



ELSEVIER

Contents lists available at ScienceDirect

JSES International

journal homepage: www.jsesinternational.org

Tranexamic acid use in arthroscopic rotator cuff repair: a systematic review and meta-analysis of randomized controlled trials



Osama Z. Alzobi, MD^a, Jawad Derbas, MD^a, Ahmad Toubasi, MD^b,
Ashraf Hantouly, MD MSc^a, Abdullah Abdullah, MD^c, Bashir Zikria, MD^{d,e},
Nedal Alkhatib, MD^{a,f,*}

^aDepartment of Orthopaedic Surgery, Surgical Specialty Center, Hamad Medical Corporation, Doha, Qatar

^bFaculty of Medicine, University of Jordan, Amman, Jordan

^cThe Moncton Hospital, Moncton, New Brunswick, Canada

^dDepartment of Orthopaedic Surgery, Johns Hopkins School of Medicine, Baltimore, MD, USA

^eAspetar Orthopaedic and Sports Medicine Hospital, Doha, Qatar

^fDepartment of Orthopaedic Surgery, Indiana University School of Medicine, Indianapolis, IN, USA

ARTICLE INFO

Keywords:

Tranexamic acid

TXA

Rotator cuff

Arthroscopy

Systematic review

Meta-analysis

Level of evidence: Level II; Systematic Review/Meta-Analysis

Background: Rotator cuff disease, a prevalent cause of shoulder disability and pain among middle-aged and older adults, has seen an uptick in arthroscopic repairs in the last 2 decades. These repairs necessitate optimal visualization and controlled hemostasis to prevent complications. This study aimed to assess the efficacy of tranexamic acid (TXA) in arthroscopic rotator cuff repairs by evaluating all available randomized controlled trials (RCTs) in the literature.

Methods: A systematic search was conducted in PubMed, Cochrane Library, Embase, Science Direct, Web of Science, Google Scholar, and CINAHL databases from inception through November 2022 for RCTs investigating the use of TXA in arthroscopic rotator cuff repair. The studies selected reported on the primary outcomes, which include visual clarity during surgery, postoperative pain, and operative time. The quality of the studies was evaluated using the RoB 2 (Risk of Bias) tool.

Results: A total of 7 studies, with level I and II of evidence, comprising 510 randomized patients (253 females, 257 males) were included, with mean ages of 59 and 58 years for the TXA and control groups, respectively. Bias was graded “Low” in 2 RCTs and “Some concerns” in 5 RCTs. Visual analog scale for pain was significantly different with TXA use at postoperative day 1 (weighted mean difference (WMD) = -0.55 ; 95% confidence interval (CI): -1.07 to -0.04 , $P = .04$). Operative time was significantly higher for the control group with a mean difference of 7.97 minutes (WMD = -7.97 ; 95% CI: -15.19 to -0.74 , $P = .04$). The impact of TXA on visual clarity during shoulder arthroscopy remains uncertain. However, postoperative shoulder swelling results were comparable in both groups (WMD = -1.71 ; 95% CI: -3.72 to 0.29 , $I^2 = 99%$ (where $I^2 =$ heterogeneity statistic), $P = .69$). Considerable heterogeneity was seen in some results.

Conclusion: Pooled data suggest that the use of TXA in shoulder arthroscopy does reduce postoperative shoulder pain and has a positive effect on decreasing operative time. However, the reduction in pain may not be clinically significant, and there is no effect on reducing shoulder swelling. The impact of TXA on visual clarity remains inconclusive, and further research is needed using methodologically rigorous articles that incorporate objective measures and controlled factors to eliminate subjective bias.

© 2024 The Authors. Published by Elsevier Inc. on behalf of American Shoulder and Elbow Surgeons. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Rotator cuff pathology is a common cause of shoulder pain and disability, especially among older adults. Studies have shown that the prevalence is around 13% in patients over 50 years of age and increases to more than 50% in patients over 80 years of age.^{8,18} Arthroscopic repair has become the preferred method due to its

advantages over open surgery, including reduced morbidity, recovery time, and complications.¹⁸ Adequate visualization during arthroscopic surgery is crucial for success and avoiding complications. Over 80% of rotator cuff repairs are repaired with arthroscopic techniques.¹⁸

Uncontrolled bleeding during arthroscopic shoulder surgeries can significantly impact visualization, which is crucial for a successful outcome. Bleeding can obscure the surgeon's view and make it challenging to identify important structures, leading to

*Corresponding author: Nedat Alkhatib MD, Indiana University Health Care, 550 University Blvd, Suite 6201, Indianapolis, IN 46202, USA.

E-mail addresses: Nda0037315@gmail.com, Nalkhati@iu.edu (N. Alkhatib).

potential complications.¹⁸ Several factors can influence bleeding during arthroscopic shoulder surgeries. Pump irrigation systems can help flush out debris and maintain a clear view, but excessive pressure can also cause tissue damage and bleeding.⁶

Thermal coagulation techniques or the addition of epinephrine to the irrigation fluid can control bleeding, but can also cause tissue damage if not used appropriately. Hypotensive anesthesia can help reduce bleeding by lowering blood pressure, but it can also increase the risk of complications in some patients.^{6,10}

Tranexamic acid (TXA) is a synthetic antifibrinolytic medication that is used to improve hemostasis and surgical visualization during arthroscopic procedures.^{7,19,24} TXA works by competitively inhibiting plasminogen conversion into plasmin, thereby reducing fibrinolysis and promoting clot formation. Several studies have investigated the use of TXA in the setting of knee, hip, and shoulder arthroplasty^{14,27} with some reporting improved hemostasis and reduced hemarthrosis-related complications, such as postoperative pain and swelling.^{7,19} Additionally, TXA has also been shown to be effective in reducing hemarthrosis and knee swelling after arthroscopic anterior cruciate ligament reconstruction without an increase in the risk of complications.³ However, the evidence on the efficacy and safety of TXA in shoulder arthroscopy is still limited.

Several recent randomized controlled trials (RCTs) have investigated the use of TXA vs. placebo in patients undergoing arthroscopic shoulder surgery.^{5,7,11,19,20,22,28} These studies have varying sample sizes and conclusions. It is worth noting that while some studies have reported a benefit of TXA in arthroscopic shoulder surgery, others have not found a significant difference in outcomes between the TXA and placebo groups. The primary objective of this systematic review and meta-analysis was to compare the outcomes of visual clarity, postoperative pain, and operative time between patients who received TXA and those who received a placebo during shoulder arthroscopy. The secondary objective was to compare postoperative shoulder swelling. The hypothesis was that the use of TXA would improve visualization during surgery, leading to a reduction in operative time and postoperative swelling and pain.

Materials and methods

Protocol

This meta-analysis was conducted with adherence to the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).²³ A protocol registration was sought in advance on the International Prospective Register of Systematic Reviews (PROSPERO) with the registration number: CRD42023466552.

Eligibility criteria

RCTs that directly compared TXA to no TXA usage in arthroscopic rotator cuff repair were sought. The inclusion criteria were studies reporting at least 1 outcome, including operative time, visual clarity scores, total irrigation fluid (L), visual analog scale (VAS) for pain intensity, and the difference in shoulder circumference. The exclusion criteria were nonrandomized clinical trials, letters, abstracts, case reports, and reviews.

Search method and strategy

PubMed, Cochrane Library, Embase, Science Direct, Web of Science, Google Scholar and CINAHL databases were systematically searched up from inception to November 2022. The search strategy involved using the following keywords (“Tranexamic Acid” OR TXA) AND (“Rotator Cuff Repair” OR RCR) AND (arthroscopy) AND “randomized controlled trials.” The search strategy was performed by 2

authors independently. The senior author resolved disagreements between the 2 authors in the search strategy. Titles and abstracts were screened, and a full-text review was conducted for eligible studies. The inter-reviewer agreement during the screening and quality assessment phases was assessed using the kappa (κ) statistic. With a priori classifications as follows: κ values of 0.91–0.99 indicated almost perfect agreement; 0.71–0.90 suggested considerable agreement; 0.61–0.70 denoted high agreement; 0.41–0.60 represented moderate agreement; 0.21–0.40 was interpreted as fair agreement; and a κ value of 0.20 or less signified no agreement.²¹

Data extraction methods

Two independent authors, J.D. and A.H., used a predesigned spreadsheet to extract data. The extracted items included the first author's surname, study year, study location, study design, age, gender, number of patients, exclusion criteria, body mass index, time to surgery, TXA protocol, operative time, additional arthroscopic procedures, follow-up duration, and all other outcome measures. Authors B.Z and N.A. resolved any potential concerns in recorded data.

Quality assessment (risk of bias assessment)

The RoB 2 (Risk of Bias) tool,^{2,26} advised by Cochrane, was utilized to evaluate the risk of bias. This tool assesses 5 domains: randomization, drift from intended interventions, missing data, outcome measurements, and selective result reporting. The ratings may be either “Low,” “High,” or “Some concerns”. The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) guidelines²⁵ were used to assess the strength of evidence for primary outcomes using the GRADEpro Guideline Development Tool (2020; McMaster University & Evidence Prime, Hamilton, Canada). Authors O.A. and A.A. independently completed the assessment. Disagreements between the reviewers were quantitatively assessed and resolved using kappa statistics.²¹

Quantitative analysis (meta-analysis)

For continuous outcomes, mean values and standard deviations were analyzed, and median and interquartile ranges presented in studies were converted to mean and standard deviation using the method described by Xiang et al.³⁰ Each outcome was assessed using a random-effects model when the heterogeneity statistic (I^2) exceeded 50%, indicative of substantial heterogeneity, whereas a fixed-effects model was employed when I^2 was below 50%, suggesting low heterogeneity. I^2 was applied to determine heterogeneity across studies. Definitions for heterogeneity were adapted from the Cochrane handbook with values below 25% indicating low heterogeneity, 25% to 50% representing moderate heterogeneity, and those over 50% signifying high heterogeneity.¹⁵ The effect size is represented by the weighted mean difference and its associated 95% confidence intervals (95% CI) for continuous outcomes, indicating the overall effect across studies. The analysis was done using Meta XL, version 5.3 (EpiGear International, Surise Beach, Australia).

Level of evidence

For each included article, the Oxford Centre for Evidence-Based Medicine criteria were used to assess the level of evidence.¹⁶

Outcomes of interest

The main focus of this study was to contrast the results related to visual clarity, postoperative pain, and surgical duration between patients administered TXA and those given a placebo during

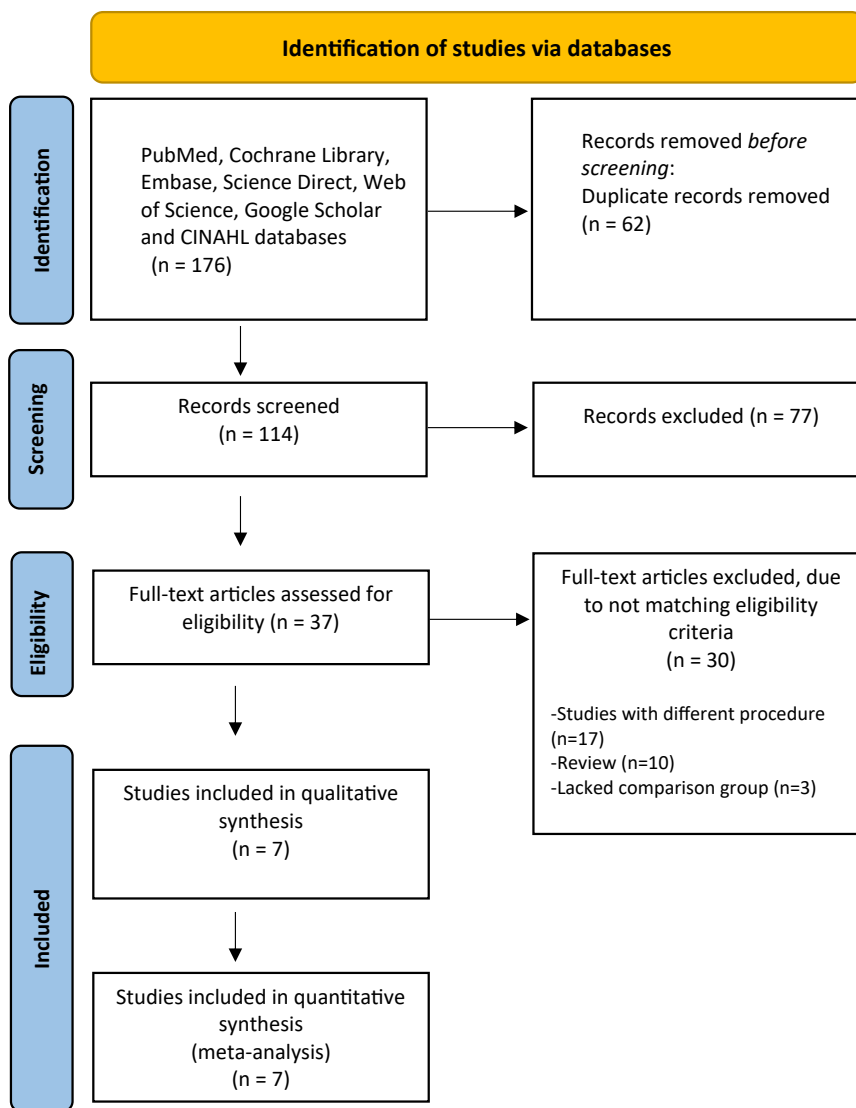


Figure 1 PRISMA flow diagram of the systematic search process detailing article identification, screening, eligibility and inclusion steps. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

shoulder arthroscopy. Additionally, a secondary goal was to evaluate differences in postoperative shoulder swelling. In a pair of studies,^{7,22} a 10-point visualization scale was employed to measure visual clarity, with 0 marking "poor" and 10 denoting "good" quality. Two other RCTs used a numeric scale,^{19,28} evaluating clarity at 15-minute intervals during the operation and grading it from 1 (poor) to 3 (clear). In a different RCT,⁵ a 1-5 scale was used. This involved both the operating surgeon and a blinded colleague who, after the procedure, watched and rated the video. For each patient, these scores were then averaged with assessments conducted every 10 minutes. Postoperative pain on the first day was assessed using the VAS, whereas postoperative shoulder swelling was determined by measuring the shoulder circumference on the same day.

Results

Study selection

The initial query search plus manual search yielded 176 results. A total of 62 duplicates were identified and removed, leaving 114 results for the screening process. Subsequently, the titles and

abstracts were screened, of which 77 studies were excluded leaving 37 studies for full-text review. Of the 37, 7 eligible studies were included in the qualitative and qualitative synthesis. The PRISMA diagram of the article search and selection process is shown in Fig. 1. The agreement level during title and abstract screening was almost perfect ($\kappa = 0.97$, 95% CI 0.931-1.00), and it reached perfect agreement during the full-text review phase ($\kappa = 1.00$).

Study and patient characteristics

Among the 7 included studies, a total of 510 randomized patients (253 females, 257 males) were included. TXA was given in 261, while 249 were not given TXA. The mean age of the TXA and the control groups was 59 (standard deviation = 2) and 58 (standard deviation = 3) years, respectively. Due to the low number of analyzed studies (<10), a funnel plot was not made. All patients underwent arthroscopic rotator cuff repair. One study conducted a preoperative interscalene brachial plexus nerve block for anesthesia.²⁰ All other trials used general anesthesia.^{5,7,11,19,20,28} Another study combined an echo-guided interscalene plexus block with general anesthesia.²⁰ Three studies used preoperative intravenous (IV) 1 g of TXA,^{19,22,28}

Table I
A summary of the characteristics of the included studies.

Publication author & year	Level of evidence	Country	Follow-up duration	Gender						Sample size		Mean age, (yrs)	
				TXA			Control			Total	TXA	Control	
				Male	Female	Total	Male	Female	Total				
Liu 2019 (5)	II	China	12 weeks	19	18	37	17	18	35	72	58.9	60.2	
Ersin 2020 (6)	II	Turkey	NM	15	17	32	11	17	28	60	49.6	53	
Gao 2020 (12)	II	China	1 week	6	24	30	5	25	30	60	62.3	62.3	
Takahashi 2021 (11)	I	Japan	1 week	24	9	33	19	14	33	66	61.6	61.6	
Nicholson 2022 (13)	II	USA	24 hrs	39	11	50	29	21	50	100	59.7	59.2	
Mackenzie 2022 (14)	I	Australia	52 weeks	34	13	47	22	20	42	89	58	58	
Bildik 2022 (15)	I	Turkey	NM	8	24	32	9	22	31	63	56.5	57.8	

TXA, Tranexamic acid; NM, not mentioned.

Table II
A summary of treatment protocols of the included studies.

Publication author & yr	TXA dose		Administration of TXA	Anesthesia measured
	Dose	Control		
Liu 2019 (5)	1 g	Saline	IV 10 minutes before surgery	General anesthesia with interscalene nerve block
Ersin 2020 (6)	10 mg/kg	Saline	IV 20 minutes before surgery	General anesthesia
Gao 2020 (12)	0.5 g	Saline	500 mg intra-articularly into the shoulder joint	General anesthesia
Takahashi 2021 (11)	1 g	Saline	IV 10 minutes before surgery	General anesthesia
Nicholson 2022 (13)	1 g	No TXA	IV before surgery	Interscalene brachial plexus nerve block before surgery
Mackenzie 2022 (14)	2 g	Saline	IV before surgery	General anesthesia with interscalene nerve block
Bildik 2022 (15)	250 mg	No TXA	Intraoperative injected into irrigation fluid	General anesthesia

TXA, Tranexamic acid; IV, intravenous.

while 1 used 2 g.²⁰ One study was performed with IV administration of 10 mg/kg TXA in 100 mL saline solution.⁷ The other 2 studies were conducted through intra-articular (IA) injection into the shoulder.^{5,11} In 1 study, 250 mg of intraoperative TXA was injected into 3 L of irrigation fluid.⁵ The other was performed by injecting 500 mg in 10 mL saline intra-articularly into the shoulder joint and subacromial space.¹¹ Follow-up durations ranged from 1 week to 1 year in 4 studies^{11,19,20,28} and were not mentioned in 3 studies.^{5,7,22} Detailed study characteristics are provided in [Tables I and II](#).

Qualitative assessment

Two studies were assessed as having a low risk of bias overall, and 5 have some concerns. In these 5 studies, unblinding of the anesthesiologist was assessed as consistently having some concerns about blinding other personnel in the operating room. Three studies were assessed to have some concerns about reporting incomplete outcome data. Two studies had unclear risk of outcome assessment data. Risk of bias evaluations for included RCTs are summarized in [Fig. 2](#). The agreement level during quality assessment was high, all kappa values exceeded 0.9. GRADE analysis certainty levels were moderate for 5 outcomes and high for 2 pooled outcomes. [Fig. 3](#) shows the GRADEpro summary.

Pooled outcomes

Postoperative pain at day 1 was measured using the VAS in 5 RCTs,^{5,19,20,22,28} with a total of 390 patients. The pooled mean difference was -0.55 (95% CI: -1.07 to -0.04, $I^2 = 52%$, $P = .04$), which is statistically significant between both groups. Forest plot of pooled outcome for VAS is shown in [Fig. 4](#).

Five RCTs calculated operative time in minutes in 361 patients.^{5,7,19,20,28} The pooled mean difference was -7.97 minutes (95% CI: -15.19 to -0.74, $I^2 = 69%$, $P = .04$), revealing a statistically significant reduction in TXA group. Forest plot of pooled outcome for operative time is shown in [Fig. 5](#).

Visual clarity was recorded in 5 RCTs with a total of 361 patients.^{5,7,19,20,28} Two studies investigated the difference in the image quality score between the TXA and control group.^{7,22} The operative surgeon completed a 10-point visualization scale; 0 was ranked as “poor” and 10 was ranked as “good”. The pooled data demonstrated no significant difference between the 2 groups, with a mean difference of 0.47 (95% CI: -0.83 to 1.77, $I^2 = 92%$, $P = .09$). In another 2 RCTs, visual clarity was rated using a numeric rating scale from grade 1 (poor) to grade 3 (clear) every 15 minutes throughout the surgery.^{19,28} Significant improvement in intraoperative visual clarity scores in favor of TXA group was only noted in grade 3 with a pooled mean difference of 9.10 (95% CI: 4.05-14.15, $I^2 = 0%$, $P = .02$). No significant difference between the groups was noted in grade 1 (mean difference, -2.60; 95% CI: -6.32 to 1.12, $I^2 = 28%$, $P = .08$). In another RCT,⁵ visual clarity was calculated using a numeric rating scale from grade 1 to 5 by the operating surgeon and another blinded surgeon who postoperatively watched the video of the arthroscopic surgery and rated the quality every 10 minutes. The average score for every single patient was calculated. Forest plots of pooled outcomes for visual clarity scores are shown in [Figs. 6–8](#).

Three RCTs assessed postoperative shoulder swelling by measuring postoperative shoulder circumference at day 1.^{11,19,28} Gao et al¹¹ reported statistical differences favoring TXA group, but Liu et al¹⁹ and Takahashi et al²⁸ reported no significant differences. The pooled mean difference was -1.71; 95% CI: -3.72 to 0.29, $I^2 = 99%$, $P = .69$), demonstrating no statistical difference between both groups. Forest plot of pooled outcomes for postoperative shoulder swelling is shown in [Fig. 9](#). Additionally, it is important to note that across the included studies, there were no reported adverse events associated with the use of TXA in arthroscopic rotator cuff repair.

Discussion

The most significant findings of the meta-analysis are that the use of TXA in shoulder arthroscopy resulted in a reduction of operative time and postoperative pain, but there was no difference



Figure 2 Summary charts for the risk of bias assessments for all included RCTs in all 5 different domains across all studies. RCT, randomized controlled trial.

Author(s):
 Question:
 Setting: Hospital
 Bibliography:

No. of studies	Study design	Certainty assessment					No. of patients		Effect		Certainty	Importance
		Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Tranexamic acid	Control	Relative (95% CI)	Absolute (95% CI)		
Operative Time												
5	randomised trials	serious ^a	not serious	not serious	not serious	none	184	177	-	MD 7.97 lower (15.19 lower to 0.74 lower)	⊕⊕⊕○ Moderate	CRITICAL
VAS Pain Score at Post-Operative Day One												
5	randomised trials	serious ^a	not serious	not serious	not serious	none	199	191	-	MD 0.55 lower (1.05 lower to 0.06 lower)	⊕⊕⊕○ Moderate	IMPORTANT
Image Quality Score												
2	randomised trials	serious ^{a,b}	not serious	not serious	not serious	none	82	78	-	MD 0.47 higher (0.83 lower to 1.77 higher)	⊕⊕⊕○ Moderate	IMPORTANT
Average Visual Clarity Score Grade 1												
2	randomised trials	not serious	not serious	not serious	not serious	none	70	68	-	MD 2.6 lower (6.32 lower to 1.12 higher)	⊕⊕⊕⊕ High	IMPORTANT
Average Visual Clarity Score Grade 3												
2	randomised trials	not serious	not serious	not serious	not serious	none	70	68	-	MD 9.1 higher (4.05 higher to 14.15 higher)	⊕⊕⊕⊕ High	IMPORTANT
Shoulder Circumference												
3	randomised trials	serious ^c	not serious	not serious	not serious	none	100	98	-	MD 1.71 lower (3.72 lower to 0.29 higher)	⊕⊕⊕○ Moderate	CRITICAL

CI: confidence interval; MD: mean difference

Explanations

- a. Surgeons were blinded in all trials. Outcome assessors blinding was not noted in one trial.
- b. Anesthesiologists were informed about allocation in two trials; therefore, some concerns of bias about blinding other personnel in the operating room.
- c. Outcome assessors blinding was not noted in one trial.

Figure 3 Summary of the GRADE assessments for all 7 primary pooled outcomes and risk ratings for the studies included within each outcome. Explanations for grades of evidence and most serious risk classifications are shown below the GRADE table. GRADE, Grading of Recommendations, Assessment, Development and Evaluation.

in postoperative shoulder swelling. Another important finding was that there were no significant adverse events or complications directly related to TXA usage. Additionally, the results of TXA's impact on visual clarity were inconclusive.

While there have been several meta-analyses investigating the use of TXA in arthroplasty surgeries, there is still a relative lack of studies examining its use in shoulder arthroscopy.^{3,4,9,14,17} Belk et al⁴ conducted a meta-analysis that included studies on both knee and shoulder arthroscopy and reported that the use of TXA was associated with improved outcomes and decreased hemarthrosis-

related complications during the early postoperative period. However, they only included 1 study specifically on shoulder arthroscopy.

Hartland et al¹⁴ conducted a meta-analysis to evaluate the effectiveness of TXA in reducing blood loss and the need for blood transfusion in patients undergoing shoulder surgery. The authors combined 8 studies, including shoulder arthroplasty, shoulder arthroscopy, and open Latarjet procedures. The authors found that overall, TXA significantly reduced perioperative blood loss and estimated drain output. However, when studies involving

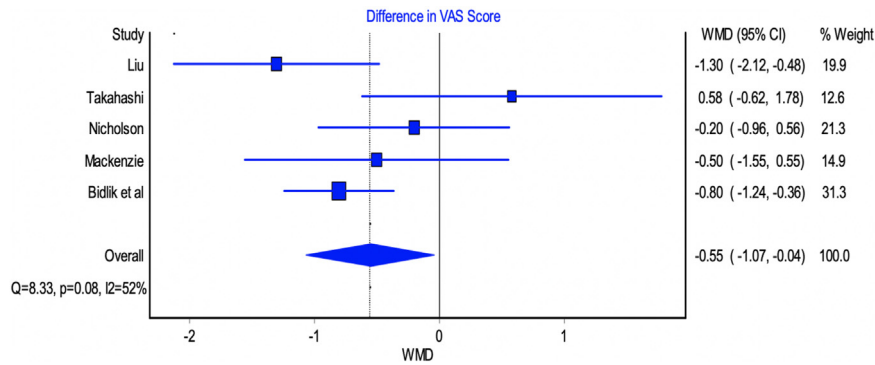


Figure 4 Forest plots from the TXA vs. no TXA main analysis for visual analog scale (VAS) for pain at postoperative day 1. TXA, Tranexamic acid; VAS, Visual analog scale; WMD, weighted mean difference; CI, confidence interval.

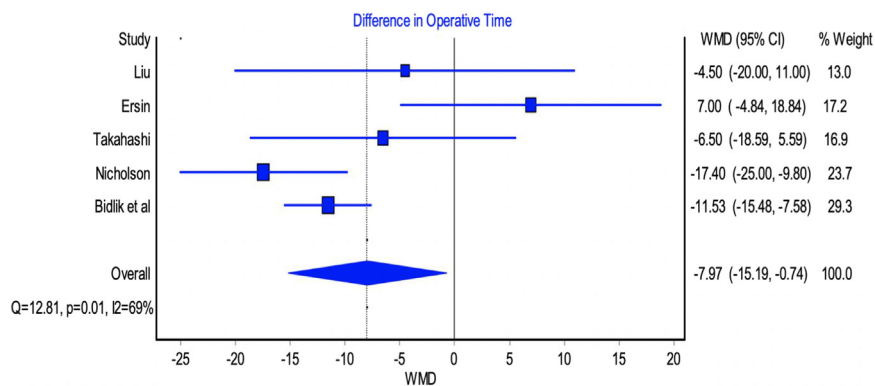


Figure 5 Forest plots from the TXA vs. no TXA main analysis for calculated operative time. TXA, Tranexamic acid; WMD, weighted mean difference; CI, confidence interval.

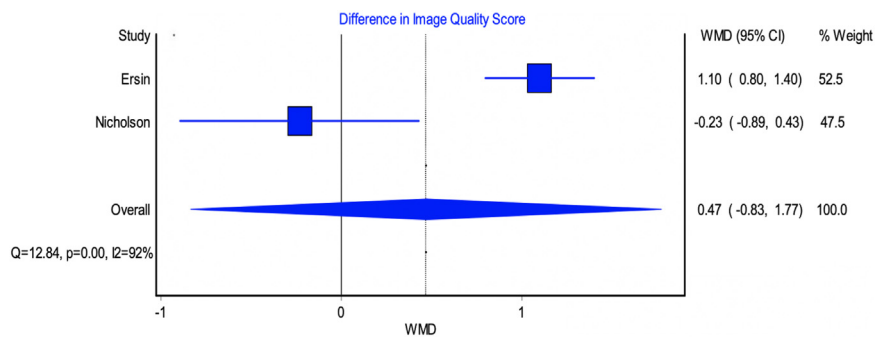


Figure 6 Forest plot from the TXA vs. no TXA main analysis for image quality score for visual clarity. TXA, Tranexamic acid; WMD, weighted mean difference; CI, confidence interval.

arthroscopic procedures were included, the statistical differences between the TXA and control groups were no longer significant for hemoglobin reduction.¹⁴ This finding may be attributed to the fact that arthroscopic shoulder surgeries are associated with minimal estimated blood loss. Therefore, the effect of TXA in reducing blood loss may be negligible in this patient population.

In this meta-analysis, the finding that TXA use in shoulder arthroscopy reduces operative time is consistent with some previous studies.¹ Better visualization and reduced bleeding during arthroscopic surgery may be contributing factors. However, the magnitude of this effect may not be clinically significant, and caution should be exercised when interpreting these results due to

significant heterogeneity among the studies. Factors such as mean arterial pressure and pump pressure may have played a role in the differences observed between studies.

This study found a significant decrease in immediate post-operative pain among the TXA group in comparison to the placebo group within the first 24 hours. However, the mean difference in the VAS was 0.55, which did not reach the minimum clinically important difference and may not have clinical significance.²⁹ Pain is an essential outcome to measure the efficacy of TXA, either through its anti-inflammatory properties or by reducing postoperative hemarthrosis.³¹ The use of TXA in hip and knee arthroplasty for reducing blood loss and pain has been widely accepted.¹² However,

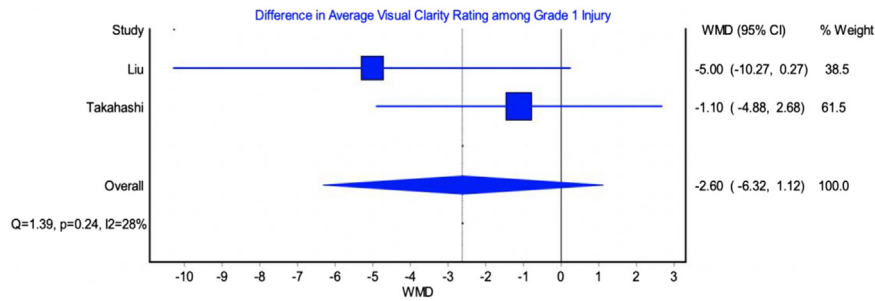


Figure 7 Forest plot from the TXA vs. no TXA main analysis for visual clarity grade 1. TXA, Tranexamic acid; WMD, weighted mean difference; CI, confidence interval.

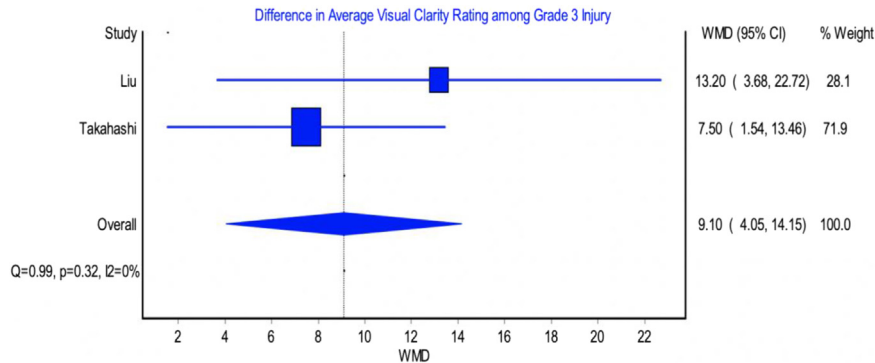


Figure 8 Forest plot from the TXA vs. no TXA main analysis for visual clarity grade 3. TXA, Tranexamic acid; WMD, weighted mean difference; CI, confidence interval.

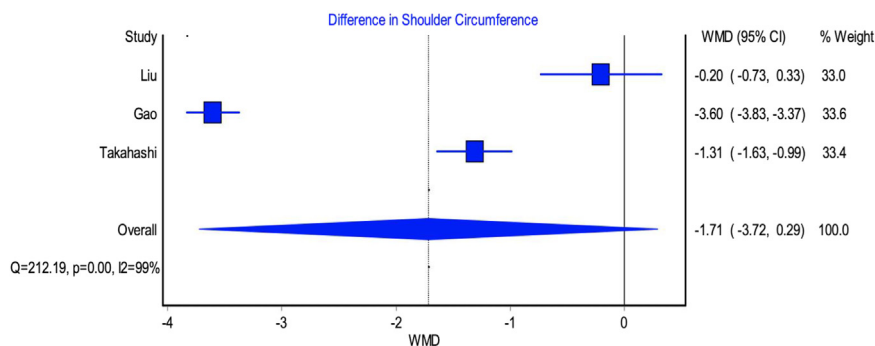


Figure 9 Forest plot from the TXA vs. no TXA main analysis for postoperative shoulder swelling. TXA, Tranexamic acid; WMD, weighted mean difference; CI, confidence interval.

its effects on hemarthrosis and pain reduction in arthroscopic procedures remain uncertain. Some studies have shown reduced pain and hemarthrosis after arthroscopic anterior cruciate ligament reconstruction with TXA, while others have not found a significant difference compared to placebo.^{3,4,28} Hartland et al,¹⁴ in their meta-analysis, found a significant reduction in shoulder pain associated with TXA use, although they included different types of shoulder surgeries.

Two of the 5 pooled studies found significant pain reduction on the first day postoperative.^{5,19} However, 1 of the pooled studies found significant postoperative pain reduction at 8 and 24 hours but not at 48 hours, and it was the only pooled study that used IA TXA rather than IV; therefore, conducting a subgroup analysis of IA vs. IV TXA use was not possible due to a limited number of studies.¹⁶ Interestingly, the pain was significantly lower with IA TXA compared to IV TXA in the setting of knee and hip arthroplasty.¹³ The relationship between pain and IA TXA through the use of TXA in irrigation fluid requires further investigation.

The analysis also showed that the use of TXA may not be effective in reducing immediate postoperative shoulder swelling. This was assessed in the involved studies by measuring the difference in shoulder circumference on the first postoperative day. Three studies^{11,19,28} investigated the effects of TXA on shoulder swelling, and only 1 of these studies¹¹ found a significant reduction in shoulder circumference on the first postoperative day. However, this effect was not sustained, and there was no significant difference in shoulder circumference between the TXA and control groups after 1 week. It is worth noting that the studies used different methods of administering TXA (IV vs. IA), which may explain the heterogeneity in the results. In addition, while TXA has been shown to be effective in reducing knee swelling, hemarthrosis, and the need for aspiration in knee arthroscopy,³ the same effect has not been demonstrated in shoulder arthroscopy studies.

Maintaining a clear visual field is important during arthroscopy as it can impact the accuracy and efficiency of the procedure and reduce the risk of complications.¹⁹ Five studies were included in

this meta-analysis that investigated the effect of TXA on visual clarity; however, due to the variability in methods used to assess visual clarity, we could not pool the data across all studies.^{5,7,19,22,28} The studies included in this meta-analysis did not provide a clear consensus on whether TXA improves visual clarity compared to placebo during arthroscopy. Ersin et al⁷ reported a decrease in the need for high pump pressure and a reduction in total fluid for irrigation. However, Nicholson et al²² found no change in the pumping pressure parameters. Takahashi et al²⁸ used a 3-grade clarity score (grade 3 being "good" and grade 1 being "poor") and found that TXA had a slight improvement in grade 3 visibility, but it was not considered clinically important. On the other hand, Liu et al¹⁹ also used the same 3-grade clarity score and found that TXA improved grade 3 visibility by 32% and decreased grade 1 visibility by 54%. Bildik et al⁵ used a 5-grade visual clarity scale and reported that TXA resulted in a significant improvement in visual clarity. The differences in results could be attributed to differences in TXA dose, pumping pressure setup, methods used to evaluate visual clarity, and subjective bias. Based on the reviewed studies, the impact of TXA on visual clarity during shoulder arthroscopy remains uncertain. The lack of consistency in methods used to assess visual clarity, the presence of a strong subjective component, and the variability in results across studies underscore the need for further research using standardized protocols and validated methods to determine the effect of TXA on visual clarity during shoulder arthroscopy.

Limitations

This meta-analysis has some limitations, including significant heterogeneity between studies due to variations in TXA dosing and administration protocols, pump pressure setups, types of irrigation fluid, and methods for assessing visual clarity. Additionally, the lack of uniform reporting on rotator cuff tear characteristics and additional concomitant surgical procedures, which could significantly influence all investigated outcomes, was not consistently available in the included papers. This makes it challenging to pool the data and draw accurate conclusions on the effectiveness of TXA in shoulder arthroscopy. Furthermore, the overall low number of studies included in our meta-analysis constitutes another limitation. Further studies that use less biased methods for assessing visual clarity and have more controlled factors are needed to clarify the effectiveness of TXA in shoulder arthroscopy.

Conclusion

Pooled data suggest that the use of TXA in shoulder arthroscopy does reduce postoperative shoulder pain and has a positive effect on decreasing operative time. However, the reduction in pain may not be clinically significant, and there is no effect on reducing shoulder swelling. The impact of TXA on visual clarity remains inconclusive, and further research is needed using methodologically rigorous articles that incorporate objective measures and controlled factors to eliminate subjective bias.

Disclaimers:

Funding: The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.
Conflicts of Interest: The authors, their immediate families, and any research foundations with which they are affiliated have not received any financial payments or other benefits from any commercial entity related to the subject of this article.
 No ethical approval was required for this review article.

References

1. Agarwalla A, Gowd AK, Yao K, Bohl DD, Amin NH, Verma NN, et al. A 15-minute Incremental increase in operative duration is associated with an additional risk of complications within 30 Days after arthroscopic rotator cuff repair. *Orthop J Sports Med* 2019;7:2325967119860752. <https://doi.org/10.1177/2325967119860752>.
2. Alkhatib N, Abdullah ASA, AlNouri M, Ahmad Alzobi OZ, Alkaramany E, Ishibashi Y. Short- and long-term outcomes in Bankart repair vs. conservative treatment for first-time anterior shoulder dislocation: a systematic review and meta-analysis of randomized controlled trials. *J Shoulder Elbow Surg* 2022;31:1751-62. <https://doi.org/10.1016/j.jse.2022.02.032>.
3. Alkhatib N, AlNouri M, Abdullah ASA, Ahmad Alzobi OZ, Alkaramany E, Sasaki E, et al. Tranexamic acid Use in anterior cruciate ligament reconstruction decreases bleeding complications: a systematic review and meta-analysis of randomized controlled trials. *Arthroscopy* 2022;38:506-518.e6. <https://doi.org/10.1016/j.arthro.2021.07.030>.
4. Belk JW, McCarty EC, Houck DA, Dragoo JL, Savoie FH, Thon SG. Tranexamic acid use in knee and shoulder arthroscopy leads to improved outcomes and fewer hemarthrosis-related complications: a systematic review of level I and II studies. *Arthroscopy* 2021;37:1323-33. <https://doi.org/10.1016/j.arthro.2020.11.051>.
5. Bildik C, Pehlivanoglu T. Arthroscopic rotator cuff repair performed with intra-articular tranexamic acid: could it provide improved visual clarity and less postoperative pain? A prospective, double-blind, randomized study of 63 patients. *J Shoulder Elbow Surg* 2023;32:223-31. <https://doi.org/10.1016/j.jse.2022.10.007>.
6. Burkhart SS, Danaceau SM, Athanasios KA. Turbulence control as a factor in improving visualization during subacromial shoulder arthroscopy. *Arthroscopy* 2001;17:209-12.
7. Ersin M, Demirel M, Büget Mİ, Edipoğlu İS, Atalar AC, Erşen A. The effect of intravenous tranexamic acid on visual clarity during arthroscopic rotator cuff repair: a randomized, double-blinded, placebo-controlled pilot study. *Acta Orthop Traumatol Turc* 2020;54:572-6. <https://doi.org/10.5152/j.aott.2020.19164>.
8. Fermont AJ, Wolterbeek N, Wessel RN, Baeyens JP, de Bie RA. Prognostic factors for successful recovery after arthroscopic rotator cuff repair: a systematic literature review. *J Orthop Sports Phys Ther* 2014;44:153-63. <https://doi.org/10.2519/jospt.2014.4832>.
9. Fillingham YA, Ramkumar DB, Jevsevar DS, Yates AJ, Shores P, Mullen K, et al. The efficacy of tranexamic acid in total knee arthroplasty: a network meta-analysis. *J Arthroplasty* 2018;33:3090-3098.e1. <https://doi.org/10.1016/j.arth.2018.04.043>.
10. Furia JP, Zambetti GJ Jr. An injection technique to create a bloodless field in arthroscopically assisted anterior cruciate ligament reconstruction. *Am J Sports Med* 1992;20:406-9.
11. Gao HL, Zhang JC, He Y, Zhai WT, Xiao LB, Shi Q. [Clinical study on the control of intra-articular hemorrhage by tranexamic acid after shoulder arthroscopy]. *Zhong Guo Gu Shang* 2020;33:238-41. <https://doi.org/10.12200/j.issn.1003-0034.2020.03.010>.
12. Gianakos AL, Hurley ET, Haring RS, Yoon RS, Liporace FA. Reduction of blood loss by tranexamic acid following total hip and knee arthroplasty: a meta-analysis. *JBJS Rev* 2018;6:e1. <https://doi.org/10.2106/JBJS.RVW.17.00103>.
13. Haratian A, Shelby T, Hasan LK, Bolia IK, Weber AE, Petrigliano FA. Utilization of tranexamic acid in surgical orthopaedic practice: indications and current considerations. *Orthop Res Rev* 2021;19:187-99. <https://doi.org/10.2147/ORR.S321881>.
14. Hartland AW, Teoh KH, Rashid MS. Clinical effectiveness of intraoperative tranexamic acid use in shoulder surgery: a systematic review and meta-analysis. *Am J Sports Med* 2021;49:3145-54. <https://doi.org/10.1177/0363546520981679>.
15. Higgins JP, Green S. *Cochrane handbook for systematic reviews of interventions: cochrane book series*. Sussex England: Wiley-Blackwell; 2008. ISBN:9780470699515.
16. Howick J, Chalmers I, Glasziou P. *The Oxford 2011 levels of evidence*. 2018. Available at: <http://www.cebm.net/index.aspx?o=5653>.
17. Kirsch JM, Bedi A, Horner N, Wiater JM, Pauzenberger L, Koueiter DM, et al. Tranexamic acid in shoulder arthroplasty: a systematic review and meta-analysis. *JBJS Rev* 2017;5:e3. <https://doi.org/10.2106/JBJS.RVW.17.00021>.
18. Kuo LT, Chen CL, Yu PA, Hsu WH, Chi CC, Yoo JC. Epinephrine in irrigation fluid for visual clarity in arthroscopic shoulder surgery: a systematic review and meta-analysis. *Int Orthop* 2018;42:2881-9. <https://doi.org/10.1007/s00264-018-4021-9>.
19. Liu YF, Hong CK, Hsu KL, Kuan FC, Chen Y, Yeh ML, et al. Intravenous administration of tranexamic acid significantly improved clarity of the visual field in arthroscopic shoulder surgery. A prospective, double-blind, and randomized controlled trial. *Arthroscopy* 2020;36:640-7. <https://doi.org/10.1016/j.arthro.2019.10.020>.
20. Mackenzie SP, Spasojevic M, Smith M, Mattern O, Piggott RP, Patel SS, et al. The effect of single-dose, preoperative intravenous tranexamic acid on early postoperative pain scores after rotator cuff repair: a double-blind, randomized controlled trial. *J Shoulder Elbow Surg* 2022;31:1399-408. <https://doi.org/10.1016/j.jse.2022.02.023>.
21. McHugh ML. Interrater reliability: the kappa statistic. *Biochem Medica* 2012;22:276-82.

22. Nicholson TA, Kirsch JM, Churchill R, Lazarus MD, Abboud JA, Namdari S. The effect of tranexamic acid for visualization on pump pressure and visualization during arthroscopic rotator cuff repair: an anonymized, randomized controlled trial. *J Shoulder Elbow Surg* 2022;31:2211–6. <https://doi.org/10.1016/j.jse.2022.06.027>.
23. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. <https://doi.org/10.1136/bmj.n71>.
24. Salameh M, Attia AK, El Khatib S, Hantouly A, Hsu R, Blankenhorn B. Tranexamic acid utilization in foot and ankle surgery: a meta-analysis. *Foot Ankle Int* 2022;43:1370–8. <https://doi.org/10.1177/10711007221114139>.
25. Schünemann H, Brożek J, Guyatt G, Oxman A. GRADE handbook for grading quality of evidence and strength of Recommendations. The GRADE working group. 2013. <https://gdt.gradepro.org/app/handbook/handbook.html>. Accessed March 8 2021.
26. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;28:l4898. <https://doi.org/10.1136/bmj.l4898>.
27. Stoicea N, Moran K, Mahmoud AR, Glassman A, Ellis T, Ryan J, et al. Tranexamic acid use during total hip arthroplasty: a single center retrospective analysis. *Medicine (Baltim)* 2018;97:e10720. <https://doi.org/10.1097/MD.00000000000010720>.
28. Takahashi R, Kajita Y, Iwahori Y, Harada Y. Tranexamic acid administration for arthroscopic rotator cuff repair: a prospective, double-blind, randomized controlled trial. *J Orthop Sci* 2023;28:328–32. <https://doi.org/10.1016/j.jos.2021.11.015>.
29. Tashjian RZ, Shin J, Broschinsky K, Yeh CC, Martin B, Chalmers PN, et al. Minimal clinically important differences in the American Shoulder and Elbow Surgeons, Simple Shoulder Test, and visual analog scale pain scores after arthroscopic rotator cuff repair. *J Shoulder Elbow Surg* 2020;29:1406–11. <https://doi.org/10.1016/j.jse.2019.11.018>.
30. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol* 2014;19:135. <https://doi.org/10.1186/1471-2288-14-135>.
31. Wang D, Luo ZY, Yu ZP, Liu LX, Chen C, Meng WK, et al. The antifibrinolytic and anti-inflammatory effects of multiple doses of oral tranexamic acid in total knee arthroplasty patients: a randomized controlled trial. *J Thromb Haemost* 2018;16:2442–53. <https://doi.org/10.1111/jth.14316>.