



## Review

# Tranexamic acid versus aminocaproic acid for blood management after total knee and total hip arthroplasty: A systematic review and meta-analysis



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## ABSTRACT

**Objective:** To compare the efficacy and safety of tranexamic acid and aminocaproic acid for reducing blood loss and transfusion requirements after total knee and total hip arthroplasty.

**Methods:** We conduct electronic searches of Medline (1966–2017.11), Embase (1980–2017.11), ScienceDirect (1985–2017.11) and the Cochrane Library (1900–2017.11). The primary outcomes, including total blood loss, hemoglobin decline and transfusion requirements. Secondary outcomes include length of hospital stay and postoperative complications such as the incidence of deep vein thrombosis and pulmonary embolism. Each outcome is combined and calculated using the statistical software STATA 12.0. Fixed/random effect model is adopted based on the heterogeneity tested by  $I^2$  statistic.

**Results:** A total of 1714 patients are analyzed across three randomized controlled trials (RCTs) and one non-RCT. The present meta-analysis reveals that TXA is associated with a significantly reduction of total blood loss and postoperative hemoglobin drop compared with EACA. No significant differences are identified in terms of transfusion rates, length of hospital stay, and the incidence of postoperative complications.

**Conclusion:** Although total blood loss and postoperative hemoglobin drop are significant greater in EACA groups, there is no significant difference between TXA and EACA groups in terms of transfusion rates. Based on the current evidence available, higher quality RCTs are still required for further research.

## 1. Introduction

Total knee arthroplasty (TKA) and total hip arthroplasty (THA) are successful surgical procedures for the treatment of end-stage joint osteoarthritis. It is reported that more than 600 thousand TKAs and 500 thousand THAs are conducted in the US annually and there is an increase in demand in the next few years [1,2]. However, the process is associated with massive perioperative blood loss which increases morbidity especially for elderly individuals. There are several protocols to reduce postoperative blood loss after total joint arthroplasty (TJA) including topical or intravenous hemostatic agents, minimally invasive procedures, controlled hypotensive anesthesia and the use of various blood-salvaging techniques [3–6].

The administration of antifibrinolytic medications for TJA has showed improved outcomes for perioperative blood management. Tranexamic acid (TXA), and epsilon aminocaproic acid (EACA) are the most commonly used antifibrinolytics, which can inhibit plasmin, plasminogen, and fibrin from combining and directly inhibit plasmin activity, thereby preventing premature clot dissolution [7]. Previous studies have confirmed that both drugs are associated with a

significantly reduction of perioperative blood loss and transfusion requirements in cardiac surgery [8,9]. Recently, the use of TXA is popular in major orthopedic surgery. Although the administration of TXA in reducing blood loss in TJA has been well-documented, the use of EACA is less studied. EACA is cheaper and does not carry any risk of anaphylaxis. As cost efficacy is becoming an important factor in providing high quality medical care, the administration of EACA leads to further research.

Currently, few studies have focused on the comparison of TXA and EACA in the clinical setting for blood management after arthroplasties. Based on the clinical similarities of these drugs, we perform a systematic review and meta-analysis to compare the efficacy and safety of TXA and EACA for reducing blood loss and transfusion requirements after TJA. We hypothesis that TXA showed similar outcomes for blood management compared with EACA in arthroplasties.

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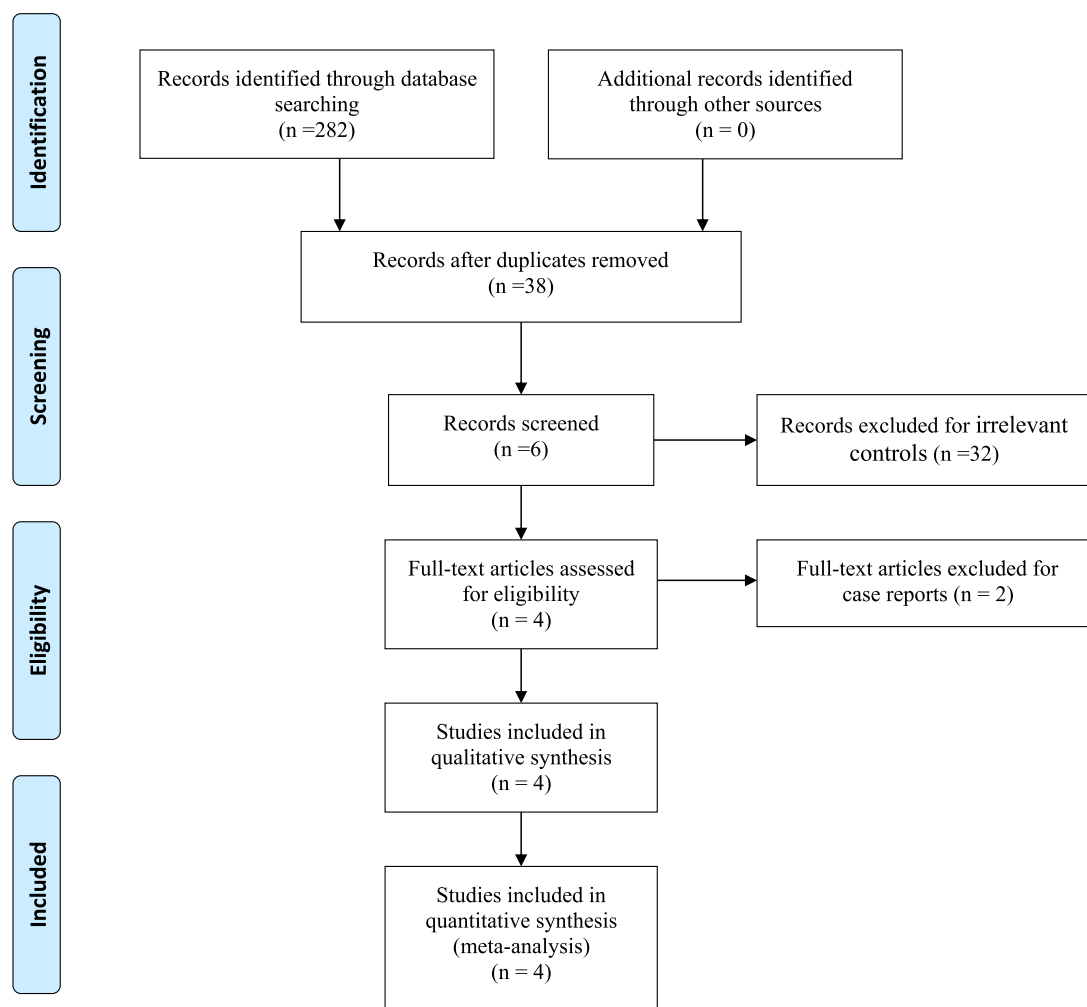


Fig. 1. Search results and the selection procedure.

## 2. Methods

### 2.1. Search strategy

We conduct electronic searches of Medline (1966–2017.11), PubMed (1966–2017.11), Embase (1980–2017.11), ScienceDirect (1985–2017.11) and the Cochrane Library (1900–2017.11). The following key words are used in combination with Boolean operators AND or OR: “total knee arthroplasty OR replacement”, “total hip arthroplasty OR replacement”, “aminocaproic acid”, “tranexamic acid” and “blood loss OR bleeding OR transfusion”. References of the included studies are also scanned for potentially relevant articles. No restrictions are placed on the publication language. Two reviewers independently assess the titles and abstracts of all the reports identified by the electronic and manual searches. Subsequently, the full text of the potential articles which meet the inclusion criteria are screened, and a final decision is made. Disagreements are resolved by consulting an additional reviewer Fig. 1.

### 2.2. Inclusion and exclusion criteria

Studies are considered eligible if they meet the following criteria: (1) Randomized control trails (RCTs) and non-RCTs; (2) Patients undergo TKA or THA, **group 1** receive intravenous TXA and **group 2** intravenous EACA; (3) The primary outcomes, including total blood loss, hemoglobin decline and transfusion requirements. Secondary outcomes include length of hospital stay and postoperative complications such as

the incidence of deep vein thrombosis (DVT) and pulmonary embolism (PE). Articles will be excluded from the present meta-analysis for incomplete data, case reports, conference abstracts or review articles.

### 2.3. Selection criteria

Two authors independently review all the abstracts of the potential studies identified by the above searches. After an initial decision, full text of the studies that potentially meet the inclusion criteria are reviewed and final decision is made. A senior reviewer is consult in case of disagreement regarding which studies to include.

### 2.4. Data extraction

A standard form for data extraction is printed for data extraction. Two authors independently extract the relevant data from the included articles. Details of incomplete data of included studies are obtained by consulting the corresponding authors. Following data are extracted: First author names, published year, study design, country, samples size, comparable baseline, anesthesia methods, surgical type, drug intervention, transfusion trigger, and follow up. Other relevant data are also extracted from individual articles.

### 2.5. Quality assessment

Two authors perform the assessment of risk of bias for included RCTs according to the Cochrane Handbook for Systematic Reviews of

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