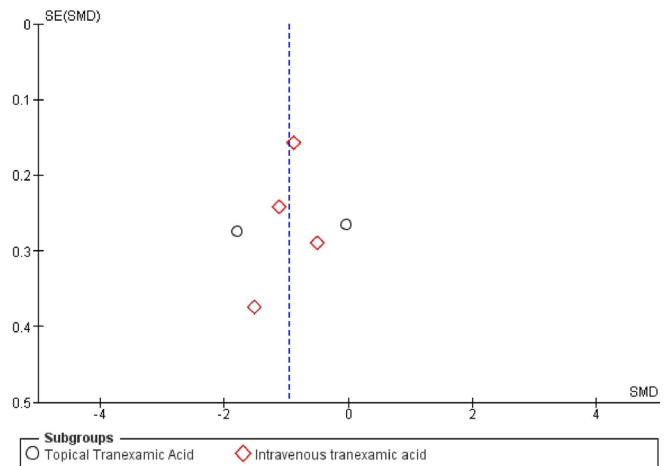

Figure 3. Funnel plot of intraoperative blood loss demonstrating publication bias. SE, standard error; SMD, standard mean difference.
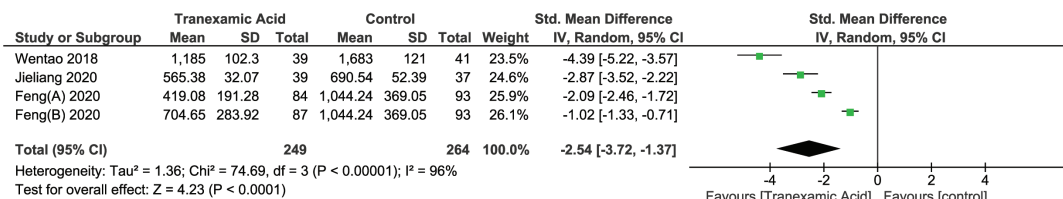
Figure 4. Forest plot showing the effect of tranexamic acid on total blood loss.

conclusions drawn by other studies that have analyzed the effect of TXA in spine surgeries in general.[9,13,14] Although this is reassuring, it must also be taken into consideration that there were significant heterogeneities present, which may affect the results.

The analysis of the effect of TXA on IBL bears some inspection. Although iTXA uniformly reduced IBL, tTXA only reduced IBL in 1 of the 2 studies, where it was used at an earlier point in the surgery than normally used, that is, just before wound closure.[9,31] More studies are desirable to look into the optimum timing of administration of tTXA. Furthermore, blood loss is known to vary based on the surgical approach being used, which may have also contributed to the heterogeneity seen in this meta-analysis.[35,36] The statistics

for TBL and HBL must be taken with caution as these are both calculated estimations, which may be prone to errors. There were also some variations in the formula used in these calculations in each of the studies.

However, there was no significant change in the rates of transfusion. Nellipovitz et al stressed that blood loss is only useful as a surrogate outcome for transfusion requirements and that estimation of blood loss can be imprecise.[5] The lack of effect on blood transfusion rates in our meta-analysis is interesting but in accordance with the variable results in other studies.[4,37–40] Of the 5 studies that reported blood transfusions, only 3 reported specific criteria for transfusions, the variability of which may have contributed to the heterogeneity of results. There are other factors that may influence
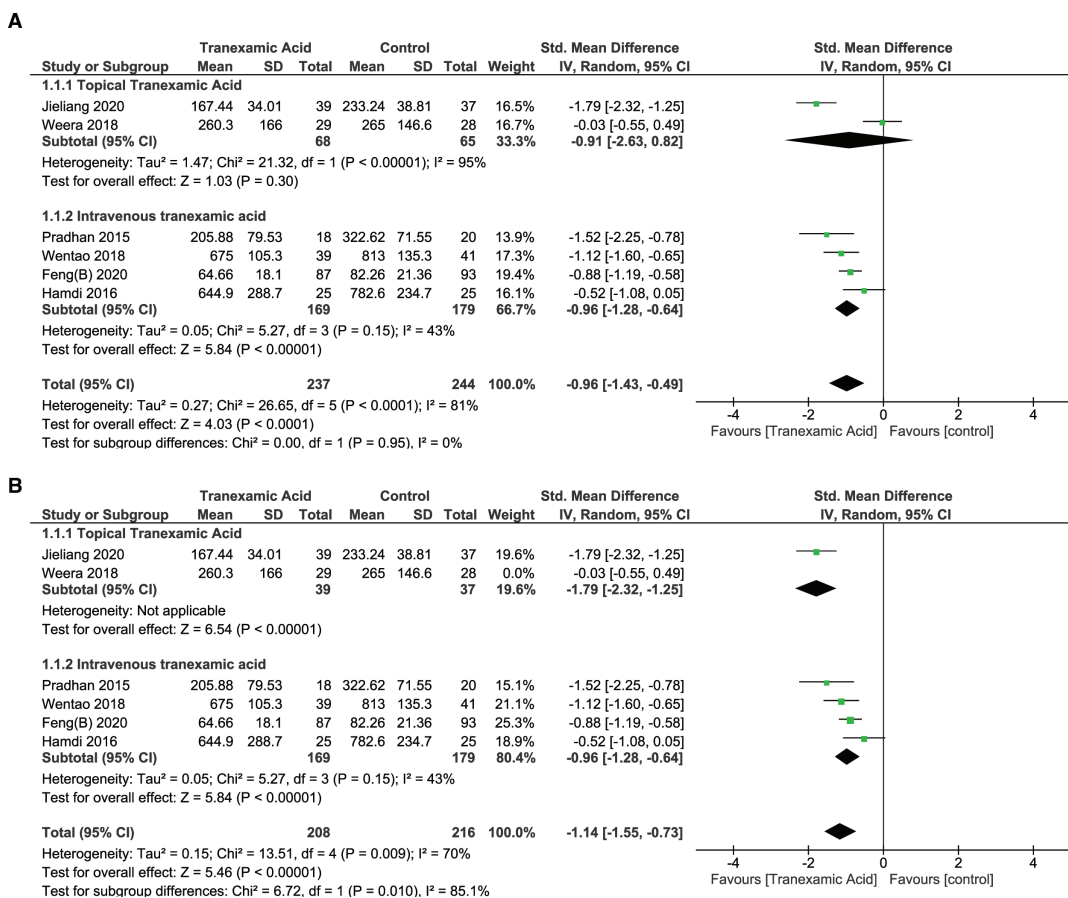
Figure 5. (A) Forest plot showing the effect of tranexamic acid (TXA) on intraoperative blood loss. (B) Forest plot showing the effect of TXA on intraoperative blood loss after leave-one-out analysis and exclusion of Weera 2018.
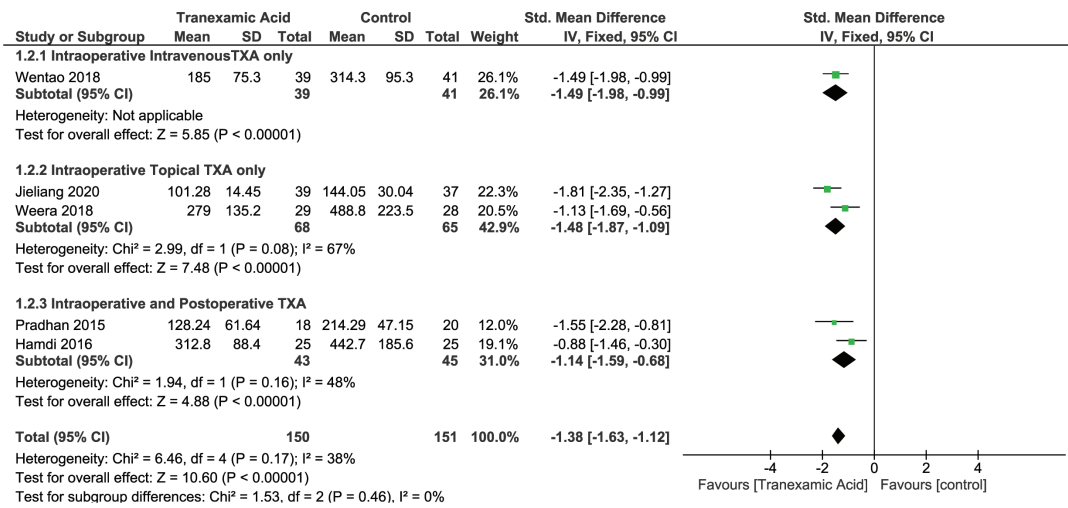
Figure 6. Forest plot showing effect of tranexamic acid on postoperative blood loss.

blood loss in these trauma patients, including poly-trauma, disseminated intravascular coagulation, and prior use of antiplatelet or anticoagulant medication. In this analysis, only a few of the included studies have mentioned the use of anticoagulants/antiplatelet medications as an exclusion criterion. This is likely to add variability to the results. Although this device is used extensively, none of the studies has mentioned the use of bipolar sealant devices/Aquamantys for decreasing blood loss during surgery.

Operative Duration

Operative duration was reported by a total of 7 studies, 3 using tTXA and 4 using iTXA. Although there was no significant overall difference in operative duration with the use of TXA, 2 outlier studies merit attention. Jieliang et al used tTXA early on in their surgery, while most other studies use instillation toward the end of the procedure.[31,41] Early use of tTXA may be an area for further research to substantiate these results.
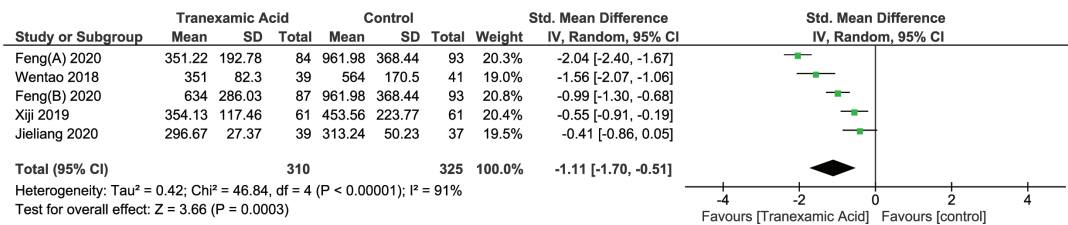
Figure 7. Forest plot showing effect of tranexamic acid on hidden blood loss.

Figure 8. Forest plot showing effect of tranexamic acid on perioperative hemoglobin levels.

A

Study or Subgroup	Tranexamic Acid Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Jieliang 2020	102.18	11.69	39	125.49	11.05	37	21.7%	-2.03 [-2.59, -1.47]
Xiji 2019	102.3	26.56	61	102.96	31.82	61	53.7%	-0.02 [-0.38, 0.33]
Weera 2018	98.6	18.2	29	91	18.6	28	24.6%	0.41 [-0.12, 0.93]
Total (95% CI)			**129**			**126**	**100.0%**	**-0.35 [-0.61, -0.09]**

Heterogeneity: Chi² = 45.91, df = 2 (P < 0.00001); I² = 96%
Test for overall effect: Z = 2.65 (P = 0.008)

B

Study or Subgroup	Tranexamic Acid Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
Jieliang 2020	102.18	11.69	39	125.49	11.05	37	0.0%	-2.03 [-2.59, -1.47]
Xiji 2019	102.3	26.56	61	102.96	31.82	61	68.6%	-0.02 [-0.38, 0.33]
Weera 2018	98.6	18.2	29	91	18.6	28	31.4%	0.41 [-0.12, 0.93]
Total (95% CI)			**90**			**89**	**100.0%**	**0.11 [-0.18, 0.41]**

Heterogeneity: Chi² = 1.77, df = 1 (P = 0.18); I² = 43%
Test for overall effect: Z = 0.75 (P = 0.45)

Figure 9. (A) Forest plot showing effect of topical tranexamic acid (tTXA) on operative duration. (B) Forest plot showing effect of tTXA on operative duration after leave-one-out analysis and exclusion Jieliang 2020.
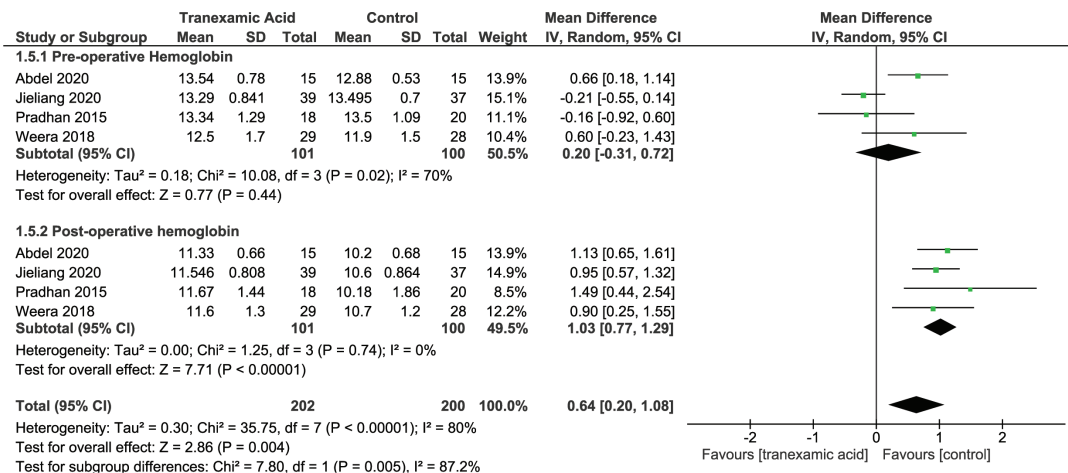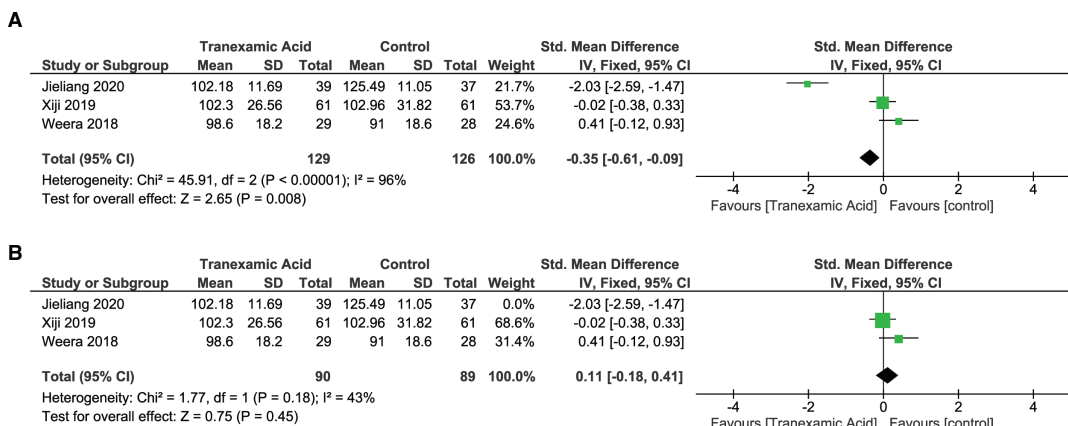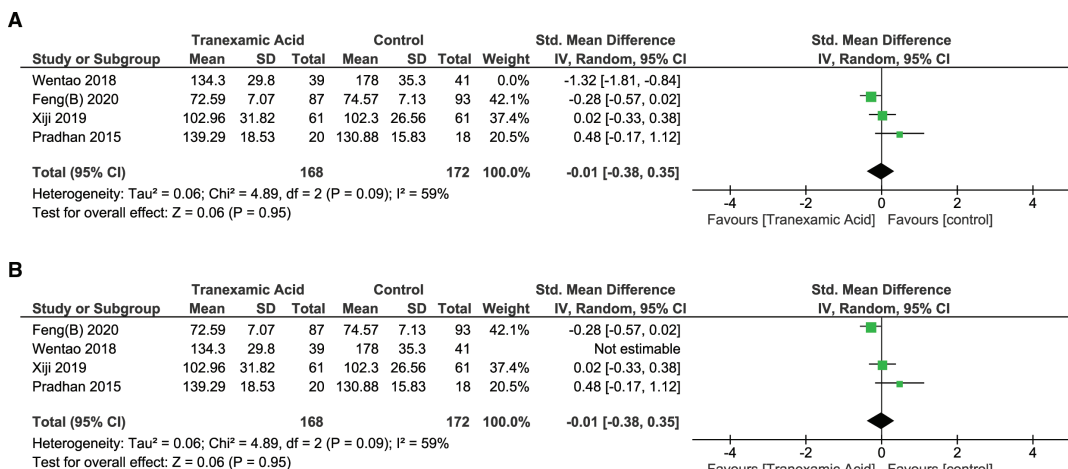
A

Study or Subgroup	Tranexamic Acid Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Wentao 2018	134.3	29.8	39	178	35.3	41	0.0%	-1.32 [-1.81, -0.84]
Feng(B) 2020	72.59	7.07	87	74.57	7.13	93	42.1%	-0.28 [-0.57, 0.02]
Xiji 2019	102.96	31.82	61	102.3	26.56	61	37.4%	0.02 [-0.33, 0.38]
Pradhan 2015	139.29	18.53	20	130.88	15.83	18	20.5%	0.48 [-0.17, 1.12]
Total (95% CI)			**168**			**172**	**100.0%**	**-0.01 [-0.38, 0.35]**

Heterogeneity: Tau² = 0.06; Chi² = 4.89, df = 2 (P = 0.09); I² = 59%
Test for overall effect: Z = 0.06 (P = 0.95)

B

Study or Subgroup	Tranexamic Acid Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Feng(B) 2020	72.59	7.07	87	74.57	7.13	93	42.1%	-0.28 [-0.57, 0.02]
Wentao 2018	134.3	29.8	39	178	35.3	41		Not estimable
Xiji 2019	102.96	31.82	61	102.3	26.56	61	37.4%	0.02 [-0.33, 0.38]
Pradhan 2015	139.29	18.53	20	130.88	15.83	18	20.5%	0.48 [-0.17, 1.12]
Total (95% CI)			**168**			**172**	**100.0%**	**-0.01 [-0.38, 0.35]**

Heterogeneity: Tau² = 0.06; Chi² = 4.89, df = 2 (P = 0.09); I² = 59%
Test for overall effect: Z = 0.06 (P = 0.95)

Figure 10. (A) Forest plot showing effect of intravenous tranexamic acid (iTXA) on operative duration. (B) Forest plot showing effect of iTXA on operative duration after leave-one-out analysis and exclusion of Wentao 2018.
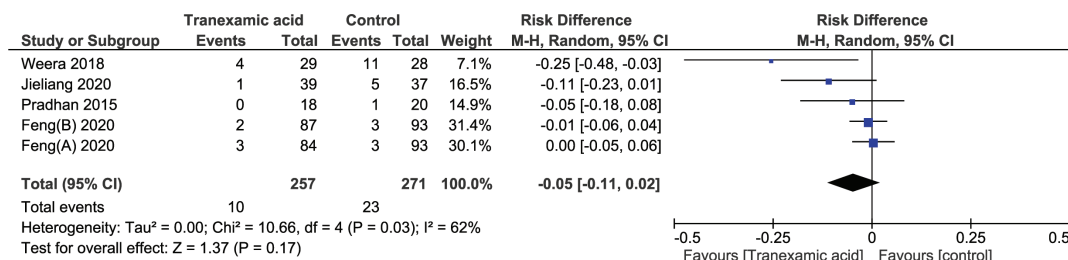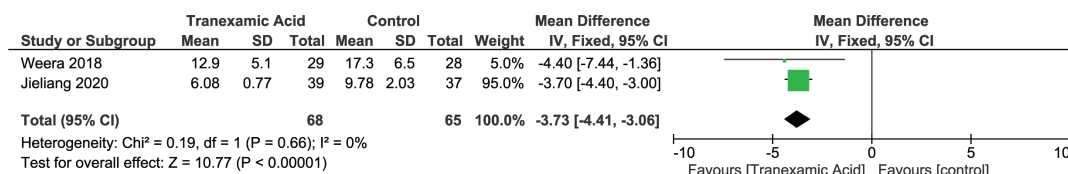
Study or Subgroup	Tranexamic acid Events	Total	Control Events	Total	Weight	Risk Difference M-H, Random, 95% CI
Weera 2018	4	29	11	28	7.1%	-0.25 [-0.48, -0.03]
Jieliang 2020	1	39	5	37	16.5%	-0.11 [-0.23, 0.01]
Pradhan 2015	0	18	1	20	14.9%	-0.05 [-0.18, 0.08]
Feng(B) 2020	2	87	3	93	31.4%	-0.01 [-0.06, 0.04]
Feng(A) 2020	3	84	3	93	30.1%	0.00 [-0.05, 0.06]
Total (95% CI)		**257**		**271**	**100.0%**	**-0.05 [-0.11, 0.02]**
Total events	10		23			

Heterogeneity: Tau² = 0.00; Chi² = 10.66, df = 4 (P = 0.03); I² = 62%
Test for overall effect: Z = 1.37 (P = 0.17)

Figure 11. Forest plot showing effect of tranexamic acid on blood transfusions.

Study or Subgroup	Tranexamic Acid Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Weera 2018	12.9	5.1	29	17.3	6.5	28	5.0%	-4.40 [-7.44, -1.36]
Jieliang 2020	6.08	0.77	39	9.78	2.03	37	95.0%	-3.70 [-4.40, -3.00]
Total (95% CI)			**68**			**65**	**100.0%**	**-3.73 [-4.41, -3.06]**

Heterogeneity: Chi² = 0.19, df = 1 (P = 0.66); I² = 0%
Test for overall effect: Z = 10.77 (P < 0.00001)

Figure 12. Forest plot showing effect of tranexamic acid on length of hospital stay.

| Study or Subgroup | Tranexamic Acid | | Control | | | Risk Difference | Risk Difference |
	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Feng(A) 2020	3	84	3	87	26.2%	0.00 [−0.05, 0.06]	
Feng(B) 2020	1	87	3	93	27.6%	−0.02 [−0.06, 0.02]	
Hamdi 2016	0	25	0	25	7.7%	0.00 [−0.07, 0.07]	
Jieliang 2020	0	39	0	37	11.7%	0.00 [−0.05, 0.05]	
Pradhan 2015	0	18	0	20	5.8%	0.00 [−0.10, 0.10]	
Weera 2018	0	29	0	28	8.7%	0.00 [−0.07, 0.07]	
Wentao 2018	13	39	14	41	12.3%	−0.01 [−0.22, 0.20]	
Total (95% CI)		**321**		**331**	**100.0%**	**−0.01 [−0.04, 0.03]**	
Total events	17		20				
Heterogeneity: Chi² = 0.66, df = 6 (P = 1.00); I² = 0%							
Test for overall effect: Z = 0.37 (P = 0.71)							

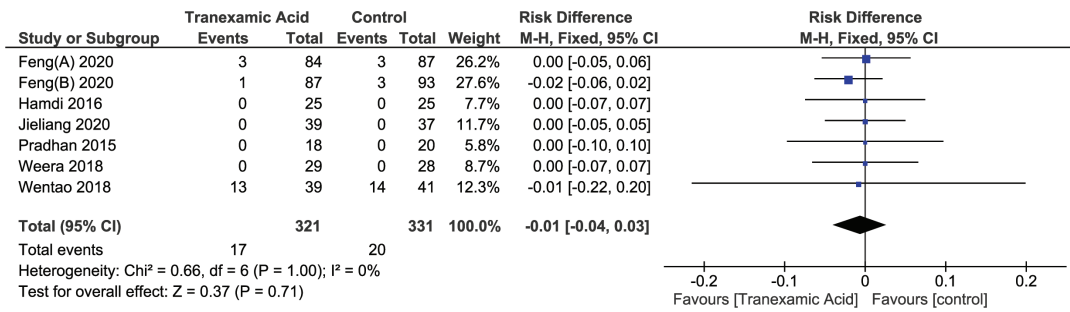Favours [Tranexamic Acid]   Favours [control]

Figure 13. Forest plot showing effect of tranexamic acid on incidence of deep vein thrombosis.

Wentao et al also showed a significant decrease in operative duration and used a continuous infusion of iTXA instead of bolus doses.[28]

Hospital Stay

A significant positive effect on length of hospital stay is noted, though this was only reported by studies using tTXA. Further studies using both iTXA and tTXA will be required to assess this outcome.

Adverse Events

The analysis also revealed that there was no significant positive effect of TXA on the incidence of DVT and PE. The absence of increased incidence of thrombotic events is in keeping with the findings of multiple studies.[3,7,42] Other adverse effects such as seizures, stroke, and myocardial infarction were not reported even in studies using tTXA. Intact dura may prove to be a barrier to excessive neuraxial penetration of TXA, an essential prerequisite to stroke and/or seizures. In this review, studies did not include patients suspected to have a cerebrospinal fluid leak. Neurological deficits may be used as a marker for possible dural injury, and this has been used as an exclusion criterion.[43,44] Whether tTXA is indicated in patients with neurological deficits is at present uncertain. Of the studies included in this review, only one specifically included patients with neurological deficits, while 3 studies excluded patients with deficits.[26,27,29,31] The rest did not specify this as a criterion. At present, patients noted to have intraoperative dural tears or those confirmed on preoperative imaging may not be ideal candidates for tTXA.

Limitations

The limitations of this study include the inclusion of both randomized and nonrandomized trials for analysis, with studies having a higher risk of bias on quality analysis. The sample size is also relatively lower, with only small studies with low sample sizes included in the analysis. The included studies have used different protocols with varying surgical interventions and drug dosing regimens. Transfusion criteria were not noted to be uniform where mentioned. The inclusion criteria in this analysis also did not include the pediatric age group. Publication bias was assessed using a funnel plot, which revealed an asymmetric scatter. This may be due to several reasons, including significant statistical heterogeneity and insufficient trials in the plot leading to decreased sensitivity. Language restrictions may have also contributed to bias.

TXA may be used in the perioperative period in spine trauma to decrease blood loss without any serious side effects. Further research is required to understand the optimum dosing and timing of both intravenous and tTXA, as well as if it has any significant effect on the duration of hospital stay and costs.
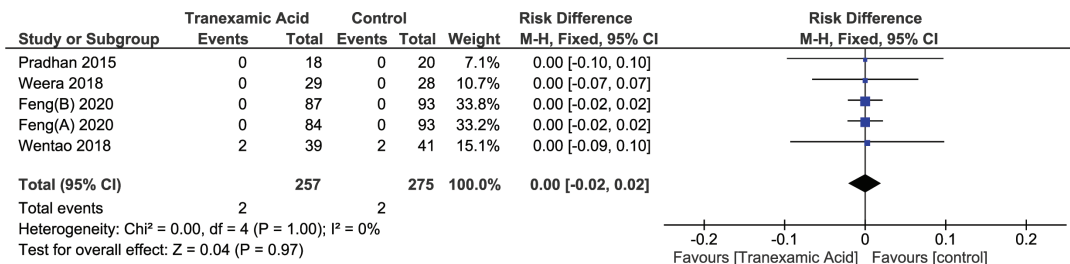
| Study or Subgroup | Tranexamic Acid | | Control | | | Risk Difference | Risk Difference |
	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Pradhan 2015	0	18	0	20	7.1%	0.00 [−0.10, 0.10]	
Weera 2018	0	29	0	28	10.7%	0.00 [−0.07, 0.07]	
Feng(B) 2020	0	87	0	93	33.8%	0.00 [−0.02, 0.02]	
Feng(A) 2020	0	84	0	93	33.2%	0.00 [−0.02, 0.02]	
Wentao 2018	2	39	2	41	15.1%	0.00 [−0.09, 0.10]	
Total (95% CI)		**257**		**275**	**100.0%**	**0.00 [−0.02, 0.02]**	
Total events	2		2				
Heterogeneity: Chi² = 0.00, df = 4 (P = 1.00); I² = 0%							
Test for overall effect: Z = 0.04 (P = 0.97)							

Favours [Tranexamic Acid]   Favours [control]

Figure 14. Forest plot showing effect of tranexamic acid on incidence of pulmonary embolism.

CONCLUSION

TXA, both intravenous and topical, has become routine adjuncts in spine surgery. However, there is less experience with TXA in spine trauma surgery. This meta-analysis has reaffirmed the use of TXA in reducing perioperative blood loss and operative duration with no added risk of adverse events, although a demonstrable effect on blood transfusion rate is uncertain. Further studies in the dose and timing of TXA, as well as patient selection, are necessary.

REFERENCES

1. Elgafy H, Bransford RJ, McGuire RA, Dettori JR, Fischer D. Blood loss in major spine surgery: are there effective measures to decrease massive hemorrhage in major spine fusion surgery? *Spine (Phila Pa 1976)*. 2010;35(9 Suppl):S47-56. doi:10.1097/BRS.0b013e3181d833f6

2. Hu SS. Blood loss in adult spinal surgery. *Haemost Spine Surg*. 2005:3–5. doi:10.1007/b139006

3. Li G, Sun TW, Luo G, Zhang C. Efficacy of antifibrinolytic agents on surgical bleeding and transfusion requirements in spine surgery: a meta-analysis. *Eur Spine J*. 2017;26(1):140–154. doi:10.1007/s00586-016-4792-x

4. Gill JB, Chin Y, Levin A, Feng D. The use of antifibrinolytic agents in spine surgery. A meta-analysis. *J Bone Joint Surg Am*. 2008;90(11):2399–2407. doi:10.2106/JBJS.G.01179

5. Neilipovitz DT. Tranexamic acid for major spinal surgery. *Haemost Spine Surg*. 2005:62–65. doi:10.1007/b139006

6. Ker K, Edwards P, Perel P, Shakur H, Roberts I. Effect of tranexamic acid on surgical bleeding: systematic review and cumulative meta-analysis. *BMJ*. 2012;344:bmj.e3054. doi:10.1136/bmj.e3054

7. Shakur H, Roberts I, Bautista R, et al. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. *Lancet*. 2010;376(9734):23–32. doi:10.1016/S0140-6736(10)60835-5

8. CRASH-3 trial collaborators. Effects of tranexamic acid on death, disability, vascular occlusive events and other morbidities in patients with acute traumatic brain injury (CRASH-3): a randomised, placebo-controlled trial. *Lancet*. 2019;394(10210):1713–1723. doi:10.1016/S0140-6736(19)32233-0

9. Winter SF, Santaguida C, Wong J, Fehlings MG. Systemic and topical use of tranexamic acid in spinal surgery: a systematic review. *Global Spine J*. 2016;6(3):284–295. doi:10.1055/s-0035-1563609

10. Earnshaw C, Poole M. *Tranexamic Acid*. 2019. www.wfsahq.org/resources/anaesthesia-tutorial-of-the-week. Accessed December 6, 2020.

11. Horrow JC, Van Riper DF, Strong MD, Grunewald KE, Parmet JL. The dose-response relationship of tranexamic acid. *Anesthesiology*. 1995;82(2):383–392. doi:10.1097/00000542-199502000-00009

12. Yu CC, Fidai MS, Kadri O, Kadado AA, Bartol S. 221. Intravenous and oral tranexamic acid are equivalent at reducing blood loss in thoracolumbar spinal fusion: a prospective randomized trial phase II. *Spine J*. 2019;19(9):S108–S109. doi:10.1016/j.spinee.2019.05.236

13. Yerneni K, Burke JF, Tuchman A, et al. Topical tranexamic acid in spinal surgery: a systematic review and meta-analysis. *J Clin Neurosci*. 2019;61:114–119. doi:10.1016/j.jocn.2018.10.121

14. Li ZJ, Fu X, Xing D, Zhang HF, Zang JC, Ma XL. Is tranexamic acid effective and safe in spinal surgery? A meta-analysis of randomized controlled trials. *Eur Spine J*. 2013;22(9):1950–1957. doi:10.1007/s00586-013-2774-9

15. Patel S, Robertson B, McConachie I. Catastrophic drug errors involving tranexamic acid administered during spinal anaesthesia. *Anaesthesia*. 2019;74(7):904–914. doi:10.1111/anae.14662

16. Lin Z, Xiaoyi Z. Tranexamic acid-associated seizures: a meta-analysis. *Seizure*. 2016;36:70–73. doi:10.1016/j.seizure.2016.02.011

17. Wong J, Abrishami A, El Beheiry H, et al. Topical application of tranexamic acid reduces postoperative blood loss in total knee arthroplasty: a randomized, controlled trial. *J Bone Joint Surg Am*. 2010;92(15):2503–2513. doi:10.2106/JBJS.I.01518

18. Liang J, Liu H, Huang X, et al. Using tranexamic acid soaked absorbable gelatin sponge following complex posterior lumbar spine surgery: a randomized control trial. *Clin Neurol Neurosurg*. 2016;147:110–114. doi:10.1016/j.clineuro.2016.06.001

19. Ehresman J, Pennington Z, Schilling A, et al. Cost-benefit analysis of tranexamic acid and blood transfusion in elective lumbar spine surgery for degenerative pathologies. *J Neurosurg Spine*. 2020;33(2):1–9. doi:10.3171/2020.1.SPINE191464

20. Mallepally AR, Mahajan R, Rustagi T, Goel SA, Das K, Chhabra HS. Use of topical tranexamic acid to reduce blood loss in single-level transforaminal lumbar interbody fusion. *Asian Spine J*. 2020;14(5):593–600. doi:10.31616/asj.2019.0134

21. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019;366:l4898. doi:10.1136/bmj.l4898

22. Slim K, Nini E, Forestier D, Kwiatkowski F, Panis Y, Chipponi J. Methodological index for non-randomized studies (MINORS): development and validation of a new instrument. *ANZ J Surg*. 2003;73(9):712–716. doi:10.1046/j.1445-2197.2003.02748.x

23. Melsen WG, Bootsma MCJ, Rovers MM, Bonten MJM. The effects of clinical and statistical heterogeneity on the predictive values of results from meta-analyses. *Clin Microbiol Infect*. 2014;20(2):123–129. doi:10.1111/1469-0691.12494

24. Garg B, Dhatt S, Chakraborty S. Use of single-dose tranexamic acid to reduce blood loss in operative thoracolumbar trauma: a comparative study. *Spine J*. 2012;12(9):S93. doi:10.1016/j.spinee.2012.08.259

25. Hamdi M, Boughariou S, Zbidi B, et al. Abstract PR372. *Anesthesia & Analgesia*. 2016;123:476. doi:10.1213/01.ane.0000492766.29483.3b

26. Sudprasert W, Tanaviriyachai T, Choovongkomol K, Jongkittanakul S, Piyapromdee U. A randomized controlled trial of topical application of tranexamic acid in patients with thoracolumbar spine trauma undergoing long-segment instrumented posterior spinal fusion. *Asian Spine J*. 2019;13(1):146–154. doi:10.31616/asj.2018.0125

27. Wang X, Yang R, Sun H, Zhang Y. Different effects of intravenous, topical, and combined application of tranexamic acid on patients with thoracolumbar fracture. *World Neurosurg*. 2019;127:e1185–e1189. doi:10.1016/j.wneu.2019.04.095

28. Wang W, Duan K, Ma M, et al. Tranexamic acid decreases visible and hidden blood loss without affecting prethrombotic state molecular markers in transforaminal thoracic interbody fusion for treatment of thoracolumbar fracture-dislocation.

Spine (Phila Pa 1976). 2018;43(13):E734–E739. doi:10.1097/BRS.0000000000002491

29. Wang F, Nan L, Feng X, et al. The efficacy and safety of multiple-dose intravenous tranexamic acid in reducing perioperative blood loss in patients with thoracolumbar burst fracture. *Clin Neurol Neurosurg*. 2020;193:105766. doi:10.1016/j.clineuro.2020.105766

30. Pradhan RL, Pandey BK. Does tranexamic acid reduce perioperative bleeding in short segment pedicle screw fixation in thoracolumbar spine fractures? *J Nepal Med Assoc*. 2015;53(199):169–173. doi:10.31729/jnma.2785

31. Shen J, Yang Z, Fu M, Hao J, Jiang W. The influence of topical use of tranexamic acid in reducing blood loss on early operation for thoracolumbar burst fracture: a randomized double-blinded controlled study. *Eur Spine J*. 2021;30(10):3074–3080. doi:10.1007/s00586-020-06626-x

32. Abdel Wanis M, Sleem A, Abdel-all M. Effect of topical use of tranexamic acid in patients with thoracolumbar fracture undergoing posterior spinal fixation and fusion. *Egyptian Journal of Orthopedic Research*. 2020;1(2):75–82. doi:10.21608/ejor.2020.162002

33. Sheng J, Liu D, Chen Y, Liu XL, Wu HH, Zheng W. Hemostasis following local versus intravenous tranexamic acid in patients undergoing posterior open reduction and internal fixation of thoracolumbar fractures: study protocol for a parallel-group, randomized controlled trial. *Clin Trials Orthop Disord*. 2018;3(4):113. doi:10.4103/2542-4157.248609

34. Lehman RA. *Columbia U. Tranexamic Acid to Reduce Blood Loss in Spine Trauma Surgery*. 2021. https://clinicaltrials.gov/ct2/show/NCT02314988. Accessed January 5, 2021.

35. Chen ZX, Sun ZM, Jiang C, et al. Comparison of hidden blood loss between three different surgical approaches for treatment of thoracolumbar fracture. *J Invest Surg*. 2019;32(8):755–760. doi:10.1080/08941939.2018.1458925

36. Yin M, Chen G, Yang J, et al. Hidden blood loss during perioperative period and the influential factors after surgery of thoracolumbar burst fracture: a retrospective case series. *Medicine (Baltimore)*. 2019;98(13):e14983. doi:10.1097/MD.0000000000014983

37. Luo W, Sun RX, Jiang H, Ma XL. The efficacy and safety of topical administration of tranexamic acid in spine surgery: a meta-analysis. *J Orthop Surg Res*. 2018;13(1):96. doi:10.1186/s13018-018-0815-0

38. Fatima N, Barra ME, Roberts RJ, et al. Advances in surgical hemostasis: a comprehensive review and meta-analysis on topical tranexamic acid in spinal deformity surgery. *Neurosurg Rev*. 2021;44(1):163–175. doi:10.1007/s10143-020-01236-z

39. Peters A, Verma K, Slobodyanyuk K, et al. Antifibrinolytics reduce blood loss in adult spinal deformity surgery: a prospective, randomized controlled trial. *Spine (Phila Pa 1976)*. 2015;40(8):E443-9. doi:10.1097/BRS.0000000000000799

40. Farrokhi MR, Kazemi AP, Eftekharian HR, Akbari K. Efficacy of prophylactic low dose of tranexamic acid in spinal fixation surgery: a randomized clinical trial. *J Neurosurg Anesthesiol*. 2011;23(4):290–296. doi:10.1097/ANA.0b013e31822914a1

41. Xiong Z, Liu J, Yi P, Wang H, Tan M. Comparison of intravenous versus topical tranexamic acid in nondeformity spine surgery: a meta-analysis. *Biomed Res Int*. 2020;2020:7403034. doi:10.1155/2020/7403034

42. Ko BS, Cho KJ, Kim YT, Park JW, Kim NC. Does tranexamic acid increase the incidence of thromboembolism after spinal fusion surgery? *Clin Spine Surg*. 2020;33(2):E71–E75. doi:10.1097/BSD.0000000000000860

43. Park JK, Park JW, Cho DC, Sung JK. Predictable factors for dural tears in lumbar burst fractures with vertical laminar fractures. *J Korean Neurosurg Soc*. 2011;50(1):11–16. doi:10.3340/jkns.2011.50.1.11

44. Luszczyk MJ, Blaisdell GY, Wiater BP, et al. Traumatic dural tears: what do we know and are they a problem? *Spine J*. 2014;14(1):49–56. doi:10.1016/j.spinee.2013.03.049

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