The Efficacy of Tranexamic Acid in Primary Total Shoulder Arthroplasty: A Systematic Review and Meta-Analysis of Level I Randomized Controlled Trials

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INTRODUCTION: Tranexamic acid (TXA) is commonly used during hip and knee arthroplasty procedures to reduce perioperative blood loss, however its role in total shoulder arthroplasty is still being established. Although prior studies have attempted to synthesize the available data regarding the efficacy of TXA in total shoulder arthroplasty, all have incorporated level III studies, and none have exclusively analyzed high-quality randomized controlled trials (RCTs). Given the difficult and sensitive nature of obtaining data in the perioperative period, the inclusion of low-quality retrospective studies calls the accuracy and validity of this reported data into question. There is significant value in limiting meta-analysis to high quality studies appropriate for treatment recommendation, and therefore the purpose of this study was to systematically review and synthesize the available level I evidence regarding the impact of TXA on the reduction of blood loss, transfusion rate, and early postoperative outcomes in patients undergoing total shoulder arthroplasty.

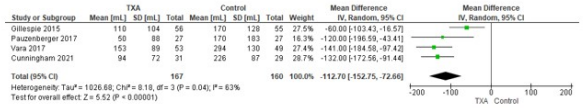
METHODS: A systematic review of the PubMed Central, MEDLINE, Embase, and Scopus databases from inception through April 2023 was performed to identify level I RCTs examining the use of TXA at the time of primary reverse or anatomic total shoulder arthroplasty. Studies were included if they met the following inclusion criteria: 1) regarded clinical outcomes of TXA use in patients undergoing primary reverse or anatomic total shoulder arthroplasty, 2) were of level I evidence, 3) included a non-TXA control, and 4) had available text written in the English language. Studies were excluded if they 1) were systematic reviews/meta-analyses, letters to the editor, elemental analyses, or case reports, and 2) were of level II-V evidence. Dichotomous outcomes were pooled into risk ratios (RR) whereas continuous outcomes were pooled into weighted mean differences (MD) using random effects meta-analysis.

RESULTS: Database searching identified 397 studies, of which 5 were deemed eligible for inclusion in our study. All included studies were double-blinded, placebo-controlled, RCTs of level I evidence. Among included studies, a total of 435 patients (219 TXA, 216 control) were identified. The weighted mean age of the TXA cohort was 68 years (range, 67-72), and 122 of the patients were female (55.7%). The weighted mean age of the control cohort was 68 years (range, 65-73), and 116 of the patients (53.7%) were female. The total dose of TXA was 2g in three studies, 1g in one study, and weight-based (20 mg/kg total) in one study. The route of administration was intravenous in four studies, and topical in one. Control patients received a normal saline placebo in all studies. Hematologic outcomes were significantly better among the TXA cohort, including lower 24-hour drain output (MD [95% CI], -112.70 mL [-152.75, -72.66]; $p < 0.001$), lower pre- to postoperative change in hemoglobin (MD [95% CI], -0.68 g/dL [-0.97, -0.39]; $p < 0.001$), and less total blood loss (MD [95% CI], -249.56 mL [-347.60, -151.52]; $p < 0.001$) **(Figure 1)**. Postoperative Visual Analog Scale for pain (VAS-Pain) scores were lower in the TXA group, but not significantly (MD [95% CI], -0.46 [-1.11, -0.19]; $p = 0.17$) **(Figure 2)**. No difference in operative time (MD [95% CI], -2.90 [-8.13, 2.33]; $p = 0.28$) or hospital length of stay (MD [95% CI], -0.06 [-0.32, 0.20]; $p = 0.65$) was observed between cohorts. Postoperative blood transfusion was required in 3/219 TXA patients (1.4%) and 7/216 control patients (3.2%) (RR [95% CI], 0.40 [0.11, 1.45]; $p = 0.16$). Overall, 1 adverse event (0.46%), a syncopal fall treated with fluids, was reported in the TXA cohort. Among the control cohort, 3 adverse events (1.4%) including 1 skin hypersensitivity reaction, 1 non-ST segment elevation myocardial infarction, and 1 deep vein thrombosis were reported. No other thromboembolic events were reported in either cohort in any study. Pooled analysis revealed no difference in the risk of postoperative complications between groups (RR [95% CI], -0.01 [-0.03, 0.02]; $I^2 = 0\%$; $p = 0.58$).

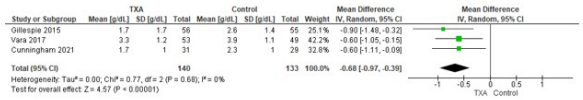
DISCUSSION AND CONCLUSION:

Among patients undergoing primary total shoulder arthroplasty, compared with placebo control, perioperative TXA reduces drain output, change in hemoglobin levels, and total blood loss without increasing the risk of adverse events or loss of operative time. TXA is safe, effective, and may be a useful adjunct in primary total shoulder arthroplasty procedures.

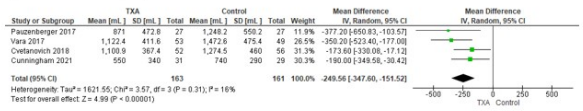
A) 24 hour/POD 1 Drain Output (mL)



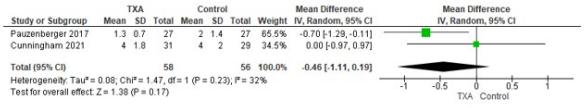
B) Pre- to Postoperative Change in Hemoglobin (g/dL)



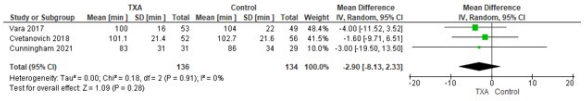
C) Total Blood Loss (mL)



A) Postoperative VAS-Pain Score



B) Operative Time (min)



C) Hospital Length of Stay (days)