

INPLASY PROTOCOL

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submission:** Not reported.

Conflicts of interest:
None declared.

INTRODUCTION

Review question / Objective: Recently, the administration of Tranexamic acid (TXA) has gradually been applied in the treatment of intertrochanteric fracture patients

Efficacy and safety of tranexamic acid for patients with intertrochanteric fractures treated with intramedullary fixation: a systematic review and meta-analysis of current evidence in randomized controlled trials

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Review question / Objective: Recently, the administration of Tranexamic acid (TXA) has gradually been applied in the treatment of intertrochanteric fracture patients undergoing intramedullary fixation surgery with promising results. However, a common limitation of all these trials is the sample size, leading to underpowered studies and possible Type II errors. The efficacy and safety of TXA for patients with intertrochanteric fractures treated with intramedullary fixation are still controversial. Therefore, we performed this systematic review and meta-analysis to evaluate the efficacy and safety of TXA for patients with intertrochanteric fractures treated with intramedullary fixation.

Information sources: Electronic databases, including Cochrane, PubMed, and EMBASE. After the electronic search is completed, manual searches were carried out on related literatures and references to find potential eligible studies.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 07 August 2022 and was last updated on 07 August 2022 (registration number INPLASY202280027).

undergoing intramedullary fixation surgery with promising results. However, a common limitation of all these trials is the sample size, leading to underpowered studies and possible Type II errors. The efficacy and safety of TXA for patients with

intertrochanteric fractures treated with intramedullary fixation are still controversial. Therefore, we performed this systematic review and meta-analysis to evaluate the efficacy and safety of TXA for patients with intertrochanteric fractures treated with intramedullary fixation.

Condition being studied: Intertrochanteric fractures are mostly related to osteoporosis and are low-violence fractures, which are more common in geriatric females. As the population ages, the incidence of intertrochanteric fractures increases rapidly, accounting for almost half of all hip fractures. Despite recent advances in orthopedic surgery techniques and instruments, the intraoperative bleed loss (IBL) in geriatric patients with intertrochanteric fractures has been significantly reduced, but they are still often accompanied by massive blood loss, especially hidden blood loss (HBL), and the prevalence of postoperative anemia is high. Tranexamic acid (TXA) is a synthetic lysine analogue that acts by inhibiting plasminogen activation. TXA has been widely used in spine, shoulder, hip, and knee surgery, showing that its efficacy is positive and can effectively reduce the amount of bleeding. Recently, the administration of TXA has gradually been applied in the treatment of intertrochanteric fracture patients undergoing intramedullary fixation surgery with promising results. However, a common limitation of all these trials is the sample size, leading to underpowered studies and possible Type II errors. The efficacy and safety of TXA for patients with intertrochanteric fractures treated with intramedullary fixation are still controversial[18]. Therefore, we performed this systematic review and meta-analysis to evaluate the efficacy and safety of TXA for patients with intertrochanteric fractures treated with intramedullary fixation.

METHODS

Participant or population: Patients were adults diagnosed with intertrochanteric fractures. The treatment method is intramedullary fixation, include PFNA,

Trochanteric femoral nail advanced, Gamma nail, short intramedullary nail, etc.

Intervention: Patients were treated with TXA.

Comparator: Patients who received placebo, saline, or blank control.

Study designs to be included: The studies were original, randomized control trials (RCTs) only.

Eligibility criteria: The inclusion criteria for this study were as follows: (1) Population: patients were adults diagnosed with intertrochanteric fractures. The treatment method is intramedullary fixation, include PFNA, Trochanteric femoral nail advanced, Gamma nail, short intramedullary nail, etc. (2) Intervention: patients were treated with TXA. (3) Comparator: patients who received placebo, saline, or blank control. (4) Outcomes: one of the following outcomes was reported. Bleeding-related outcomes consisting of total blood loss (TBL), IBL, HBL, postoperative drainage (POD), blood transfusion rate (BTR), postoperative hemoglobin (Hb) on day 1 or day 3, postoperative hematocrit (Hct) on day 1 or day 3. Non-bleeding-related outcomes include the length of hospital stays and surgical time. Thromboembolic events were defined as deep vein thrombosis, pulmonary embolism, myocardial infarction, or ischemic stroke. Other complications include wound complications (wound hematoma or infection), respiratory infection, and renal failure. And postoperative mortality. (5) Study design: the studies were original, randomized control trials (RCTs) only.

Information sources: Electronic databases, including Cochrane, PubMed, and EMBASE. After the electronic search is completed, manual searches were carried out on related literatures and references to find potential eligible studies.

Main outcome(s): Bleeding-related outcomes consisting of total blood loss (TBL), IBL, HBL, postoperative drainage (POD), blood transfusion rate (BTR),

postoperative hemoglobin (Hb) on day 1 or day 3, postoperative hematocrit (Hct) on day 1 or day 3. Non-bleeding-related outcomes include the length of hospital stays and surgical time. Thromboembolic events were defined as deep vein thrombosis, pulmonary embolism, myocardial infarction, or ischemic stroke. Other complications include wound complications (wound hematoma or infection), respiratory infection, and renal failure. And postoperative mortality.

Quality assessment / Risk of bias analysis:

According to Cochrane Collaboration for Systematic Reviews, the methodological quality of trials included in this study was evaluated independently by two reviewers. The following items were considered: random sequence generation, allocation sequence concealment, blinding of participants and personnel, blinding of outcomes assessment, incomplete outcome data, selective reporting, and other bias. Each item was assessed as "Low risk of bias," "Unclear risk of bias," or "High risk of bias." If the item was reported incorrectly, the judgment was "High risk of bias." If the item was reported inadequately, the judgment was "Unclear risk of bias." If the item was reported correctly and adequately, the judgment was "Low risk of bias." Disagreements between the two reviewers were resolved by discussion and consensus. In case of persisting disagreement, this was resolved by a third reviewer.

Strategy of data synthesis: The statistical analysis was independently performed with RevMan software (Version 5.4; Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2020) by two reviewers. The mean difference (MD) between groups of TXA and control was reported with 95% confidence interval (95% CI) and performed to evaluate continuous variables such as TBL. The risk ratio (RR) with 95% CI was performed to evaluate dichotomous outcomes such as BTR. To measure heterogeneity between studies, we used the I^2 statistic. Furthermore, heterogeneity was accepted, and the randomized-effects model was

performed, when I^2 was $>50\%$. Otherwise, the fixed-effects model was performed. Forest plots were used to graphically represent the difference in outcomes of groups of TXA and control and for all included studies. If P values were <0.05 , the results were considered statistically significant.

Subgroup analysis: None.

Sensitivity analysis: A sensitivity analysis was performed by individually removing each study to determine whether the pooled results changed.

Country(ies) involved: China.

Keywords: tranexamic acid; intertrochanteric fractures; hip fractures; intramedullary fixation; proximal femoral nail autorotation.

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