Safety and Efficacy of Tranexamic Acid in Spinal Surgery: A Systematic Review and Meta-Analysis

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Abstract:

Background: Tranexamic acid (TXA) has gained popularity in spinal surgery because of its potential to reduce blood loss. However, concerns regarding its safety and efficacy remain.

This systematic review and meta-analysis aimed to evaluate the efficacy of TXA in reducing blood loss and its safety profile in spinal surgeries.

Methods: A comprehensive search was conducted in electronic databases for randomized controlled trials and prospective studies evaluating the use of TXA in spinal surgery. The primary outcomes were intraoperative and total estimated blood loss (EBL), and the secondary outcomes included the incidence and types of complications associated with TXA use. Meta-analyses were performed using random-effects models.

Results: Thirteen studies involving 1,213 participants were included in the meta-analysis. The use of TXA was associated with significant reductions in both intraoperative (mean difference: −46.56 mL [−73.85, −19.26], p<0.01]) and total EBL (mean difference: −210.17 mL [−284.93, −135.40], p<0.01) while also decreasing the need for blood transfusions (risk ratio: 0.68 [0.51, 0.90], p<0.01). No significant difference was found in the incidence and types of thrombotic complications when TXA was used in spinal surgery. Subgroup analysis showed consistent results in instrumentation and fusion surgery and different doses of TXA.

Conclusions: TXA is effective in reducing intraoperative and overall blood loss in spinal surgery without increasing the risk of complications. These findings support the use of TXA to improve patient outcomes. However, caution should be exercised because of the heterogeneity among the included studies. Further research is needed to confirm these findings and explore potential long-term complications.

Keywords:

Tranexamic Acid, Spinal Surgery, Blood Loss, Complications, Systematic Review, Meta-Analysis

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Introduction

Spinal surgery is a crucial procedure addressing a variety of conditions such as scoliosis, herniated disks, and spinal stenosis. However, despite its effectiveness, there is a notable association of spinal surgery with considerable intraoperative and postoperative blood loss[1,2)]. Excessive bleeding during these surgeries can result in complications, including anemia, thromboembolism, and the necessity for blood transfusions. This can subsequently prolong hospital stays, increase direct costs, and lead to suboptimal patient outcomes[3,4)]. As such, strategies and interventions that reduce intraoperative and postoperative blood loss are vitally important.

Tranexamic acid (TXA), a recognized antifibrinolytic agent, is a promising measure to decrease blood loss during surgical interventions[5)]. An increasing array of studies indicates TXA's efficacy in curtailing blood loss across diverse surgeries, including cardiac, orthopedic, and spinal operations[6-8)].

However, the safety of using TXA remains under scrutiny, especially concerning potential thromboembolic occurrences.

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Intriguingly, the mechanism that enables TXA to diminish blood loss might concurrently amplify risks such as deep vein thrombosis, pulmonary embolism, and other critical thromboembolic issues[9,10].

Bearing these aspects in focus, our objective is to deliver an enriched systematic review and meta-analysis, delving deep into the benefits and potential hazards of TXA application in spinal surgery.

Materials and Methods

The protocol for this systematic review was registered on PROSPERO (No. CRD42023443939). The systematic reviews and meta-analyses were performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and adhered prepublished protocol[11,12].

Interventions

The intervention of interest is the intraoperative use of TXA in patients undergoing spine surgery. This encompasses any dosage and method of administration of TXA, except topical use (e.g., intravenous and oral), that is given during the surgical procedure.

Outcomes

Studies report on the efficacy of TXA, measured as a reduction in intraoperative or postoperative blood loss, reduction in the need for blood transfusions, and/or other relevant outcomes. Studies also report on the incidence and types of complications associated with TXA.

Study design

We included randomized controlled trials (RCTs) and prospective cohort studies as these study designs provide the highest level of evidence.

Inclusion criteria

We included studies involving patients of any age and gender who have undergone any type of spine surgery.

Exclusion criteria

Studies that do not involve the use of TXA or do not involve its intraoperative use (e.g., only postoperative usage) were excluded. We also excluded studies where TXA was used but the dosage, timing, or method of administration was not clearly described. We also excluded case reports, case series, reviews, and retrospective studies, as these study designs are more prone to bias and provide a lower level of evidence.

Systematic search

We conducted a comprehensive search on MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials from inception to July 10, 2023, for RCTs or prospective studies comparing intravenous or oral TXA and placebo or no intervention in patients undergoing spine surgery. We did not apply any language or time restrictions to the searches. We manually examined the reference lists of pertinent studies to find more related articles.

Trial selection and data extraction

Two authors independently screened articles for inclusion on the basis of the title and abstracts and reviewed relevant articles as full text. Disagreements were resolved by discussion and referral to a third author if necessary. Two authors extracted the study characteristics from each included study, including the year of publication, study population, number of participants, name of comparators, dose of treatment, indication for treatment, name and categories of adverse events, and data evaluating potential biases within the research.

Data extraction and statistical analyses

We conducted analysis to establish the effects of TXA on intraoperative and total estimated blood loss (EBL). Additionally, we conducted subgroup analysis in patients receiving instrumentation and fusion surgery. Subanalysis was also performed between those who received either low-dose (TXA dose of ≤2 g per day) or high-dose TXA (TXA dose of >2 g per day) and the control group. Random-effects analysis was used for meta-analysis for the comparisons of EBL between the two groups. We then investigated whether the administration of TXA was associated with an increased risk of any thrombotic events (thromboembolism [TE], vein thrombosis [VT], pulmonary embolism [PE], and venous thromboembolism [VTE]) and seizures.

Two of us independently assessed the methodological quality of the included studies based on the Cochrane Risk of Bias tool. For the complications, because many studies showed no event in both groups, we assessed risk difference (RD) to provide accurate results. We operated under the assumption that all studies had a consistent true effect size, given the rarity of TEs. The only perceived variability in effect size across studies might arise from the differences in the number of participants. Nevertheless, to test the sturdiness of our results, we conducted a sensitivity analysis with a random-effects model. We also conducted another sensitivity analysis using risk ratio (RR) for effect size, incorporating studies with zero cell frequencies (using a continuity correction of 0.5) or excluding them. We undertook an additional analysis of total TEs, segmented by study size. To assess the level of heterogeneity, we used the I^2 statistics. All statistical computations were conducted using Review Manager Software 5 (RevMan Version 5.4. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2020) and SPSS statistics version 28 (IBM, Chicago, USA). Heterogeneity among the trials was explored by inspection of forest plots and calculation of I^2 statistics. We performed random-effects analyses using the DerSimonian-Laird estimator for tau^2, reporting the most conservative summary estimate with the broadest confidence interval for the compari-

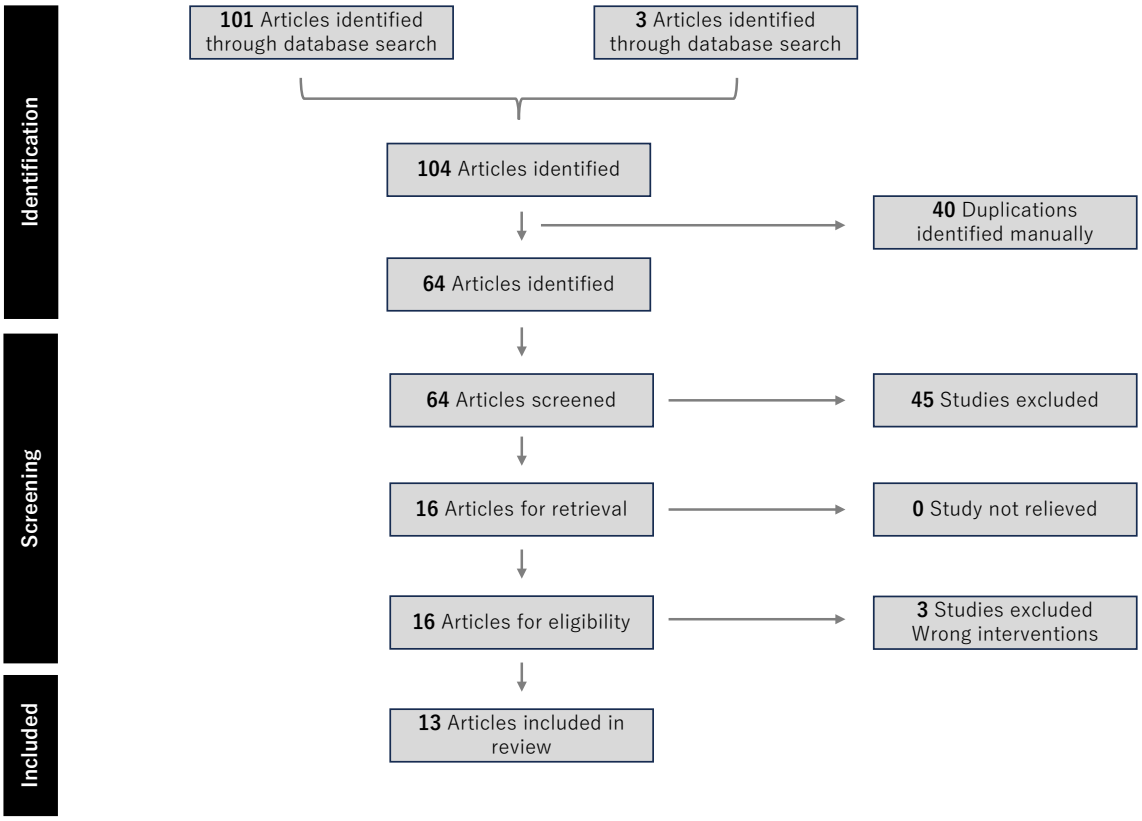


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) Flow Diagram Showing Study Selection.

sons of EBL[12].

Quality assessment

Two authors independently assessed the risk of systematic errors (bias) of the trials, adhering to the guidelines set by the Cochrane Handbook, version 6.1. To evaluate the risk of bias in the individual RCTs, we used the revised uniform criteria of RevMan 5.4. To evaluate the risk of bias in the individual prospective studies, we used the revised uniform criteria of the Risk Of Bias In Non-randomized Studies - of Interventions (ROBINS-I) tool.

Results

Literature search

In total, we screened 104 abstracts, of which 64 were eligible for full-text review. Thirteen trials with 1,213 participants were eligible for inclusion in the meta-analysis[13-25] (Fig. 1).

Description of included studies

Table 1 summarizes the characteristics of the included trials. Seven (53.8%) trials were in instrumentation and fusion surgery, two trials (15.4%) were in decompression alone surgery, and four (30.8%) trials were in both instrumentation and fusion surgery and decompression alone surgery.

The most common route of administration was intravenous injection alone, which was used in 12 studies. Administration involving oral TXA alone was used in only one study. Among 13 trials, 5 trials (38.4%) used high-dose TXA treatment, 6 trials (46.2%) used low-dose TXA treatment, and 2 trials (15.4%) used both high-dose and low-dose TXA treatments.

Risk of bias in individual trials

Among 11 RCTs and 2 prospective studies, 11 trials were deemed to be at a low risk of bias (Fig. 2). A total of 11 trials were judged at a low risk of bias for the randomization process; 2 trials, for deviations from selecting the reported result; and 1 trial, for missing outcome data. All remaining RCTs had a low risk of bias in all domains. Overall, the included studies had a low risk of bias.

Estimated blood loss

Overall, TXA use was associated with decreased intraoperative EBL (mean difference [MD]=−46.56 mL, 95% confidence interval [CI]: [−73.85, −19.26 mL], $p<0.00001$, $I^2=61\%$) and total EBL (MD=−210.17 mL, 95% CI: [−284.93, −135.40 mL], $p<0.00001$, $I^2=84\%$) in patients undergoing spine surgery (Fig. 3A-3D). However, certainty in effect estimates were lowered because of important imprecision and inconsistency. Significant heterogeneity was detected among the studies for total EBL ($I^2=84\%$).

A subgroup analysis was conducted to examine the effects of TXA in specific surgical contexts. In instrumentation and

Table 1. Summary of the Characteristics of the Included Trials.

Study ID	Authors	Study design	Country	Sample size	Age	Diagnosis	Type of surgery	Dose of TXA	Method
100	Reyes-Sánchez A et al. 2023	RCT	Mexico	60 patients	Control: 56.56±19.39 y TXA: 48.7±20 y	Complex spine surgery	>4 levels TL spine	1,950 mg	Oral
101	Raksakietisak M et al. 2015	RCT	Thailand	80 patients	Control: 53.1±11.7 y TXA: 52.6±12.8 y	Various types of surgery	Instrumentation and fusion or >3 levels laminectomy	2 doses of 15 mg/kg (or 1 g/70 kg)	IV
102	Zhu X et al. 2020	RCT	China	150 patients	Control: 56±9.5 y low TXA: 54.8±10.3 y, high TXA: 56±9.9 y	Lumbar degenerative disease	1 or 2 level PLIF	loading dose 15 mg/kg	IV
103	Shi H et al. 2017	RCT	China	96 patients	Control: 55.87±13.14 y TXA: 53.76±12.0 y	Lumbar degenerative disease	PLIF	loading dose 30 mg/kg, followed by 2 mg/kg/h	IV
104	Tsutsumimoto T et al. 2011	RCT	Japan	40 patients	Control: 65.8±11.8 y TXA: 68.0±11.0 y	Cervical spondylotic myelopathy	French-door cervical laminoplasty	15 mg/kg	IV
105	Kim KT et al. 2017	RCT	Korea	72 patients	Control: 65.2±7.0 y low TXA: 63.6±7.6 y, high TXA: 61±9.0 y	Lumbar degenerative disease	PLIF	High TXA: 10 mg/kg, followed by 2 mg/kg/h Low TXA: 5 mg/kg followed by 1 mg/kg/h	IV
51	Kushioka J et al. 2017	Prospective study	Japan	60 patients	Control: 71.5±7.0 y TXA: 67.8±12.0 y	Lumbar degenerative disease	Single-level PLIF	2,000 mg	IV
106	Elmose S et al. 2019	RCT	Denmark	233 patients	Control: 51.1±14.9 y TXA: 48.9±15.4 y	Lumbar degenerative disease	Elective primary decompression or/and discectomy over 1 to 2 levels	10 mg/kg	IV
107	Colomina MJ et al. 2017	RCT	Spain	95 patients	Control: 50.8 y TXA: 59.2 y	Complex spine surgery	Instrumentation and fusion	Loading dose 10 mg/kg, followed by 2 mg/kg/h	IV
108	Elwatidy S et al. 2008	RCT	Saudi Arabia	64 patients	Control: 49.75±21.04y, TXA: 51.56±19.08 y	Various types of surgery	Various spinal surgeries	Loading dose of 2 g or 30 mg/kg, followed by 100 mg/h or 1 mg/kg/h	IV
52	Seddighi A et al. 2017	Prospective study	Not specified	40 patients	Control: 43.7±10.255 y TXA: 49.85±12.209 y	Lumbar degenerative disease	Various spinal surgeries	Loading dose of 10 mg/kg, followed by 0.5 mg/kg/h	IV
109	Stejskal P et al. 2023	RCT	Czech Republic	162 patients	(LAMP) Control: 67.8±9.0 y, TXA: 66.1±9.9 y (PLIF) Control: 55.7±9.6 y, TXA: 55.3±9.9 y	Lumbar degenerative disease	Single-level decompression and stabilization	15 mg/kg/h	IV
110	Sethna NF et al. 2005	RCT	Not specified	44 patients	Control: 14±2 y, TXA: 13.6±1.8 y	Scoliosis	PSF or A/PSF	Loading dose of 50 mg/kg, followed by 5 mg/kg/h	IV

fusion surgery, the use of TXA was associated with a significant decrease in both intraoperative EBL and total EBL. For intraoperative EBL, the subgroup analysis showed an MD of −103.94 mL (95% CI: [−160.09, −47.79 mL], p<

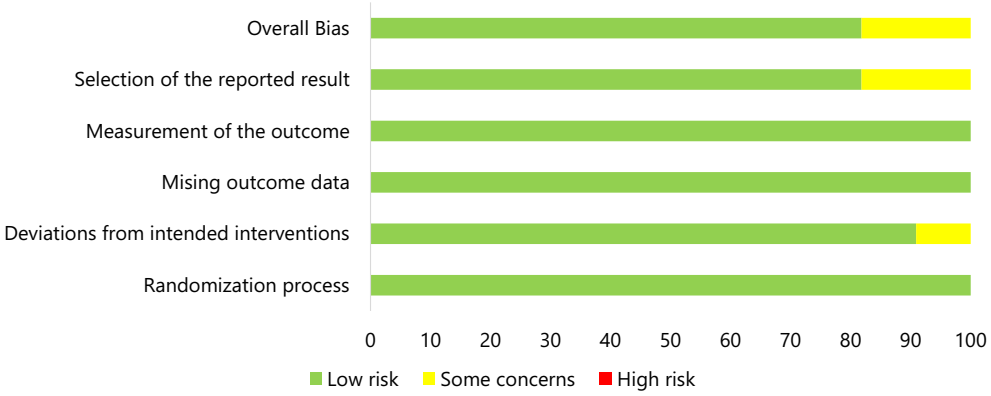


Figure 2. Risk of Bias Summary.
Review authors' judgments regarding each risk of bias item for each included RCT study.

0.00001, I^2=69%) in favor of TXA use (Fig. 4A, 4B). This indicates a reduction in blood loss during the surgical procedure when TXA was administered. Similarly, for total EBL, the subgroup analysis revealed an MD of −307.01 mL (95% CI: [−418.39, −195.64 mL], p<0.00001, I^2=62%) in favor of TXA use (Fig. 4C, 4D).

The subgroup analysis showed that high-dose TXA had an MD of −362.60 mL (95% CI: [−441.53, −283.67 mL], p <0.00001, I^2=0%), indicating a substantial reduction in total blood loss (Fig. 5C, 5D). Similarly, low-dose TXA demonstrated an MD of −80.06 mL (95% CI: [−130.44, −29.68 mL], p=0.002, I^2=59%), indicating a statistically significant decrease in total blood loss (Fig. 6C, 6D). However, concerning intraoperative EBL, a significant reduction was observed only with high-dose TXA (Fig. 5A, 5B). The subgroup analysis showed an MD of −99.51 mL (95% CI: [−164.61, −34.41 mL], p<0.00001, I^2=81%) in favor of high-dose TXA (Fig. 5A, 5B). By contrast, low-dose TXA had an MD of −33.20 mL (95% CI: [−70.29, 3.89 mL], p=0.06, I^2= 49%), which did not reach statistical significance (Fig. 6A, 6B).

Blood transfusions

TXA use was associated with a decreased need for blood transfusions in patients undergoing spine surgery (RR [random-effects model]=0.68, 95% CI: [0.51, 0.90], I^2=15%, p=0.007) (Table 2, Fig. 7A, 7B). This result was consistent for both the random-effects and fixed-effect statistical models (RR [fixed-effect model]=0.63, 95% CI: [0.49, 0.81], I^2= 15%, p=0.003), and we observed a certain publication bias when evaluating either the funnel plot or thrombotic events (Fig. 7C, 7D).

Thrombotic events

We found no evidence that TXA administration increased the risk of thrombotic events (RD=0.00, 95% CI: [−0.01, 0.01], I^2=0%, p=0.84, and RR [random-effects model]=1.46, 95% CI: [0.65, 3.31], I^2=0%, p=0.36) (Fig. 8A, 8B). This result was consistent for both the random-effects and fixed-effect statistical models (RR [fixed-effect model]=1.47, 95% CI: [0.65, 3.32], I^2=0%, p=0.35), and we observed no evidence of publication bias when evaluating either the funnel plot or thrombotic events (Fig. 8C, 8D).

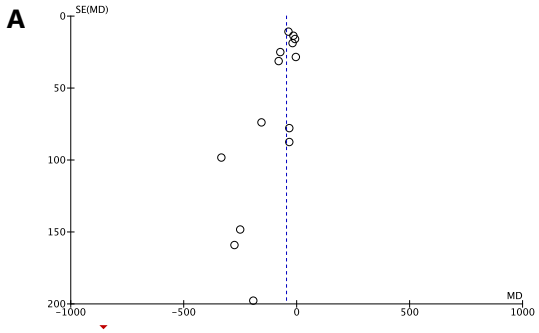
Discussion

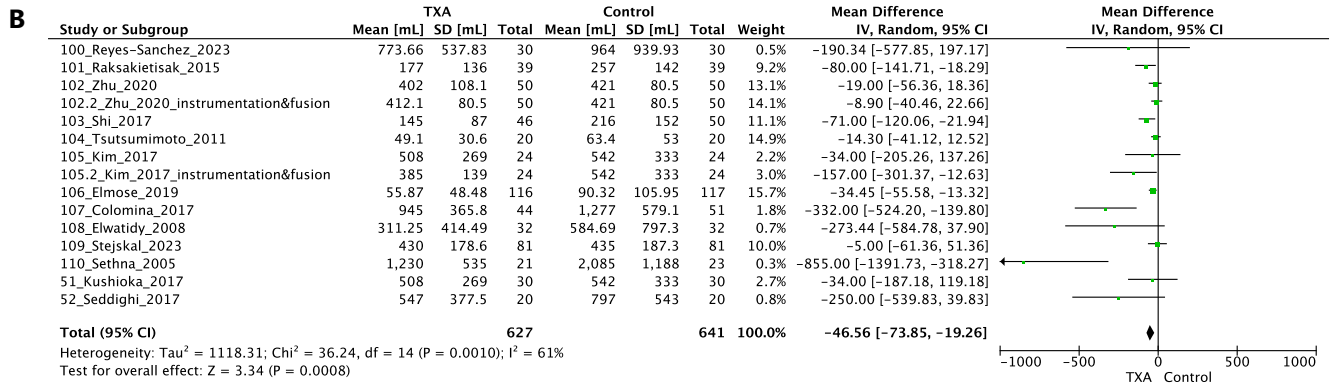
Comparison with existing meta-analyses and systematic reviews

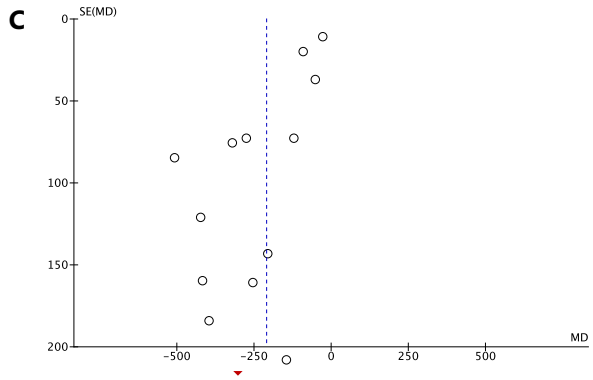
Blood loss during elective spine surgery can have a significant impact on surgical outcomes and can increase the risk of complications[1,2]. Excessive blood loss can lead to hemodynamic instability, causing a drop in blood pressure and a reduction in tissue perfusion[1,2]. This can result in inadequate oxygen delivery to vital organs, potentially leading to organ dysfunction or failure. Significant blood loss may also necessitate blood transfusions to maintain hemoglobin levels and restore adequate oxygen-carrying capacity. However, blood transfusions carry their own risks, including infections, transfusion reactions, and immunological complications[26]. TXA has emerged as a promising intervention for reducing blood loss in various types of surgeries, including general surgery, orthopedic surgery, and spine surgery[6-8].

A prior meta-analysis conducted by Ma et al. centered on TXA's application in total knee arthroplasty[6]. Although this was not directly related to spinal surgery, it did probe TXA's efficacy and safety concerning blood loss reduction. Such insights hint at TXA's potential advantages in managing blood loss, and these findings could be inferred for spinal operations. On a similar note, a systematic review by Ker et al. delved into TXA's impact on surgical bleeding, spanning a range of surgical contexts[27]. The results demonstrated that TXA was effective in reducing blood loss by 30% across diverse surgical procedures without increasing the risk of adverse events. In comparison to the existing meta-analyses and systematic reviews, the present study specifically focused on evaluating the safety and efficacy of TXA in spinal surgeries.

The results of the present study align with the findings of previous meta-analyses and systematic reviews. It demon-







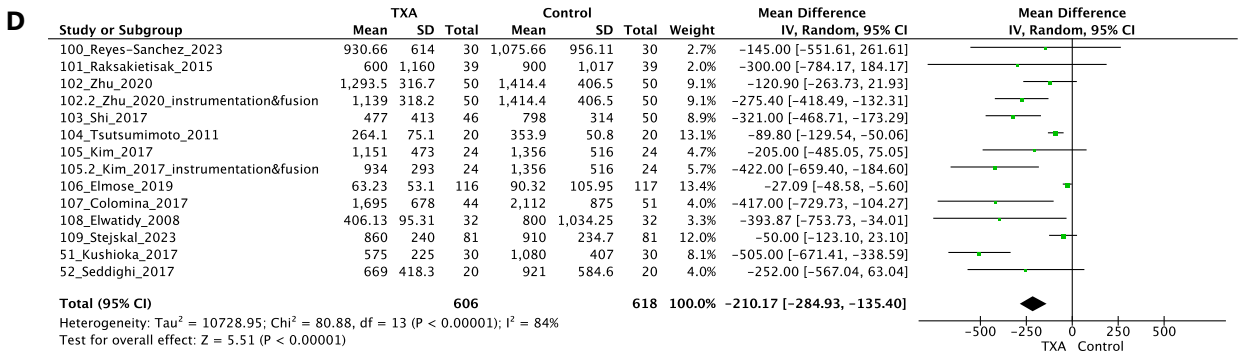


Figure 3. Comparisons of Intraoperative and Total Blood Loss between the TXA and Control Groups.

A. Figure illustrating the funnel plot of intraoperative blood loss in a meta-analysis comparing the TXA and control groups, indicating a certain publication bias.

B. Forest plot showing the effect of TXA on intraoperative blood loss.

C. Figure illustrating the funnel plot of total blood loss in the two groups, indicating a certain publication bias.

D. Forest plot showing the effect of TXA on total blood loss.

SD, standard deviation; CI, confidence interval; TXA, tranexamic acid. The black diamond signifies that the mean difference is in favor of TXA. The size of each square depends on the weight of each study. A green square is given to continuous outcomes.

strated that the use of TXA in spinal surgery significantly reduced both intraoperative and total EBL. Importantly, the present study also examined the safety profile of TXA and found no significant difference in the incidence and types of complications associated with its use in spine surgery. This finding is consistent with the previous literature, suggesting

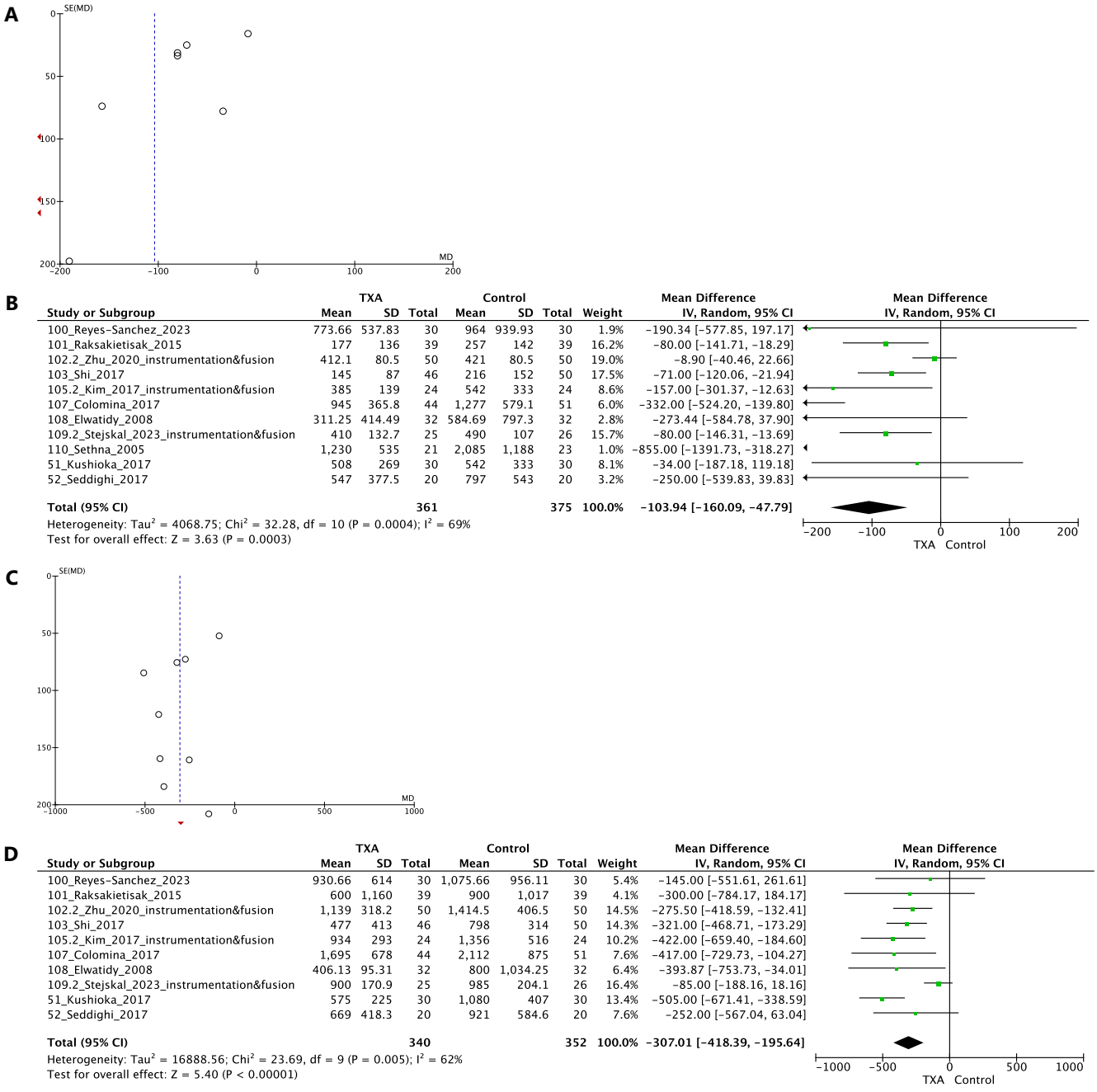


Figure 4. Comparisons of Intraoperative and Total Blood Loss of Patients Receiving Instrumentation and Fusion Surgery between the TXA and Control Groups.

A. Figure illustrating the funnel plot of intraoperative blood loss of patients receiving instrumentation and fusion surgery in a meta-analysis comparing the TXA and control groups, indicating a certain publication bias.

B. Forest plot showing the effect of TXA on intraoperative blood loss of patients receiving instrumentation and fusion surgery.

C. Figure illustrating the funnel plot of total blood loss of patients receiving instrumentation and fusion surgery in the two groups, indicating a certain publication bias.

D. Forest plot showing the effect of TXA on total blood loss of patients receiving instrumentation and fusion surgery.

SD, standard deviation; CI, confidence interval; TXA, tranexamic acid. The black diamond signifies that the mean difference is in favor of TXA. The size of each square depends on the weight of each study. A green square is given to continuous outcomes.

that TXA can effectively reduce EBL in spine surgery without increasing the risk of complications.

In our meta-analysis, the intraoperative EBL in patients receiving low-dose TXA failed to show significant reduction and total EBL was significantly reduced in patients receiving low-dose TXA when compared with the control group. The study by Qiu et al. supports our findings[8]. They compared the EBL between standard-dose TXA and high-dose intravenous TXA (TXA>2 g/day) in spine surgery and concluded that high-dose intravenous TXA decreased the intraoperative blood loss.

There was considerable variability in the dosage, timing,

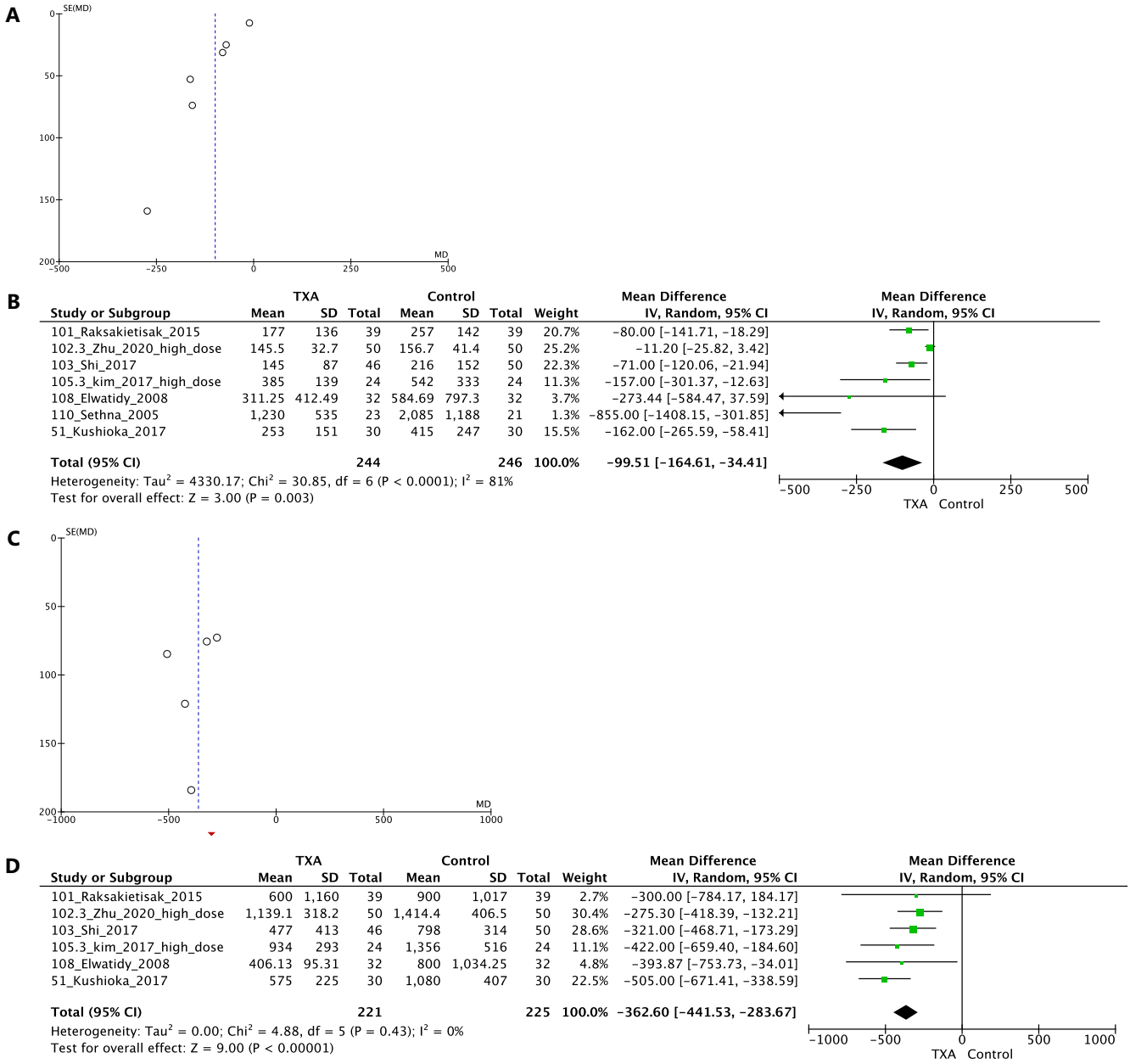


Figure 5. Comparisons of Intraoperative and Total Blood Loss between the High-Dose TXA and Control Groups.
A. Figure illustrating the funnel plot of intraoperative blood loss of patients in a meta-analysis comparing the high-dose TXA and control groups, indicating a certain publication bias.
B. Forest plot showing the effect of high-dose TXA on intraoperative blood loss.
C. Figure illustrating the funnel plot of total blood loss of patients in the two groups, indicating a certain publication bias.
D. Forest plot showing the effect of high-dose TXA on total blood loss.
SD, standard deviation; CI, confidence interval; TXA, tranexamic acid. The black diamond signifies that the mean difference is in favor of TXA. The size of each square depends on the weight of each study. A green square is given to continuous outcomes.

and route of TXA administration in clinical settings. This heterogeneity may affect the consistency and generalizability of the findings, and it highlights the need for standardized protocols in future research.

Blood transfusions

A standout conclusion from our systematic review and meta-analysis was the notable decline in blood transfusion requirements when TXA was used in spinal surgeries. The data revealed that with TXA treatment, there was a 32% decrease in the likelihood of necessitating blood transfusions relative to the control group. This is especially meaningful in clinical practice because blood transfusions carry various potential complications such as the spread of infections, immune responses, and escalated healthcare expenses[26].

This reduced reliance on blood transfusions further bolsters the mounting evidence vouching for TXA's positive impacts in spinal surgery. However, it remains paramount for healthcare practitioners to weigh individual patient specifics, surgical nuances, and established institutional guide-

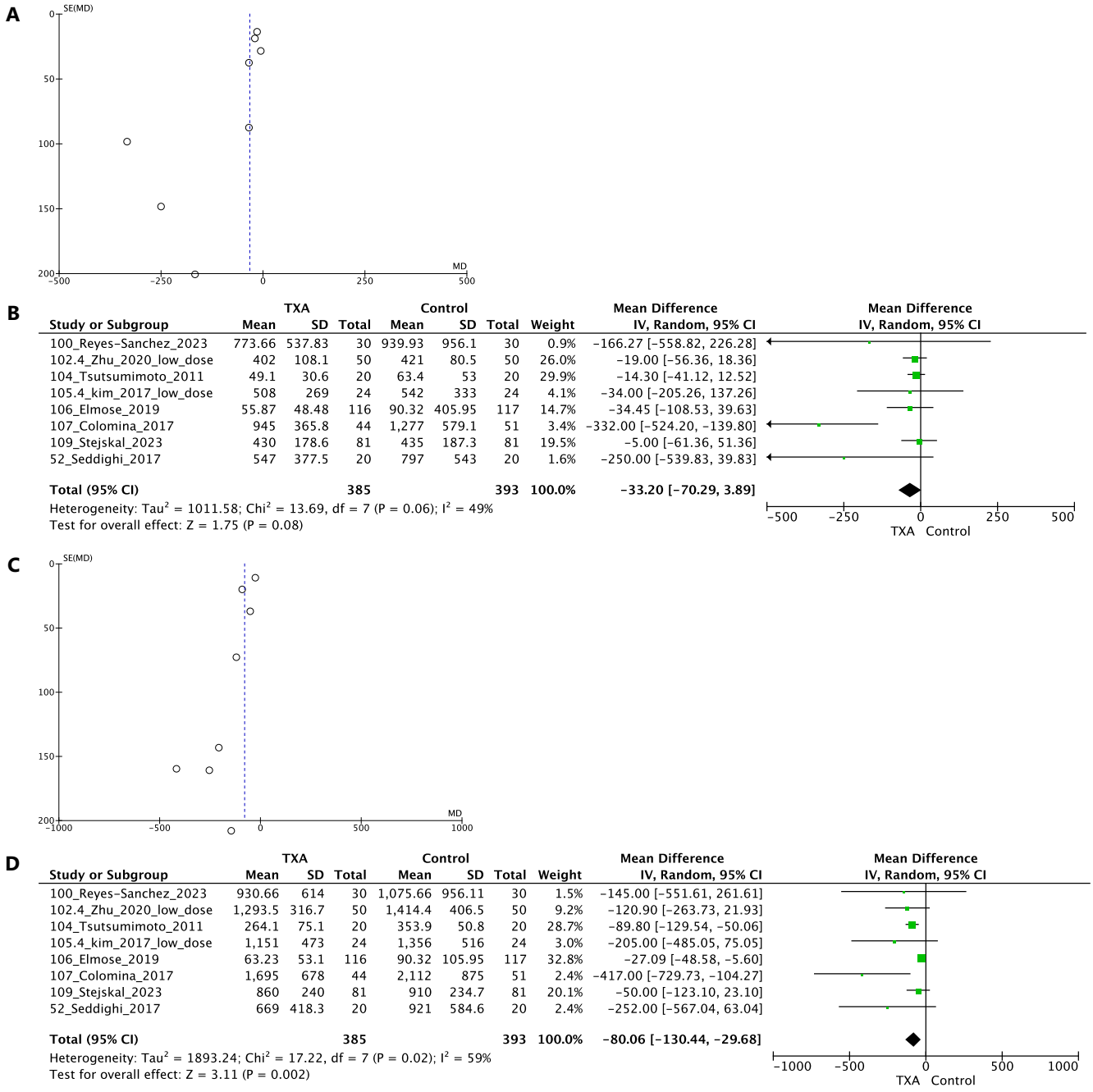


Figure 6. Comparisons of Intraoperative and Total Blood Loss between the Low-Dose TXA and Control Groups.
A. Figure illustrating the funnel plot of intraoperative blood loss of patients in a meta-analysis comparing the low-dose TXA and control groups, indicating a certain publication bias.
B. Forest plot showing the effect of low-dose TXA on intraoperative blood loss.
C. Figure illustrating the funnel plot of total blood loss of patients in the two groups, indicating a certain publication bias.
D. Forest plot showing the effect of low-dose TXA on total blood loss.
SD, standard deviation; CI, confidence interval; TXA, tranexamic acid. The black diamond signifies that the mean difference is in favor of TXA. The size of each square depends on the weight of each study. A green square is given to continuous outcomes.

lines during their decision-making processes.

Safety considerations and thromboembolic events

Although the safety profile of TXA in spinal surgery appears favorable, concerns regarding potential thromboembolic events persist[11-13]. The mechanism of action of TXA, which involves the inhibition of fibrinolysis, raises concerns regarding the risk of thromboembolic complications, including deep vein thrombosis (DVT) and PE[5-9]. Thromboembolic events are serious risks associated with the use of TXA in various surgical procedures.

Several studies, including both retrospective and prospective investigations, have examined the incidence of thromboembolic events in different types of surgeries[5-9]. For instance, Chen et al. reported that administering TXA after valve surgery and/or coronary artery bypass reduced the re-

Table 2. Summary of the Blood Transfusion and Thrombotic Complications of the Included Trials.

Study ID	Authors	Transfusion	Incidence of thromboembolic complications
100	Reyes-Sánchez A et al. 2023	Control: 1.03±1.12 U TXA: 0.86±1.4 U	No serious thromboembolic complications occurred.
101	Raksakietisak M et al. 2015	Control: 13/40 TXA: 5/40	No serious thromboembolic complications occurred.
102	Zhu X et al. 2020	Control: 8/50 Low TXA: 6/50 High TXA: 3/50	15 patients (4 from group A, 6 from group B, and 5 from group C) developed intramuscular VT.
103	Shi H et al. 2017	Control: 4/42 TXA: 1/50	No serious thromboembolic complications occurred.
104	Tsutsumimoto T et al. 2011	0	No serious thromboembolic complications occurred.
105	Kim KT et al. 2017	0	No serious thromboembolic complications occurred.
51	Kushioka J et al. 2017	0	No serious thromboembolic complications occurred.
106	Elmose S et al. 2019	0	No serious thromboembolic complications occurred.
107	Colomina MJ et al. 2017	Control: 34/51 TXA: 23/44	Thromboembolic complications occurred in 2 patients (4.5%) in the TXA group and in 1 patient (2%) in the control group.
108	Elwatidy S et al. 2008	Control: 12/32 TXA: 4/32	No serious thromboembolic complications occurred.
52	Seddighi A et al. 2017	Control: 0.45 U/case TXA: 0.4 U/case	No serious thromboembolic complications occurred.
109	Stejskal P et al. 2023	(LAMP) Control: 3/56 TXA: 2/55 (PLIF) Control: 1/26 TXA: 2/26	1 patient in TXA and 4 patients in the control developed a symptomatic postoperative wound hematoma requiring surgical evacuation.
110	Sethna NF et al. 2005	Control: 15/21 TXA: 14/23	No serious thromboembolic complications occurred.

quirements for blood products without increasing the risk of seizures following cardiac surgery[28]. Similarly, Ivasyk et al. retrospectively reviewed pediatric patients who underwent primary or revision posterior spinal fusions and found that the incidence of seizures, stroke, PE, or DVT in the TXA group was not significantly different from that in the control group[29]. By contrast, Clohisy et al. reported that one seizure and one arrhythmia occurred in patients who received high-dose TXA and one DVT and one PE occurred in patients who received low-dose TXA in adult spinal deformity surgery[30].

Importantly, our analysis also revealed that the use of TXA in spinal surgery did not significantly increase the incidence or types of complications compared to control groups. Although our meta-analysis did not find a significant increase in thrombotic events with the use of TXA, the number of events reported in the included studies was relatively small. It is essential to continue monitoring and assessing the safety profile of TXA to optimize its use in clinical practice and ensure patient safety.

Study limitations

Although the present study provides valuable insights into the safety and efficacy of TXA in spine surgery, several limitations must be acknowledged. First, potential publication bias: Even with our inclusive criteria (ignoring language or date limitations), the risk of publication bias lingers. This bias could affect the overall estimation of treatment effects. Second, quality of included studies: The reliability of our results heavily depends on the caliber of the studies that we have incorporated. Although we emphasized RCTs and prospective cohorts, the methodology's consistency and potential biases within these studies might vary. Third, potential confounders: Different surgical approaches, perioperative practices, and patient demographics might introduce variables. We strived to control these confounders, but some inherent disparities might remain. Fourth, variability in TXA regimens: There was considerable variability in the dosage, timing, and route of TXA administration across the included studies. This heterogeneity may affect the consistency and generalizability of the findings, and it highlights the need for standardized protocols in future research.

From the collated evidence, TXA emerges as a viable solution to decrease blood loss during spinal surgeries without jeopardizing patient safety. Its use can potentially lead to improved patient outcomes, shorter hospital stays, and reduced need for blood transfusions. The findings of the present study are in line with the conclusions drawn from previous meta-analyses and systematic reviews, contributing to more comprehensive understanding of the benefits and risks of TXA in spine surgery. Physicians should consider incorporating TXA into their perioperative management strategies for spinal surgery patients. However, individual patient characteristics, surgical considerations, and institutional protocols should be taken into account when making treatment decisions.

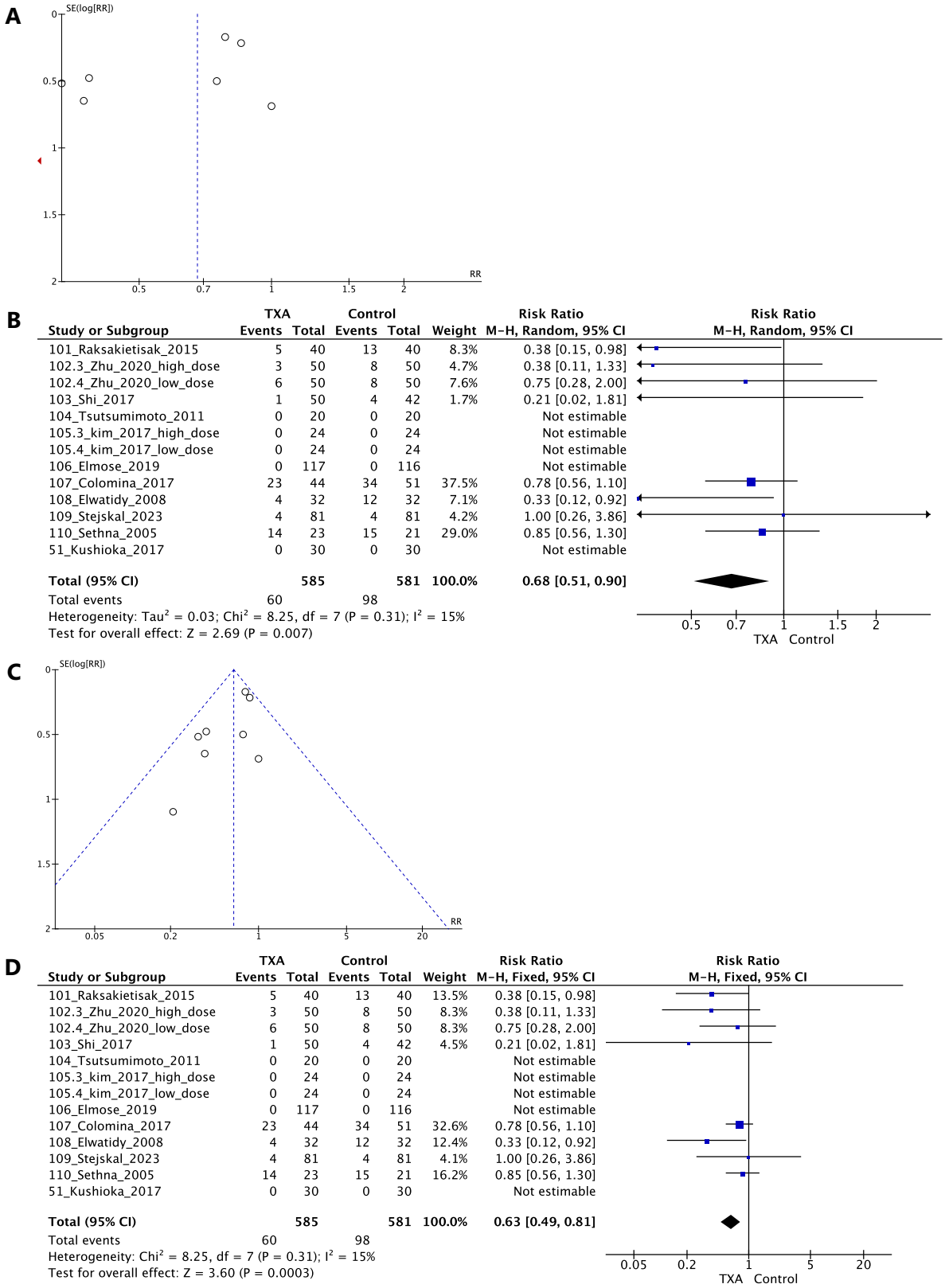


Figure 7. Comparisons of the Need for Blood Transfusion between the TXA and Control Groups.

A. Figure illustrating the funnel plot of risk ratio of the need for blood transfusion in a meta-analysis comparing the TXA and control groups, indicating a minimum publication bias in a random-effects model.

B. Forest plot of risk ratio showing the effect of TXA on the need for blood transfusion in a random-effects model.

C. Figure illustrating the funnel plot of risk ratio of the need for blood transfusion in a meta-analysis comparing the TXA and control groups, indicating a minimum publication bias in a fixed-effect model.

D. Forest plot of risk ratio showing the effect of TXA on the need for blood transfusion in a fixed-effect model.

CI, confidence interval; TXA, tranexamic acid. The black diamond signifies that the risk ratio is in favor of TXA. The size of each square depends on the weight of each study.

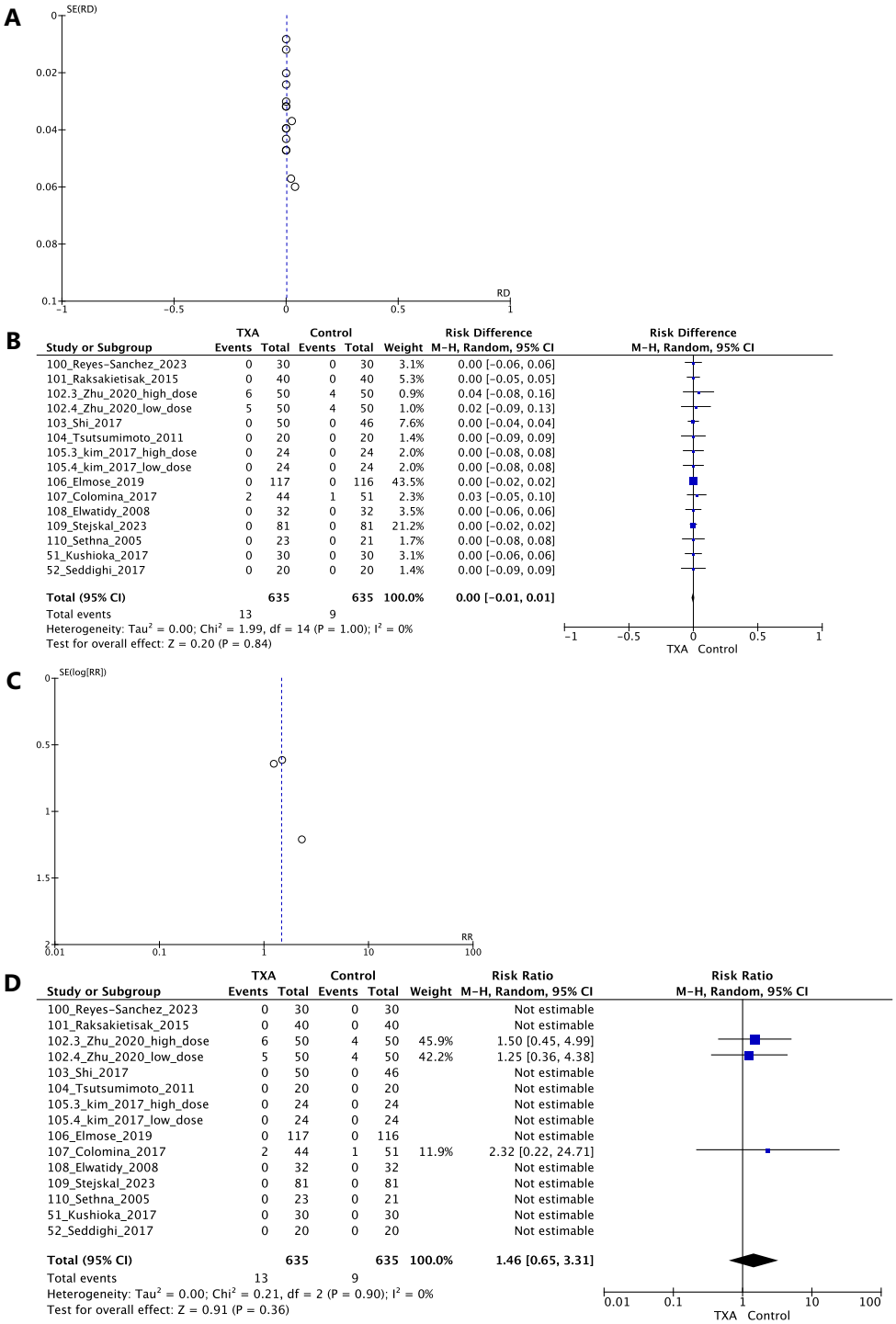


Figure 8. Comparisons of the Incidence of Thrombotic Events between the TXA and Control Groups.

A. Figure illustrating the funnel plot of risk difference of the incidence of thrombotic events in a meta-analysis comparing the TXA and control groups, indicating a minimum publication bias in a random-effects model.

B. Forest plot of risk difference showing the effect of TXA on the incidence of thrombotic events in a random-effects model.

C. Figure illustrating the funnel plot of risk ratio of the incidence of thrombotic events in a meta-analysis comparing the TXA and control groups, indicating a minimum publication bias in a random-effects model.

D. Forest plot of risk ratio showing the effect of TXA on the incidence of thrombotic events in a random-effects model.

CI, confidence interval; TXA, tranexamic acid. The size of each square depends on the weight of each study.

Conclusion

This study adds to the expanding body of literature that endorses the use of TXA in spinal surgery. It offers clinicians critical evidence to guide their clinical decisions and underscores the possible advantages of TXA in enhancing surgical results. Ongoing research is essential to determine the ideal dosage, delivery methods, and criteria for patient selection when utilizing TXA in spinal procedures.

Conflicts of Interest: The authors declare that there are no relevant conflicts of interest.

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Author Contributions: M.Y. designed the study; K.Y., H.F., and M.Y. performed the experiments and analyzed the data; S.E. provided critical reagents; M.Y. supervised the experiments; K.Y. and M.Y. wrote the manuscript.

Ethical Approval: The study did not require approval from the relevant institutional ethical review board because this study did not include any interaction or intervention with human subjects or include any access to identifiable private information.

Informed Consent: Consent was not required because this study involved no human subject.

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