# Clinical Use of Tranexamic Acid in High Tibial Osteotomy

## A Systematic Review and Meta-analysis

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**Background:** High tibial osteotomy (HTO) can cause postoperative hemorrhage. The use of tranexamic acid to reduce the hemorrhage is still controversial.

**Purpose:** To investigate the efficacy and safety of tranexamic acid in HTO.

**Study Design:** Systematic review; Level of evidence, 4.

**Methods:** Using PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, the authors conducted a comprehensive search of the Embase, Cochrane Library, PubMed, Web of Science, MEDLINE, and Foreign Medical Literature Retrieval Service databases between their inception and January 1, 2023. All clinical studies comparing the use of tranexamic acid versus no tranexamic acid during HTO were collected. The primary outcome measures were hemoglobin decrease, drainage volume, and blood loss, and the secondary outcome measures were wound complications, blood transfusion, and postoperative thrombosis. All indicators were analyzed using meta-analysis software. Results were reported as mean differences or risk ratios with 95% confidence intervals.

**Results:** Of 152 initial results, 9 studies involving 908 patients were included. The tranexamic acid group had lower indicators for total blood loss, hemoglobin decrease, and total drainage volume ($P < .00001$ for all). There were no differences between patients with versus without tranexamic acid in wound complications, including hematoma ($P = .21$) or infection ($P = .18$), nor were there any group differences in the prevalence of blood transfusion ($P = .21$) or postoperative thrombosis ($P = .36$).

**Conclusion:** Tranexamic acid was able to effectively reduce postoperative hemorrhage in patients undergoing HTO without affecting the rates of wound complications, blood transfusion, or postoperative thrombosis.

**Keywords:** high tibial osteotomy; tranexamic acid; meta-analysis

High tibial osteotomy (HTO) redistributes the strength of the knee joint to the normal anatomic site by correcting the alignment of the lower extremity through osteotomy, to slow down the degenerative changes of the knee joint, which is beneficial to the treatment of osteoarthritis with abnormal alignment. Therefore, as a part of the step-by-step treatment of knee osteoarthritis, HTO has become an active and effective treatment before knee arthroplasty.

At the same time, HTO is accompanied by many postoperative complications and risks.[4,17] Because of the involved osteotomy correction, the bone space needs to be opened during the HTO procedure. This causes soft tissue damage around the surgical site and inevitable vascular damage.[26] During the perioperative period, it is accompanied by hemorrhage, which leads to local complications of the wound, such as local hematoma, delayed healing, osteofascial compartment syndrome, and even superficial wound infection.[11,23,35] These postoperative complications and risks will affect the patient's early functional recovery and increase the economic burden. In order to better improve the prognosis, in recent years, many surgeons have used tranexamic acid (TXA) in HTO.

TXA is a synthetic analog of the amino acid lysine in its chemical structure, and it acts mainly by competitively blocking the lysine binding site of plasminogen as an

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antifibrinolytic drug.[5] TXA has been shown to reduce blood loss in other orthopaedic procedures, such as total knee arthroplasty,[15,38] total hip replacement,[1,40] and periacetabular osteotomy.[18,39] In addition, TXA can reduce hemorrhage during orthopaedic surgery at various doses without increasing the risk of thrombosis.[7,12,43] Current modes of administration of TXA include intravenous (IV), topical, or oral.[30,34,41] The clinical applications of TXA have not been widely studied and recognized in HTO.

In this study, we aimed to investigate the efficacy and safety of TXA in HTO. It was hypothesized that TXA would effectively reduce postoperative hemorrhage in patients undergoing HTO and it would not affect the prevalence of wound complications, blood transfusion, or postoperative thrombosis.

## METHODS

### Search Strategy

This systematic review was conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The comprehensive retrieval of studies from the Embase, Cochrane Library, PubMed, Web of Science, MEDLINE, and Foreign Medical Literature Retrieval Service databases was conducted by 2 independent reviewers (Z.X. and L.L.) between their inception and January 1, 2023. The search terms for retrieval were as follows: "Tranexamic Acid or Tranexamic Acid [MeSH] or TXA" and "tibia* or tibia[MeSH]" and "osteotom* or osteotomy[MeSH]." References of included studies were searched to avoid missing relevant studies. The search process did not restrict the language and country of the publication.

### Inclusion and Exclusion Criteria

The inclusion criteria for studies were as follows: (1) patients who received opening-wedge HTO; (2) intervention group received application of TXA; (3) control group received placebo; (4) primary indicators of comparative results were hemoglobin decrease, drainage volume, and blood loss, with other indicators including wound complications, blood transfusion, and postoperative thrombosis; and (5) studies were comparable in design. The exclusion criteria were as follows: (1) patients who did not receive HTO or received HTO in combination with multiple other surgeries; (2) no blank control group; (3) no postoperative bleeding-related indicators were involved in the results; (4) non–English-language articles; and (5) reviews, commentaries, or cell experiment articles. All duplicate studies were removed.

### Data Extraction and Quality Assessment

Data extraction and quality assessment were performed independently by 2 reviewers (Z.X. and L.L.). Any disputes were resolved through discussions with all members of the group. The following data were retrieved: first author, study design, sample size, general patient information, the primary indicators of comparative results, and the other results. The primary outcome measures were hemoglobin decrease, drainage volume, and blood loss, and the secondary outcome measures were the prevalence of wound complications, blood transfusion, and postoperative thrombosis.

The Cochrane Collaboration's risk of bias tool was used to assess the quality of prospective comparative studies. The Newcastle-Ottawa Scale (NOS) was used to assess the quality of retrospective comparative studies.

### Statistical Analysis

Data between the TXA and control groups were analyzed using Review Manager 5.3 of the Cochrane Collaboration Group. Risk ratios (RRs) with 95% confidence intervals were calculated for dichotomous variables, and mean differences (MDs) with 95% confidence intervals were calculated for continuous variables. The $P$ value and $I^2$ statistic were used to assess heterogeneity by standard chi-square test. When $I^2 < 50\%$ or $P \geq .1$, the fixed-effects model was adopted. If this condition could not be met, the random-effects model was adopted. We also performed subgroup analyses according to the method of TXA administration.

## RESULTS

### Literature Search and Selection

The process of retrieval is shown in Figure 1. A total of 152 studies were included in the preliminary search of various databases. After screening, 9 studies[¶] including 908

[¶]References 4, 6, 16, 17, 21, 24, 28, 31, 33.

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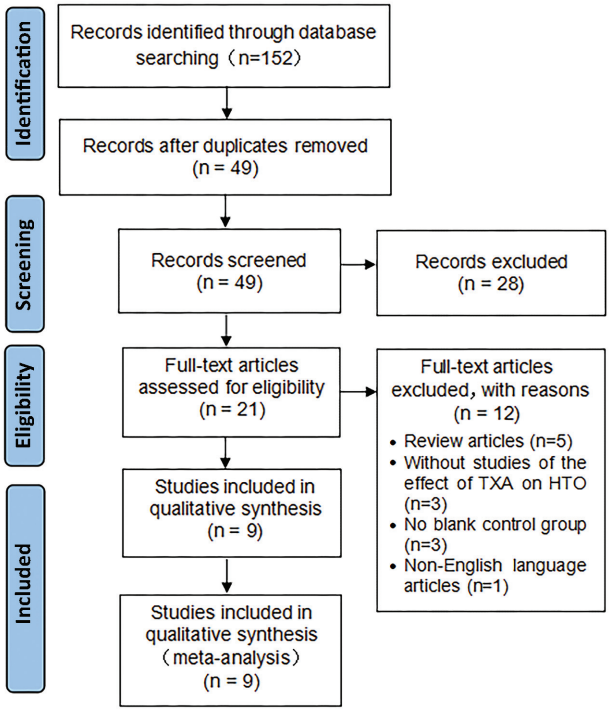


**Figure 1.** PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flowchart of the study selection process. HTO, high tibial osteotomy; TXA, tranexamic acid.

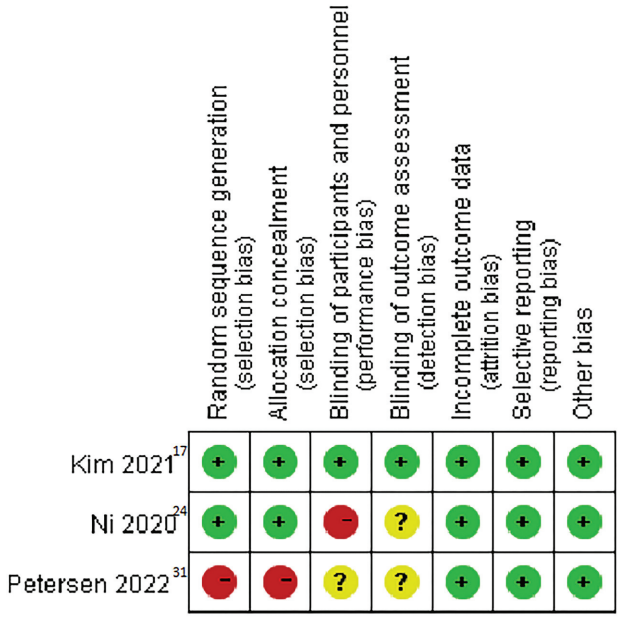


**Figure 2.** Assessment of quality for the prospective comparative studies according to the Cochrane risk of bias tool. Green indicates low risk of bias, yellow indicates unclear risk of bias, and red indicates high risk of bias.

patients were selected. There were 3 prospective comparative studies[17,24,31] and 6 retrospective comparative studies.[4,6,16,21,28,33] As for the method of TXA administration, 2 studies[6,21] opted for combined IV/topical application, 1 study[4] used IV or topical application, 1 study[33] used topical application, and 5 studies[16,17,24,28,31] used IV application.

## Quality Assessment

The quality of the 3 prospective comparative studies as assessed by the "deviation risk" of the Cochrane Collaboration is shown in Figure 2. The NOS scores of the 6 retrospective comparative studies as assessed by the NOS are shown in Table 1; 2 studies scored 8 and 4 studies scored 7, indicating good quality overall.

## Characteristics of the Included Studies

Baseline information is presented in Table 2. The methods used to assess thrombosis in the studies included in the meta-analysis are shown in Table 3.

## Total Blood Loss

Total blood loss after HTO was evaluated in 7 included studies[4,6,16,17,21,24,28] involving 881 patients (Figure 3). The heterogeneity of the studies was statistically significant ($P < .00001$; $I^2 = 87\%$). Significant differences were found between the TXA and control groups in total blood loss (MD, –273.96; 95% CI, –326.57 to −221.35; $P < .00001$). The results of the subgroup analysis according to method of TXA administration were as follows: IV (MD, –326.38; 95% CI, –393.01 to −259.75; $P < .00001$), topical (MD, –209.00; 95% CI, –288.45 to −129.55; $P < .00001$), and combined IV/topical (MD, –188.44; 95% CI, –383.33 to 6.45; $P = .06$). No significant differences were found among the subgroups ($P = .06$).

## Drainage Volume

Six studies[4,16,17,24,28,33] reported postoperative day (POD) 1 drainage volume (Figure 4A), of which 3 studies[4,16,33] reported POD2 drainage volume (Figure 4B). Eight studies[4,16,17,21,24,28,31,33] reported data on total drainage volume (Figure 4C).

The heterogeneity of studies with POD1 drainage volume was statistically significant ($P < .00001$; $I^2 = 96\%$), and significant differences were found between the TXA and control groups (MD, −129.50; 95% CI, −172.36 to −86.64; $P < .00001$). The results of the subgroup analysis were as follows: IV (MD, −139.66; 95% CI, −175.47 to −103.86; $P < .00001$) and topical (MD, −96.80; 95% CI, −134.56 to −59.03; $P < .00001$), with no significant differences found among the subgroups ($P = .11$).

The heterogeneity of studies with POD2 drainage volume was not significant ($P = .52$; $I^2 = 0\%$), and no significant differences were found between the TXA and control groups (MD, −2.82; 95% CI, −6.44 to 0.81; $P = .13$). The results of the subgroup analysis were as follows: IV (MD,

TABLE 1
Newcastle-Ottawa Scale Scores for Retrospective Comparative Studies[a]

| | Selection Items (max 4 points) | | | | | Outcome/Exposure Items (max 3 points) | | | |
|---|---|---|---|---|---|---|---|---|---|
| Study | 1 | 2 | 3 | 4 | Comparability (max 2 points) | 5 | 6 | 7 | Total (max 9 points)[b] |
| Bian (2021)[4] | ★ | ★ | ★ | ★ | ★ | ★ | ★ | ★ | 8 |
| Chen (2020)[6] | ★ | ★ | ★ | ★ | ★ | ★ | ★ | — | 7 |
| Kim (2018)[16] | ★ | ★ | ★ | ★ | ★ | — | ★ | ★ | 7 |
| Luo (2022)[21] | ★ | ★ | ★ | ★ | ★★ | ★ | — | — | 7 |
| Palanisamy (2018)[28] | ★ | ★ | ★ | ★ | ★★ | ★ | — | — | 7 |
| Suh (2018)[33] | ★ | ★ | ★ | ★ | ★★ | ★ | ★ | — | 8 |

[a]Newcastle-Ottawa Scale items: 1 = representativeness of the exposed cohort; 2 = selection of the nonexposed cohort; 3 = ascertainment of exposure; 4 = demonstration that outcome of interest was not present at start of study; 5 = assessment of outcome; 6 = was follow-up long enough for outcomes to occur; 7 = adequacy of follow-up of cohorts. Dash represents no point.

[b]Scoring: Good quality = 3 or 4 stars in selection domain *and* 1 or 2 stars in comparability domain *and* 2 or 3 stars in outcome/exposure domain. Fair quality = 2 stars in selection domain *and* 1 or 2 stars in comparability domain *and* 2 or 3 stars in outcome/exposure domain. Poor quality = 0 or 1 star in selection domain *or* 0 stars in comparability domain *or* 0 or 1 star in outcome/exposure domain.

TABLE 2
Baseline Characteristics of the Included Studies[a]

| | Sample Size | | | BMI, $kg/m^2$ | | Age, y | | Sex, Male/Female | |
|---|---|---|---|---|---|---|---|---|---|
| Study | All | TXA | Control | TXA | Control | TXA | Control | TXA | Control |
| Bian (2021)[4] | 191 | IV: 72<br>Topical: 64 | 55 | IV: 25 ± 4<br>Topical: 25 ± 4 | 24 ± 3 | IV: 56 ± 5<br>Topical: 54 ± 7 | 56 ± 6 | IV: 13/59<br>Topical: 9/55 | 10/45 |
| Chen (2020)[6] | 100 | 52 IV/topical[b] | 48 | 27.3 ± 4.0 | 28.5 ± 4.2 | 58.3 ± 10.4 | 56.6 ± 10.2 | 20/32 | 22/26 |
| Kim (2018)[16] | 150 | 75 IV | 75 | 26.3 ± 3.1I | 26.4 ± 2.6 | 55.0 ± 6.8 | 55.7 ± 5.5 | 17/58 | 14/61 |
| Kim (2021)[17] | 73 | 37 IV | 36 | — | — | 54.9 ± 9.2 | 55.3 ± 7.0 | 10/27 | 9/27 |
| Luo (2022)[21] | 60 | 30 IV/topical[b] | 30 | 26.6 ± 2.9 | 27.6 ± 3.0 | 60.3 ± 2.6 | 60.5 ± 2.7 | 19/11 | 20/10 |
| Ni (2020)[24] | 100 | 50 IV | 50 | 23.2 ± 1.5 | 23.5 ± 1.3 | 52.5 ± 2.8 | 52.9 ± 3.1 | 10/40 | 12/38 |
| Palanisamy (2018)[28] | 152 | 66 IV | 86 | 27 ± 2 | 26 ± 2 | 58 ± 5 | 57 ± 6 | 7/59 | 9/77 |
| Petersen (2022)[31] | 52 | 26 IV | 26 | — | — | 51.1 ± 6.9 | 52.9 ± 7.1 | 16/10 | 15/11 |
| Suh (2018)[33] | 30 | 15 topical | 15 | 28.1 ± 3.9 | 26.1 ± 2.7 | 60 ± 5.6 | 56 ± 5.7 | 3/12 | 4/11 |

[a]Data are reported as mean ± SD or No. of patients. Dashes indicate data not available. BMI, body mass index; IV, intravenous; TXA, tranexamic acid.

[b]Combined intravenous and topical.

TABLE 3
Methods of Evaluating Thrombosis

| Study | Method |
|---|---|
| Bian (2021)[4] | No routine screening. Doppler ultrasound applied when thrombotic symptoms present. |
| Chen (2020)[6] | Doppler ultrasound applied when thrombosis was suspected or before discharge. |
| Kim (2018)[16] | Routine computed tomography venography on postoperative day 5. Doppler ultrasound applied when thrombotic symptoms present. |
| Luo (2022)[21] | Doppler ultrasound applied when thrombosis was suspected. |
| Ni (2020)[24] | Routine Doppler ultrasound on postoperative day 5. Examination performed when thrombotic symptoms were found during follow-up. |
| Palanisamy (2018)[28] | No routine screening. Thrombosis data collected from outpatient follow-up records. |
| Petersen (2022)[31] | The Wells score was applied to evaluate the risk of thrombosis, and Doppler ultrasound applied for screening when the score $\geq$2. |

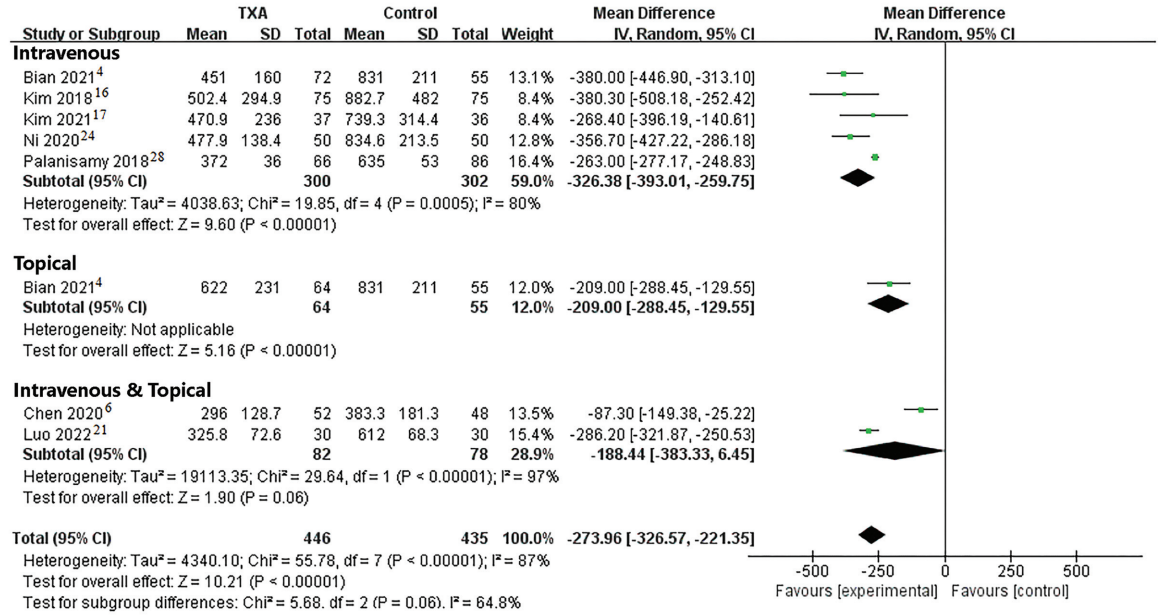


**Figure 3.** Forest plot of studies on total blood loss. IV, inverse variance; TXA, tranexamic acid.

−3.68; 95% CI, −8.53 to 1.17; $P$ = .14) and topical (MD, −1.73; 95% CI, −7.18 to 3.71; $P$ = .53), with no significant differences found among the subgroups ($P$ = .60).

The heterogeneity of studies on total drainage volume was statistically significant ($P$ < .00001; $I^2$ = 95%), and significant differences were found between the TXA and control groups (MD, −147.28; 95% CI, −192.64 to −101.92; $P$ < .00001). The results of the subgroup analysis were as follows: IV (MD, −157.69; 95% CI, −208.05 to −107.33; $P$ < .00001), topical (MD, −89.74; 95% CI, −102.73 to −76.76; $P$ < .00001), and combined IV/topical (MD, −164.50; 95% CI, −194.27 to −134.73; $P$ < .00001). Significant differences were found among the subgroups.

## Hemoglobin Decrease

The decrease in hemoglobin was reported on POD1 in 4 studies[16,17,24,33] (Figure 5A), on POD2 in 5 studies[16,17,24,28,31] (Figure 5B), and on POD5 in 3 studies[16,17,24] (Figure 5C).

The heterogeneity of studies on POD1 hemoglobin decrease was statistically significant ($P$ = .10; $I^2$ = 51%), and significant differences were found between the TXA and control groups (MD, –0.91; 95% CI, –1.20 to −0.61; $P$ < .00001). There were significant differences in the subgroup analysis: IV (MD, −0.99; 95% CI, −1.31 to −0.67; $P$ < .00001) and topical (MD, −0.60; 95% CI, −1.07 to −0.13; $P$ = .01). No significant differences were found between the 2 subgroups ($P$ = .17).

The heterogeneity of studies with POD2 hemoglobin decrease was not significant ($P$ = .43; $I^2$ = 0%). There were significant differences in POD2 hemoglobin decrease between the TXA and control groups (MD, −0.95; 95% CI, −1.11 to −0.79; $P$ < .00001). Similarly, the heterogeneity of studies with POD5 hemoglobin decrease was not significant ($P$ = .18; $I^2$ = 41%), and there were significant differences in POD5 hemoglobin decrease between the TXA and control groups (MD, −1.01; 95% CI, −1.27 to −0.75; $P$ < .00001).

## Wound Complications

Eight studies monitored wound complications, including hematoma (Figure 6A) and infection (Figure 6B).[4,6,17,21,24,28,31,33]

The heterogeneity of hematoma studies was not significant ($P$ = .91; $I^2$ = 0%), and there were no differences between the TXA and control groups (RR, 0.53; 95% CI, 0.20-1.42; $P$ = .21). Subgroup analysis indicated differences according to TXA administration: IV (RR, 0.54; 95% CI, 0.10-2.94; $P$ = .48), topical (RR, 0.93; 95% CI, 0.13-6.62; $P$ = .94), and combined IV/topical (RR, 0.37; 95% CI, 0.08-1.81; $P$ = .22).

The heterogeneity of infection studies was not significant ($P$ = .95; $I^2$ = 0%), and there were no significant differences in infection between TXA and controls (RR, 0.48; 95% CI, 0.17-1.39; $P$ = .18). Subgroup analysis indicated no significant differences: IV (RR, 0.59; 95% CI, 0.14-2.46; $P$ = .47), topical (RR, 0.29; 95% CI, 0.01 to 6.91; $P$ = .44), and combined IV/topical (RR, 0.41; 95% CI, 0.06-2.70; $P$ = .35).

## Postoperative Thrombosis

Seven studies[4,6,16,21,24,28,31] provided data on postoperative thrombosis (Figure 7). Postoperative thrombosis was found only in the study of Chen et al.[6] There was no difference in the prevalence of postoperative thrombosis between TXA and controls (RR, 0.46; 95% CI, 0.09-2.41; $P$ = .36).

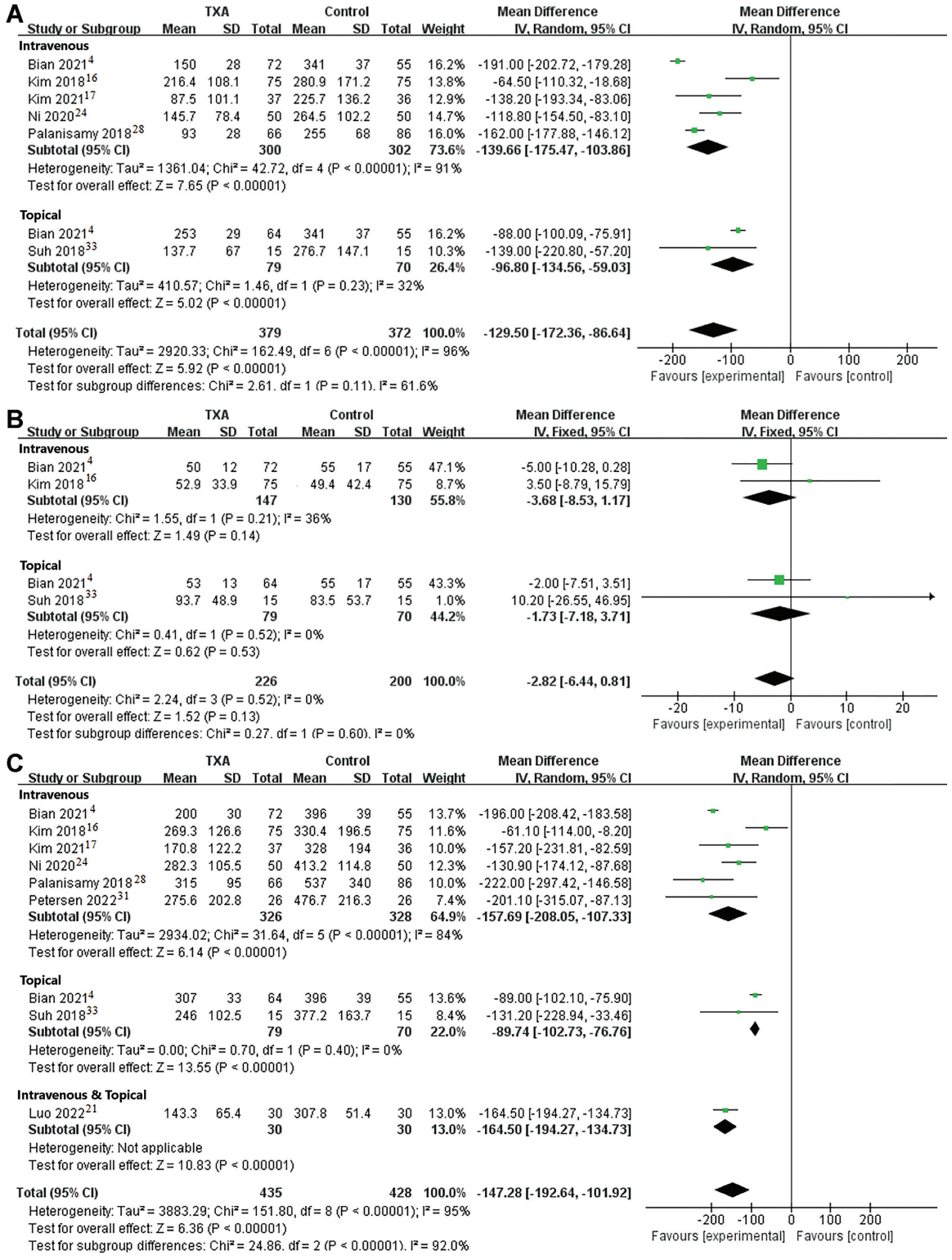


**Figure 4.** Forest plots of studies on (A) postoperative day (POD) 1 drainage volume, (B) POD2 drainage volume, and (C) total drainage volume. IV, inverse variance; TXA, tranexamic acid.

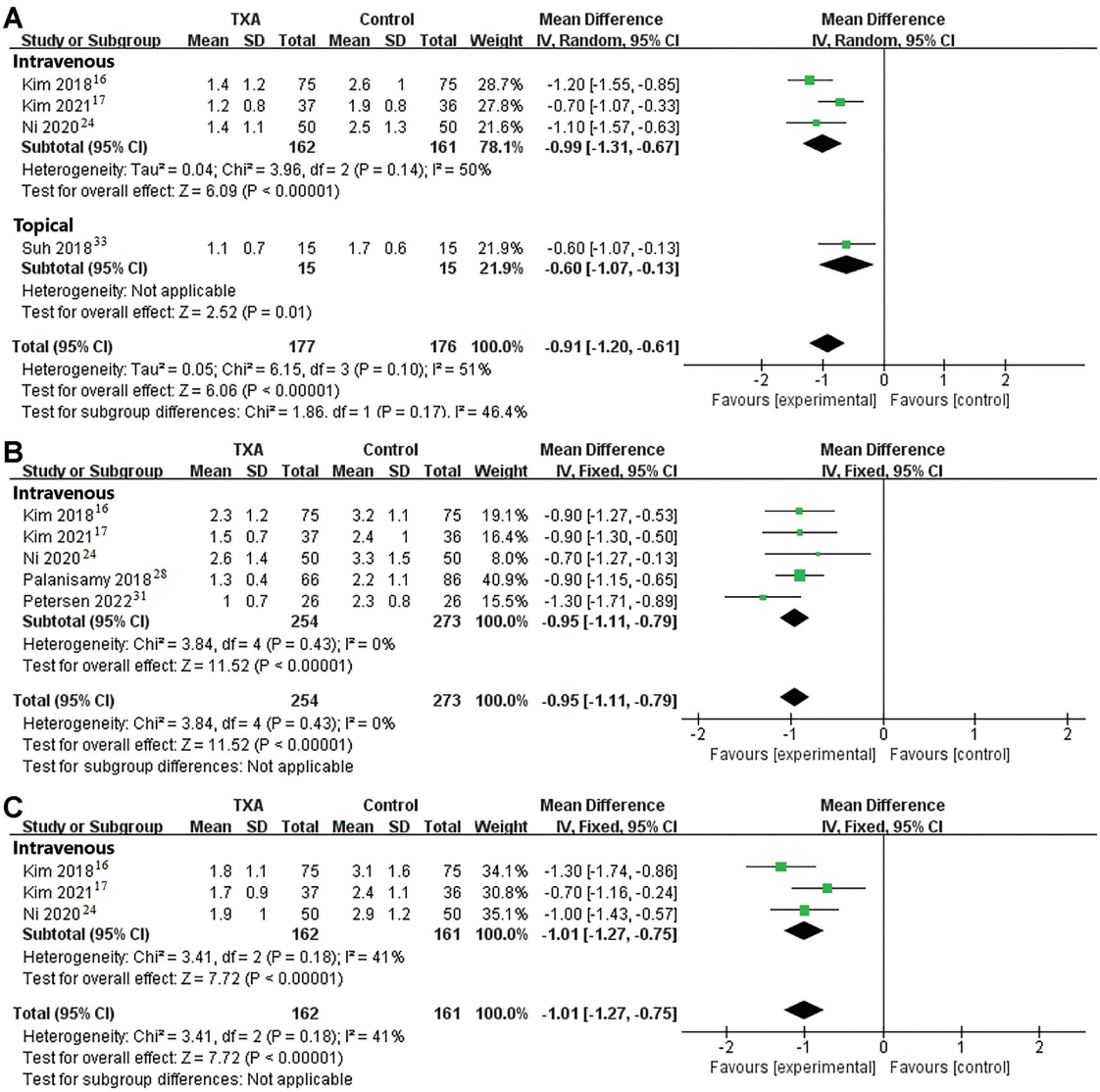


**Figure 5.** Forest plots of studies on hemoglobin decrease at (A) postoperative day (POD) 1, (B) POD2, and (C) POD5. IV, inverse variance; TXA, tranexamic acid.

## Blood Transfusion

Eight studies reported data on blood transfusion (Figure 8).[4,6,16,17,21,24,28,31] The heterogeneity of blood transfusion studies was not significant ($P$ = .82; $I^2$ = 0%). There were no differences in prevalence of blood transfusion between TXA and controls (RR, 0.25; 95% CI, 0.03-2.21; $P$ = .21).

## DISCUSSION

The study findings indicated that TXA reduced postoperative hemorrhage in HTO and did not affect the prevalence of wound complications, blood transfusion, or postoperative thrombosis.

TXA has widespread application in orthopaedic surgery, and related studies have confirmed that TXA could reduce postoperative hemorrhage.[8,9,25,36] TXA reduced blood loss in knee surgery, especially total knee arthroplasty.[10,19,29,37] In this meta-analysis, TXA significantly reduced postoperative hemorrhage, including total blood loss, hemoglobin decrease, and total drainage volume. Significant differences were found among the 2 groups, and the TXA group had lower indicators: total blood loss, hemoglobin decrease, and total drainage volume ($P$ < .00001 for all). Among them, TXA effectively reduced the drainage volume of POD1 ($P$ < .00001) but failed to significantly reduce the drainage volume of POD2 ($P$ = .13). This is because there was more hemorrhage in POD1 and the effect of TXA was more significant. In terms of total hemorrhage, the clinical effect of TXA was worthy of recognition. Besides, wound complications, including hematoma ($P$ = .21) and infection ($P$ = .18), had no difference between the 2 groups. No difference was found in postoperative thrombosis ($P$ = .36) and blood transfusion ($P$ = .21).

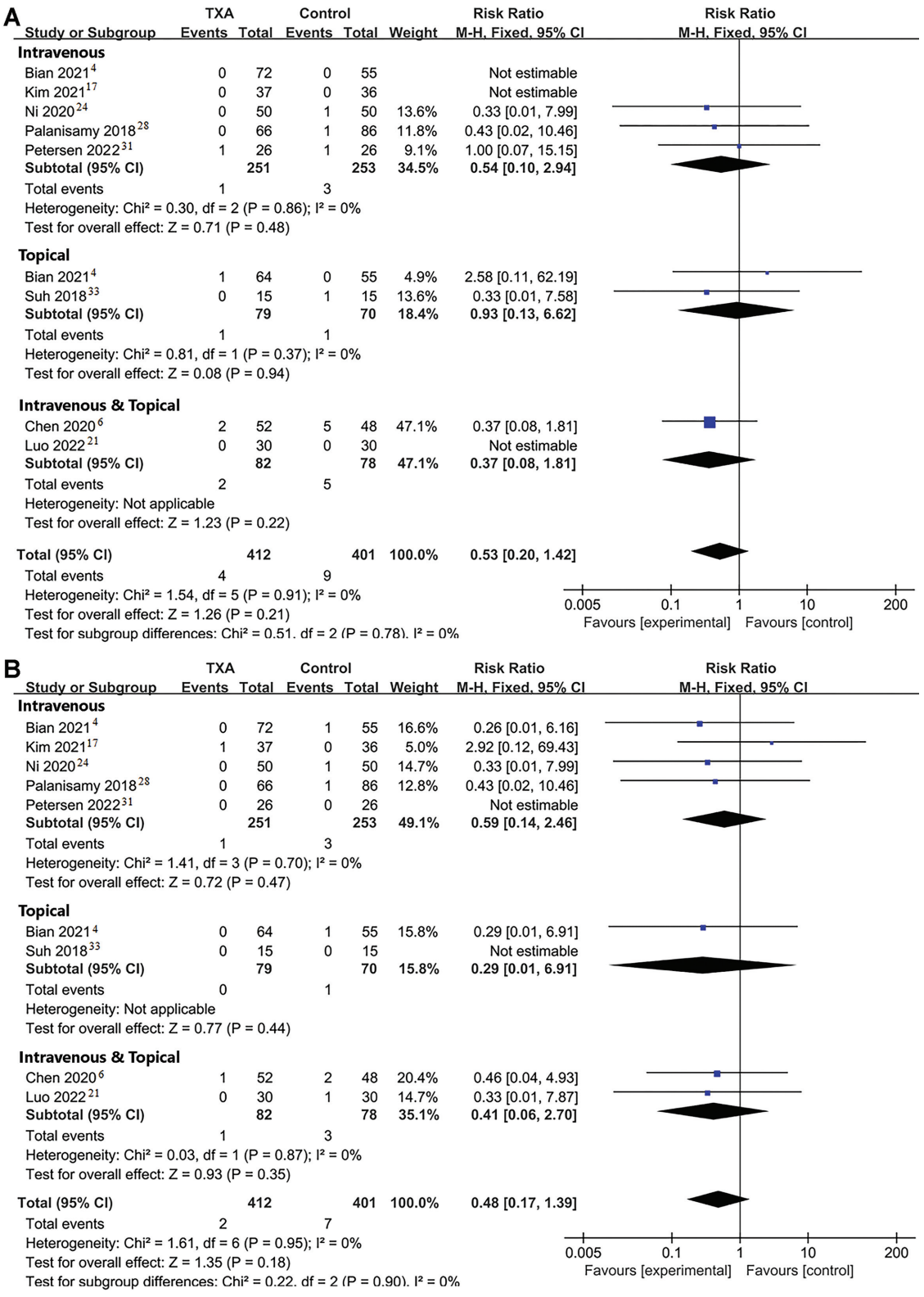


**Figure 6.** Forest plots of studies on (A) hematoma and (B) infection. M-H, Mantel-Haenszel; TXA, tranexamic acid.

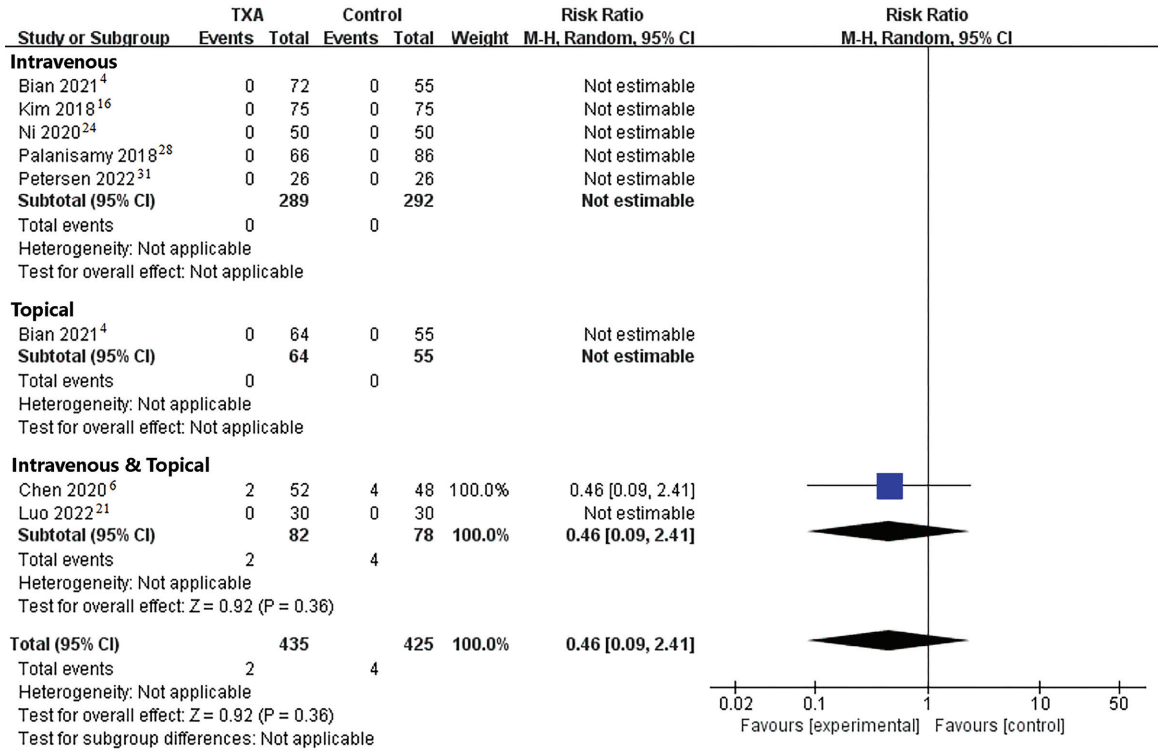


**Figure 7.** Forest plot of studies on postoperative thrombosis prevalence. M-H, Mantel-Haenszel; TXA, tranexamic acid.

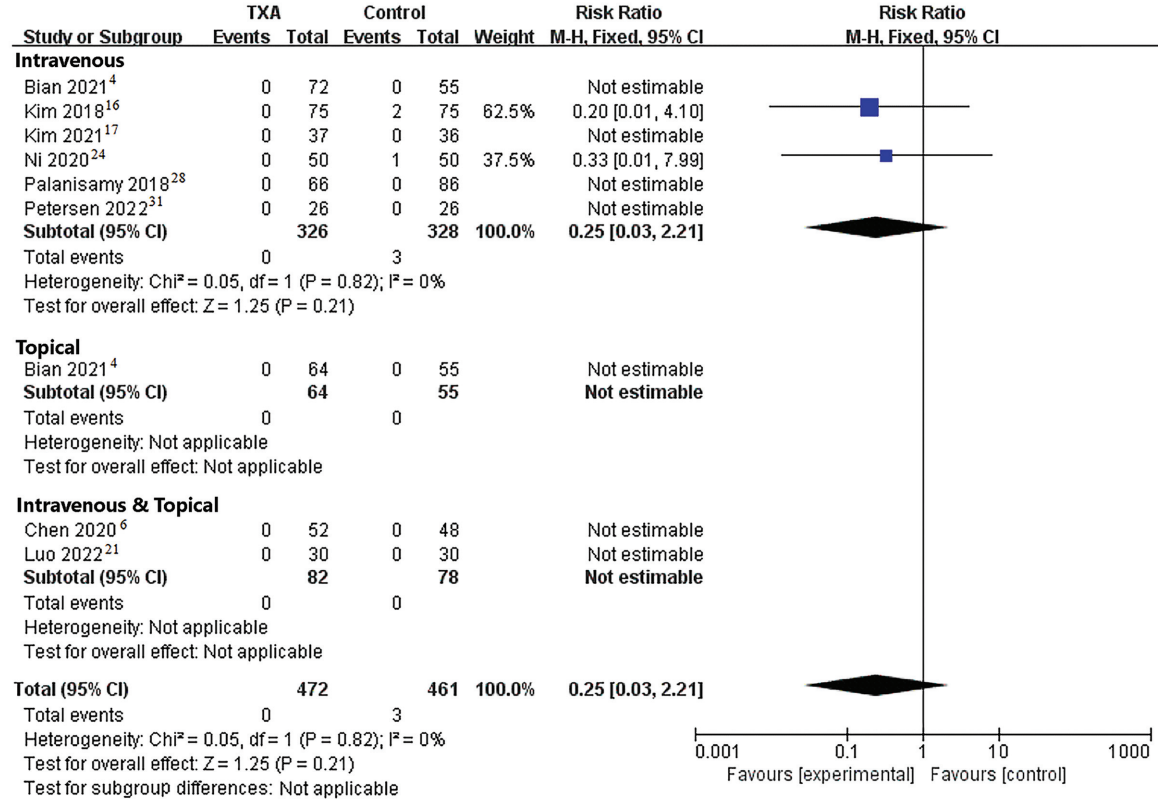


**Figure 8.** Forest plot of studies on blood transfusion prevalence. M-H, Mantel-Haenszel; TXA, tranexamic acid.

Our subgroup analysis of hemorrhage-related outcomes according to TXA administration route showed that either IV or topical application was able to effectively reduce total blood loss ($P < .00001$ for both), but combined IV/topical application did not lead to significant differences compared with controls ($P = .06$). Subgroup analysis also showed that total drainage volume was reduced after TXA through all 3 routes of administration ($P < .00001$ for all). The reasons for the different hemorrhage-related results mainly came from the study of Chen et al.[6] Compared with other included studies, the amount of postoperative hemorrhage reported by Chen et al[6] was less, and the effect of TXA was less significant than in other studies. This could be related to the differences in TXA medication regimens and perioperative hemostasis management. When total blood loss from the Chen et al[6] study was excluded, the subgroup analysis led to the following conclusions: the IV route and the combined IV/topical route were superior to the topical route in improving hemorrhage, and although the difference was not significant, it did exist.

Several studies have shown that TXA after HTO or distal femoral osteotomy reduces hemoglobin decrease.[6,16,24,28,32,33] Our analysis indicated that TXA was able to effectively improve postoperative hemoglobin level, which could help reduce the incidence of postoperative anemia. At POD1, POD2, and POD5, TXA was found to effectively improve hemoglobin decrease. However, we found no advantage of TXA in terms of the prevalence of blood transfusion. Our results indicated that moderate heterogeneity was found in the meta-analysis of hemoglobin decrease on POD1 ($P = .10$; $I^2 = 51\%$). Based on the subgroup analysis using a random-effects model, there was a significant improvement for POD1 hemoglobin with either IV or topical administration. Although there was no significant difference in the effect of the 2 routes of administration, it was observed that IV administration was more advantageous than the topical route.

The meta-analysis for wound complications included data from 8 studies[4,6,17,21,24,28,31,33] and indicated that TXA had no effect on wound complications, including hematoma and infection. Subgroup analysis according to different administration methods showed that there was no difference within each subgroup. Similarly, a meta-analysis analyzing the management of wound complications of osteotomy found that TXA did little to reduce wound complications.[39] However, Ma et al[22] noted a significant reduction in wound complications after applying TXA. There is still no consensus on the effect of TXA on wound complications in HTO.

TXA did not significantly increase the prevalence of postoperative thrombosis, which was reported in 7 studies.[4,6,16,21,24,28,31] Of these, only 1 study[6] showed thrombotic events, in 2 patients in the TXA group and 4 patients in the control group. The optimal dose of TXA was considered safe based on its mechanism of action, which inhibited only wound fibrinolysis and did not affect the systemic circulatory system.[3] In fact, reviews have indicated that many studies have shown that TXA had no effect on thrombosis,[2,14] which is reliable for the clinical use of TXA.

It is clear that, as previously mentioned, there are many studies with different results and much controversy regarding wound complications and postoperative thrombosis. In HTO, the effects of TXA were different among different routes of administration, although not statistically significant. This difference should not be overlooked. In fact, in other orthopaedic procedures, some studies proved the advantages of TXA through the IV combined with topical route over the IV or topical route alone.[13,20,27] In addition, a meta-analysis indicated that a single dose of IV-administered TXA was superior to a single dose of topically administered TXA.[42] More studies are needed to draw accurate and significant conclusions on these issues.

We did not conduct a meta-analysis on the dose of TXA administration because the dose of TXA varies. As for the IV route, 2 studies used repeated IV 2 doses of 2 g TXA,[17,28] and Kim et al[16] used repeated IV 3 doses of 10 mg/kg TXA. Three other studies used single doses of 1 g,[31] 10 mg/kg,[4] and 50 mg/kg,[24] respectively. As for the topical route, the regimens were single doses of 2 g[33] and 10 mg/kg[4], respectively. As for the IV combined with topical route, Chen et al[6] used 1 g IV combined with 1 g topical administration. Luo et al[21] used repeated doses of 1 g twice by IV route, combined with 3 g topical administration. All these different dose regimens can reduce the postoperative hemorrhage, but there are no studies comparing the effects of different regimens in HTO.

### Limitations

Several limitations exist in this review. As there are still few published articles about TXA during the HTO perioperative period, we were only able to include 3 prospective comparative studies and 6 retrospective comparative studies. Second, although subgroup analyses were performed for different administration routes, each subgroup included fewer studies and inevitably increased bias. Studies with larger sample sizes and longer follow-up are needed to improve statistical confidence because of the lower rates of some indicators such as blood transfusion and postoperative thrombosis.

## CONCLUSION

Our systematic review demonstrated that TXA could effectively reduce postoperative hemorrhage in HTO, and it did not affect wound complications, blood transfusion, and postoperative thrombosis.

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