

# Tranexamic Acid in Shoulder Arthroplasty. A Comprehensive Review

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## ABSTRACT

**Objectives:** Total shoulder arthroplasty (TSA) represents a major orthopedic procedure with significant blood loss and transfusion rates up to 43%. Tranexamic acid (TXA), a synthetic amino acid derivative, functioning by inhibiting the conversion of plasminogen to plasmin, has been proven to reduce blood loss in total knee or hip arthroplasty. However, very few studies exist regarding shoulder arthroplasty. The aim of the present review is to evaluate its effectiveness in shoulder arthroplasty.

**Materials and methods:** A meticulous electronic search was performed to find articles reporting the results of TXA administration in TSA or reverse total shoulder arthroplasty (RTSA). Patients' demographics, dose and timing of TXA administration, the type of control group, mean hemoglobin reduction, transfusion rate and total blood loss were evaluated. A total of eight studies including 981 patients were identified. Five hundred and thirty patients (group 1) received TXA, while the remaining 451 comprised the control group (group 2).

**Results:** The mean postoperative reduction in hemoglobin in group 1 was found to be 2.14 g/dL (SD=0.62), compared to 2.71 g/dL (SD=0.57) of group 2; *p*-value <0.0001. Transfusion rate in group 1 was found to be 1.9%, compared to 4.9% in group 2; *p*-value=0.009. Total blood loss was found to be 714.6 mL (SD=410.4) in group 1, compared to 911.8 mL (SD=529.7) in group 2; *p*-value <0.0001.

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**Conclusions:** *The present review has shown that TXA administration in shoulder arthroplasty has effectively reduced blood loss, postoperative hemoglobin decline and need for transfusion. More research is needed, since optimization of route, timing and dosage of TXA remain to be determined.*

**Keywords:** blood management, shoulder arthroplasty, joint replacement, transfusion rate, tranexamic acid.

## INTRODUCTION

Total shoulder arthroplasty (TSA) procedures are steadily increasing, worldwide, since they provide pain relief and good functional outcomes in cases where the native glenohumeral joint has been affected by trauma, infection or arthritis (1, 2). The introduction of reverse total shoulder arthroplasty (RTSA) has expanded indications for shoulder arthroplasty, offering good function and pain relief in patients suffering from concomitant rotator cuff deficiency (1-4).

Total shoulder arthroplasty represents a major orthopedic procedure with significant blood loss (5). Blood transfusion rates following TSA range from 7.4% to 43%, while RTSA has been identified as independent risk factor for transfusion. Furthermore, there is a high risk of postoperative hematoma following RTSA, ranging from 1% to 20% (5-8).

A plethora of measures have been studied in order to minimize perioperative blood loss in TSA, including controlled hypotensive anesthesia, drug intervention, various blood-salvaging techniques and minimally invasive surgery (9, 10). Tranexamic acid (TXA), a synthetic amino acid derivative that functions by competitively inhibiting the conversion of plasminogen to plasmin, has been successfully administered through various routes [intravenous (iv), oral and topical route], aiming to reduce perioperative blood loss and subsequent need for blood transfusions in both total hip (THA) and total knee arthroplasty (TKA) (9-12). However, data regarding the safety and efficacy of TXA in TSA or RTSA is scarce (5).

The present study aims to evaluate the administration of TXA in patients undergoing TSA or RTSA, by reviewing data from the available literature. □

## MATERIALS AND METHODS

A meticulous electronic search of PubMed, Medline, Cochrane and Embase databases was performed by two independent investigators to identify articles reporting the results of TXA administration in TSA or RTSA. All databases were searched through November 2020. A structured search using “tranexamic acid”, “shoulder arthroplasty or replacement”, “reverse shoulder arthroplasty” “intravenous”, “oral” and “topical” as mesh terms was conducted.

Citations in each article were reviewed to retrieve additional references that were not located during the initial search. The present review is limited to original articles (prospective and retrospective studies as well as clinical trials encompassing a control group) written in English and published in peer-reviewed journals. Duplicate as well as irrelevant articles (e.g., articles studying the use of TXA in different shoulder procedures) were excluded.

The following data were extracted from retrieved articles: the study origin, patients' demographics, including age, gender, body mass index (BMI), American Society of Anesthesiologists (ASA) classification, procedure type (TSA or RTSA), dose and timing of TXA administration, as well as the type of control group. Furthermore, mean hemoglobin reduction, transfusion rate and total blood loss were evaluated.

A total of eight studies (four prospective and four retrospective studies) evaluating TXA administration in TSA or RTSA have been identified through an electronic meticulous literature search, all fulfilling the inclusion criteria (13-20). Six studies originated from USA, one from Korea and one from Austria.

A total of 981 patients [461 (47%) males and 520 (53%) females] were evaluated. Four hundred eighty six patients underwent TSA, while

**TABLE 1.** Dosage, timing and route of tranexamic acid administration as well as the type of control group in each study

Study	Year	Origin	Sample	Route of TXA administration	Dosage and timing	Control group
Gillespie R et al [13]	2015	USA	111	Topical	100 mL N/S 0.9% + 2 gr TXA for 5 min intraoperative during closure of thoraco-deltoid space	Same technique with 100 mL N/S 0.9%
Abildgaard JT et al [14]	2016	USA	171	I.V.	1 gr TXA following anesthesia	nothing
Friedman RJ et al [15]	2016	USA	194	I.V.	20 mg/kg during skin preparation prior to incision	nothing
Pautzenberger L et al [16]	2017	Austria	54	I.V.	100 mL N/S 0.9% +1 gr TXA 30 min prior to surgery, Repeat dosage during wound closure	100 mL N/S 30 min prior surgery
Vara AD et al [17]	2017	USA	102	I.V.	10 mg/kg TXA 60 min prior to surgery, repeat dosage during wound closure	N/S 0.9% same volume as TXA group
Kim SH et al [18]	2017	Korea	48	I.V.	500 mg TXA 60 min prior to surgery	nothing
Cvetanovich GL et al [19]	2018	USA	108	I.V.	10 mL N/S 0.9% + 1 gr TXA 10 min prior to incision	10 mL N/S 0.9%
Belay ES et al [20]	2020	USA	193	I.V.	Not available	nothing

495 were subjected to RTSA. Three hundred ninety five patients received TXA and comprised group 1, including 251 (47.4%) males and 279 (52.6%) females, with a mean age of 69 [standard deviation (SD) 2.8], mean BMI 28.3 kg/m<sup>2</sup> (SD 2.8) and mean ASA score 2.6 (SD 0.2). The remaining 451 [215 (47.7%) males and 236 (52.3%) females], with a mean age of 69.3 (SD 3.8), mean BMI 29.6 kg/m<sup>2</sup> (SD 2.2) and mean ASA score 2.6 (SD 0.2), comprised the control group (group 2).

Table 1 highlights the dosage, timing and route of TXA administration as well as the type of control group in each study. It is of note that, in seven studies, TXA was administered intravenously, while in one study the topical route was preferred.

Data was recorded and analyzed using Microsoft Excel 2010 (Microsoft Corporation, Red-

mond, Washington). Two-sided Fisher’s exact tests were used for transfusion rates between the two groups, while t-tests were used for comparison of the mean value of remaining parameters. Statistical analysis was carried out at the 5% level of significance using IBM-SPSS 24. □

### RESULTS

The mean postoperative reduction in hemoglobin in group 1 was found to be 2.1 g/dL (SD 0.57), compared to 2.68 g/dL (SD 0.62) of group 2; p-value <0.0001. Transfusion rate in group 1 was found to be 1.9%, compared to 4.9% of group 2; p-value 0.009. Total blood loss was found to be 714.6 mL (SD 410.4) in group 1, compared to 911.8 mL (SD 529.7) in group 2; p-value <0.0001.

None of the included studies reported any complications related to TXA administration. □

## DISCUSSION

Total shoulder arthroplasty and RTSA have been widely indicated for various glenohumeral joint pathologies, including end-stage shoulder arthropathy, cuff tear arthropathy, traumatic shoulder injuries, tumors, as well as prior arthroplasty failure (3, 4). However, shoulder arthroplasty has been associated with a considerable risk of perioperative blood loss, while blood transfusion rate was ranging from 4.3% to 43% (5). There are many complications of blood transfusions such as allergic reactions, immunosuppression, infection and transfusion-related cardiopulmonary injury. Furthermore, patients receiving perioperative blood transfusion have a higher risk of medical complications, including myocardial infarction, pneumonia, sepsis, cerebrovascular, as well as venous thromboembolic events and surgical complications, including periprosthetic infections, periprosthetic fractures and mechanical complications (21). Additionally, RTSA has been reported as an independent risk factor for blood transfusion, since the reverse design of implant geometry as well as the lack of intact cuff contributes to a greater potential dead space in RTSA, resulting in more bleeding. Therefore, the need for intra-and-post-operative blood management is of utmost importance in shoulder arthroplasty (6, 22).

The present review has evaluated the use of TXA in shoulder arthroplasty. The main findings of this study are that the TXA administration in shoulder arthroplasty significantly reduces total blood loss, postoperative change in hemoglobin level as well as transfusion rate. Similar results have been reported from studies as well as meta-analyses in total knee or hip replacement surgeries, where TXA has already been used (10, 12, 23-25). It is of note that, in theory, TXA has potential for thrombosis, since it acts by competitively inhibiting fibrinolysis (9, 11). However, many studies in patients undergoing total knee or hip arthroplasty have not exhibited an increased thromboembolic risk (23-25). Nevertheless, in patients with a history of pulmonary embolism or deep vein thrombosis, the topical use seems more proper (26).

The present review has several limitations. There is heterogeneity in extracted data from existing studies. All studies included TSA as well as RTSA and therefore, the analysis includes both procedures. Furthermore, different ways were used to calculate total blood loss for each study, including drainage volume, the Nadler's and Gross formula. Timing, dosage and route of TXA administration varied across the existing studies. It is also of note that complications have been not reported in any study, while only two studies had a brief follow-up (45 and 90 days). Nevertheless, despite these limitations, the present review evaluates almost 1000 patients in a control-setting of TXA use in TSA or RTSA. Therefore, it represents a sample more than enough to draw adequate conclusions.

These limitations may also provide guidance for future research. The optimum administration route for shoulder arthroplasty should be evaluated (oral, iv, topical). Data regarding *per os* administration of TXA in patients undergoing shoulder arthroplasty is scarce. Optimum dosage for TXA use in shoulder arthroplasty should also be defined. Therefore, complications should be carefully evaluated through follow-up with triplex for thromboembolic events. □

## CONCLUSION

The present review has shown that TXA administration, either iv or topical, in shoulder arthroplasty has effectively reduced blood loss, postoperative hemoglobin decline and need for transfusion. Despite heterogeneity of data, substantial reduction of transfusion rates and significant reduction of postoperative hemoglobin change and blood loss has been revealed. It seems patients undergoing shoulder arthroplasty benefit from TXA administration. Optimization of route, timing and dosage of TXA remains to be determined. More data and research are of paramount importance towards this direction. □

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