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ORIGINAL ARTICLE

# Interaction of preoperative chemoprophylaxis and tranexamic acid use does not affect transfusion in acetabular fracture surgery

Harsh Wadhwa[1] · Matthew Rohde[1] · Yousi Oquendo[1] · Michael J. Chen[1] · Seth S. Tigchelaar[1] · Michael Bellino[1] · Julius Bishop[1] · Michael J. Gardner[1]

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## Abstract

**Purpose** While the effects of tranexamic acid (TXA) use on transfusion rates after acetabular fracture surgery are unclear, previous evidence suggests that holding deep vein thrombosis (DVT) chemoprophylaxis may improve TXA efficacy. This study examines whether holding DVT chemoprophylaxis in patients receiving TXA affects intraoperative and postoperative transfusion rates in acetabular fracture surgery.

**Methods** We reviewed electronic medical records (EMR) of 305 patients who underwent open reduction and internal fixation of acetabular fractures (AO/OTA 62) and stratified patients per the following perioperative treatment: (1) no intraoperative TXA (noTXA), (2) intraoperative TXA and no preoperative DVT prophylaxis (opTXA/noDVTP), or (3) intraoperative TXA and preoperative DVT prophylaxis (opTXA/opDVTP). The primary outcomes were need for intraoperative or postoperative transfusion. Risk factors for each primary outcome were assessed using multivariable regression.

**Results** Intraoperative or postoperative transfusion rates did not significantly differ between opTXA/opDVTP and opTXA/noDVTP groups (46.2% vs. 36%, $p=0.463$; 15.4% vs. 28%, $p=0.181$). Median units transfused did not differ between groups ($2\pm1$ vs. $2\pm1$, $p=0.515$; $2\pm1$ vs. $2\pm0$, $p=0.099$). There was no association between preoperative DVT chemoprophylaxis and TXA with intraoperative or postoperative transfusions. EBL, preoperative hematocrit, and IV fluids were associated with intraoperative transfusions; age and Charlson Comorbidity Index (CCI) were associated with postoperative transfusions.

**Conclusion** Our findings suggest holding DVT prophylaxis did not alter the effect of TXA on blood loss or need for transfusion.

**Keywords** Acetabular fracture · TXA · DVT · Anticoagulants · Transfusions

## Introduction

The incidence of deep venous thrombosis (DVT) and pulmonary embolism (PE) in pelvic and acetabular fractures has been shown to be as high as 61% and 10%, respectively [1–3]. Venous thromboembolism (VTE) chemoprophylaxis has been shown to reduce rates of DVTs and PEs [4]. However, bleeding complications and transfusions lead to worse outcomes, putting patients at risk for anemia, reduced wound healing, increased length of stay, infection, and VTE [5–7].

Tranexamic acid (TXA) is synthetic lysine derivative that inhibits fibrin degradation and has been shown to effectively reduce perioperative bleeding in total joint arthroplasty [8–11]. Previous literature in total hip arthroplasty has shown that TXA efficacy is not affected by anticoagulants and may balance the risk of increased bleeding [12]. The effect of TXA on transfusion during and after acetabular fracture surgery is less clear [1, 8, 13]. One previous study demonstrated that TXA efficacy was reduced by concomitant DVT chemoprophylaxis; however, TXA dosing was not standardized throughout the study [1]. This study aims to compare the efficacy of a standard TXA dosing regimen with and without preoperative DVT prophylaxis in acetabular fracture surgery. We hypothesized that holding DVT prophylaxis would improve TXA efficacy.

✉ Matthew Rohde
rohde.matt1@gmail.com

[1] Department of Orthopaedic Surgery, Stanford School of Medicine, Stanford, CA 94305, USA

## Methods

This protocol was approved by the Institutional Review Board (protocol #56,011) and performed in accordance with the ethical standards and national laws. Patients with acute acetabular fractures who underwent open reduction and internal fixation (ORIF) between 2004 and 2020 were retrospectively reviewed using Current Procedural Terminology (CPT) codes 27,226, 27,227, and 27,228. Patients with pathologic fractures, concomitant injuries and procedures, fractures treated with percutaneous fixation, and patients < 18 years old were excluded from the study. Any fractures treated with a combined dual anterior and posterior approach or extended iliofemoral approach were excluded. The procedures were performed at a single institution's Level 1 trauma center by one of three fellowship trained orthopedic traumatologists.

Patients were stratified into three cohorts: (1) patients who received no intraoperative TXA (noTXA), (2) patients who received intraoperative TXA and no preoperative DVT prophylaxis (opTXA/noDVTP), and (3) patients who received intraoperative TXA and preoperative DVT prophylaxis (opTXA/opDVTP). TXA was administered intravenously (1 g) prior to surgical incision and prior to wound closure (1 g). Patients given TXA were selected at the discretion of the surgeon, and no patients had contraindications for receiving TXA. Intraoperative blood transfusions were performed in accordance with surgeon discretion. In patients without concomitant diseases, postoperative blood transfusions were performed for patients with a hemoglobin < 7 g/dL. In patients with concurrent cardiac disease or other risks to acute anemia, postoperative blood transfusions were performed for patients with a hemoglobin of less than 7–8 g/dL.

Patient demographics, body mass index, Charlson Comorbidity Index (CCI), American Society of Anesthesiologists (ASA) score, Injury Severity Score (ISS), tobacco use, diabetes mellitus, fracture type, and surgical approach were collected. Fracture type was classified using the AO-OTA classification [14]. Surgical approach was grouped into the posterior approach (including Kocher-Langenbeck and Gibson approach), full ilioinguinal approach, iliofemoral/ilioinguinal lateral window, and anterior intrapelvic. The primary outcomes assessed were intraoperative and postoperative transfusions. Secondary outcomes included length of stay (LOS), operative time, IV fluids, estimated blood loss (EBL), perioperative complications (infection, venous thromboembolism (VTE), postoperative delirium, postoperative ileus, urinary retention), cell saver use, and preoperative and postoperative cell count and coagulation factors (hemoglobin, hematocrit, international normalized ratio (INR), platelets). EBL was determined subjectively based on volume of fluid in the suction container, subtracting amount administered for irrigation. VTE included any DVT or PE recorded in the patient chart during admission. Infection included any documented accounts of sepsis, pneumonia, or urinary tract infection during admission.

Continuous variables were compared using analysis of variance (ANOVA) and Kruskal–Wallis with a two-sided significance level of $p < 0.05$. Categorical variables were compared using chi-squared and Fisher's exact tests. Multivariate logistic regression was used to assess risk factors for intraoperative or postoperative transfusion. Each variable was assessed for significance using backward variable elimination until only significant ($p < 0.05$) or trending ($p < 0.10$) predictors remained. Interaction between variables, specifically preoperative VTE chemoprophylaxis and TXA use, was analyzed. Intraoperative blood transfusion was additionally assessed via logistic regression as a predictor for postoperative blood transfusion. Statistical analysis was performed using SAS Enterprise Guide (Cary, NC).

To determine sample size, a power analysis was conducted, which determined that 305 patients were necessary to provide a power of 80%. ANOVA with a two-sided significance of $\alpha = 0.05$ was used to detect a 20% difference in transfusion rates.

## Results

Three hundred and five patients were included in the study with an average age of 52 years. Two hundred and twenty-five patients were male. Two hundred and sixteen patients received no treatment (noTXA), 50 patients received TXA without DVT prophylaxis (opTXA/noDVTP), and 39 patients received TXA treatment with preoperative DVT prophylaxis (opTXA/opDVTP). Baseline demographics did not differ between groups, aside from ISS score, which was lower in the opTXA/opDVTP group ($p < 0.01$). Demographic data are summarized in Table 1. All patients receiving TXA received perioperative IV infusion and did not receive intraoperative topical TXA.

After controlling for other variables, TXA use and preoperative DVT chemoprophylaxis were not associated with intraoperative transfusions ($p = 0.931$, $p = 0.854$) (Fig. 1A). EBL, preoperative hematocrit, and IV fluids were shown to be associated with intraoperative transfusion ($p < 0.001$, $p = 0.004$, $p = 0.048$). Age, diabetes, CCI, ISS, fracture pattern, surgical approach, operative time, and preoperative hemoglobin were not associated with intraoperative transfusion. Results of multivariable logistic regression for intraoperative transfusions are shown in Fig. 1A.

TXA use and preoperative DVT chemoprophylaxis were not associated with postoperative transfusion ($p = 0.074$, $p = 0.513$) (Fig. 1B). Age and CCI were associated with

**Table 1** Baseline demographics for patients receiving no treatment (nT), patients receiving TXA only (TnD), and patients receiving TXA and preoperative deep vein thrombosis (DVT) chemoprophylaxis (TyD)

| | noTXA | opTXA/noD-VTP | opTXA/opD-VTP | *p* value |
|---|---|---|---|---|
| | *N* (%) | *N* (%) | *N* (%) | |
| *N* | 216 | 50 | 39 | |
| Age | 52.5 (19–93) | 50.1 (22–83) | 51.3 (21–96) | 0.54 |
| Female sex | 55 (25.5) | 12 (24.0) | 13 (33.3) | 0.55 |
| Diabetes | 24 (11.1) | 7 (14) | 4 (10.3) | 0.81 |
| Tobacco use | 63 (29.1) | 15 (25.8) | 8 (20.5) | 0.52 |
| BMI | 27.7 ± 6.8 | 29.7 ± 6.6 | 26.9 ± 4.6 | 0.87 |
| CCI | 1 ± 2.25 | 1 ± 2 | 1 ± 2.5 | 0.46 |
| ISS | 9 ± 9 | 9.5 ± 17 | 4 ± 1 | **< 0.01** |
| ASA | | | | 0.57 |
| 1 | 47 | 7 | 9 | |
| 2 | 92 | 23 | 22 | |
| 3 | 70 | 19 | 8 | |
| 4 | 7 | 1 | 0 | |

postoperative transfusions ($p = 0.016$, $p = 0.0081$). Operative time and IV fluids were associated with EBL ($p = 0.0025$, $p < 0.001$). The remaining variables were not associated with postoperative transfusions or EBL. Results of multivariable logistic regression for operative transfusion are shown in Fig. 1B.

There was no difference in EBL ($p = 0.09$), intraoperative ($p = 0.46$), and postoperative transfusions ($p = 0.18$) between opTXA/noDVTP and opTXA/opDVTP (Table 2). The opTXA/noDVTP group had a smaller postoperative drop in platelets relative to the opTXA/opDVTP group (2.04 ± 59.6 vs. 28.9 ± 38.5; $p = 0.007$). Patients in the noTXA group had a longer mean operative time (251.5 min; $p < 0.01$), but there was no difference in mean operative time between patients in the opTXA/noDVTP group and opTXA/opDVTP group (218.7 min, 202.5 min). While patients in the noTXA control group had a higher mean volume of IV fluids (2992.9 mL; $p = 0.01$), opTXA/noDVTP and opTXA/opDVTP groups showed similar results (2451.0 mL, 2560.3 mL). Length of stay and perioperative complications were similar between groups. Table 2 summarizes outcomes data from this cohort.

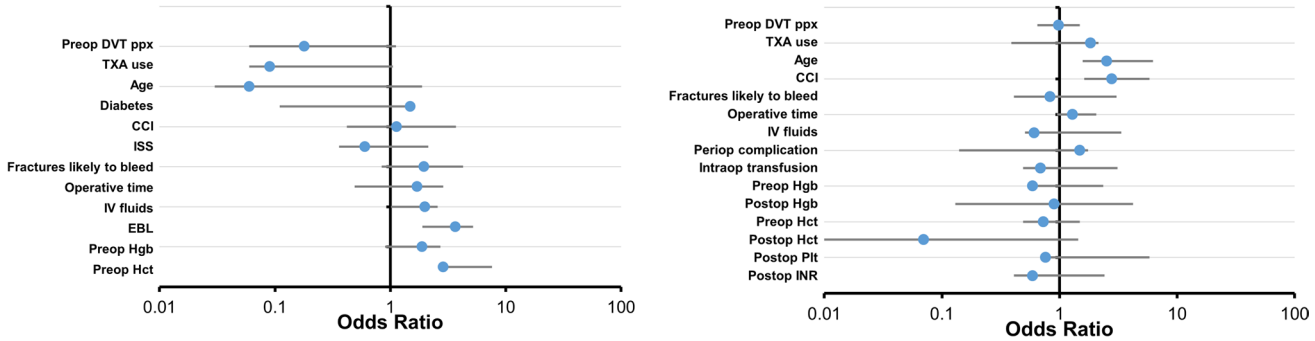


**Fig. 1** **A** Independent predictors of intraoperative transfusion (left) and postoperative transfusion (right). **B** Results of multivariable logistic regression analysis are displayed as odds ratios with 95% confidence intervals

**Table 2** Inpatient outcomes after acetabular fracture open reduction and internal fixation (ORIF) among patients receiving no treatment (nT), TXA but no DVT chemoprophylaxis (TnD), and TXA with DVT chemoprophylaxis (TyD). Continuous variables are described as means and ranges. Categorical variables are described as frequencies and percentages

| | noTXA | opTXA/noDVTP | opTXA/opDVTP | *p* value |
|---|---|---|---|---|
| Length of stay | 10.7 (2–60) | 17.9 (2–384) | 7.2 (2–21) | 0.97 |
| Operative time | 251.5 (46–967) | 218.7 (95–489) | 202.5 (96–357) | **< 0.01** |
| Perioperative complication | 38 (17.5) | 9 (18) | 6 (15.4) | 0.94 |
| IV Fluids | 2992.9 (250–7500) | 2451.0 (1000–4000) | 2560.3 (250–6000) | **0.01** |
| EBL | 600 (0–3400) | 500 (150–3500) | 500 (100–5000) | 0.09 |
| *Transfusion* | | | | |
| Intraoperative | 98 (45.4) | 18 (36) | 18 (46.2) | 0.46 |
| # units | 2 ± 1 | 2 ± 1 | 2 ± 1 | 0.52 |
| Postoperative | 64 (29.8) | 14 (28) | 6 (15.4) | 0.18 |
| # units | 2 ± 0 | 2 ± 0 | 2 ± 1 | 0.10 |

Bolded values for significance values $p < 0.05$

## Discussion

Patients undergoing acetabular fracture surgery are at an increased risk of VTE postoperatively which must be balanced against the risk of perioperative bleeding. The purpose of this study was to determine if preoperative DVT chemoprophylaxis modifies TXA efficacy in acetabular fracture surgery. Our present study found that holding DVT chemoprophylaxis in patients who received TXA did not affect number of intraoperative or postoperative transfusion rates. Patients did experience a significantly lower reduction in platelets compared to TXA with DVT prophylaxis.

Transfusion rates as high as 57% have been reported in pelvic and acetabular fractures [15], and allogenic blood transfusions put patients at risk for transfusion-associated complications, infection, and increased mortality [16, 17]. Evidence regarding TXA use for this indication is mixed. While one RCT found that TXA decreases transfusion [1, 18], more recent evidence finds no such difference [8, 13, 19]. Notably Cohen-Levy et al. [1] found that holding DVT prophylaxis and administering TXA prior to surgery and 3 h following resulted in a 20.7% reduction in blood product transfusion. However, our study found that holding DVT prophylaxis did not improve TXA efficacy in reducing blood transfusions intraoperatively or postoperatively. Interestingly, it did improve postoperative platelet levels. The difference observed between these studies may be attributable to variation in TXA administration as the current study administered 1 g of TXA prior to surgery and 1 g following wound closure, while the other administered 1–3 g initially and 1 g after 3 h.

TXA is safe and effective for reducing blood loss and transfusions in patients undergoing total joint arthroplasty while receiving DVT prophylaxis [20–22]. Additionally, choice of DVT chemoprophylaxis has been shown to not significantly effect TXA efficacy [12, 23]; however, these studies compared patients receiving anticoagulants with or without TXA use and did not compare TXA without chemoprophylaxis. Interestingly, a study by Sharfman et al. compared TXA efficacy in patients receiving VTE chemoprophylaxis versus TXA and intermittent pneumatic compression device (IPCD) without chemoprophylaxis. The study found TXA with IPCD and discontinuation of enoxaparin completely eliminated blood transfusions and did not increase the rate of thromboembolic events in patients undergoing total joint arthroplasty [24]. Not administering enoxaparin reduced transfusion rates by 19.1%, and addition of TXA further reduced transfusion rates by 5.6%., but the study did not assess interaction of TXA and enoxaparin.

Yakkanti et al. attempted to develop recommendations for bleeding and VTE prophylactic protocols for acetabular and pelvic fractures. They advised routine use of intraoperative TXA and DVT chemoprophylaxis postoperatively [25]. These recommendations were made in part due to the literature showing no increase in DVT, PE, and bleeding rates, while some lower quality evidence shows a direct benefit [25]. A meta-analysis by Shu et al. supported these findings with TXA reducing blood transfusions without increase in risk of VTE, DVT, or PE. Our present study found no increase in DVT, PE, or infection rates postoperatively ($p = 0.938$). While no clear benefit in transfusion and bleeding rates was shown, we observed that patients receiving TXA experienced shorter operative times ($p < 0.01$), which has been reported elsewhere in the literature [1, 26]. In our cohort, patients prescribed TXA with DVT chemoprophylaxis had lower ISS severity scores than patients given TXA without DVT chemoprophylaxis ($p < 0.0001$). This study attempted to control for this difference in demographics using multivariable regression, but ultimately these cohorts may be fundamentally different.

There are several limitations in this study. This study was retrospective in nature which inherently introduces bias. For example, patients were not prospectively randomized into each cohort and there was no standardized protocol for which patients were selected to receive TXA; patients may have been more likely to receive TXA if they were perceived to have a higher risk of bleeding. Additionally, topical TXA was not evaluated in the present study. Future prospective studies comparing standardized approaches to TXA administration with and without preoperative anticoagulant use could better assess the efficacy of TXA in acetabular and pelvic fractures.

## Conclusion

Holding DVT chemoprophylaxis does not affect IV TXA efficacy in reducing blood loss and transfusion rates in acetabular fracture surgery. There was no association between TXA administration and intraoperative or postoperative transfusion rates.

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**Conflict of interest** The authors have no competing interests to declare that are relevant to the content of this article.

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