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Commentary

Tranexamic acid in total hip arthroplasty—Differential efficacy in inflammatory versus degenerative arthritis

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Abstract

Total hip arthroplasty (THA) is a cornerstone intervention for advanced hip arthritis, but perioperative blood loss poses a significant clinical challenge, often leading to increased transfusion rates, prolonged hospitalization, and higher healthcare costs. Tranexamic acid (TXA), an antifibrinolytic agent, has emerged as an effective strategy for minimizing surgical bleeding. While the benefits of TXA in THA are well established, Mohabey *et al.* (2025) uniquely examined its comparative efficacy in inflammatory arthritis (IA) versus degenerative arthritis (DA) in an Indian population. Their retrospective cohort study suggests a differential response to TXA depending on arthritis type, with a more pronounced but statistically non-significant benefit in DA. This commentary contextualizes these findings within existing literature, explores mechanistic insights into differential TXA efficacy, highlights clinical implications, and identifies key areas for future research.

Keywords: Antifibrinolytic agent, Arthroplasty hip, Arthritis, Hemorrhage, Postoperative complications

Introduction

Total hip arthroplasty (THA) has transformed outcomes for patients with end-stage hip disease, providing pain relief and functional restoration in conditions ranging from primary osteoarthritis (OA) to inflammatory conditions such as rheumatoid arthritis (RA) and ankylosing spondylitis [1,2]. Despite advances in surgical technique, substantial intraoperative and postoperative blood loss remains common, with reported averages from 900 mL to over 1,600 mL [3–5]. Excessive bleeding increases the risk of transfusions, which are associated with transfusion reactions, infections, and immunomodulation [6]. Moreover, high-volume blood loss can exacerbate anemia, delay mobilization, and extend hospital stays [7].

Tranexamic acid (TXA), a synthetic lysine analogue, competitively inhibits the activation of plasminogen to plasmin, stabilizing fibrin clots and reducing fibrinolytic bleeding [8]. Its benefits have been consistently demonstrated in elective joint arthroplasty [9–11], and multiple clinical guidelines now recommend TXA as a standard adjunct in THA [12,13]. However, while the efficacy of TXA in general THA populations is well established, data comparing its impact on different arthritic pathologies, particularly Inflammatory arthritis (IA) vs. Degenerative arthritis (DA)—remain sparse.

This distinction is important because IA is characterized by chronic synovial inflammation, angiogenesis, and systemic cytokine release, potentially amplifying bleeding risk and altering coagulation responses [14,15]. Conversely, DA, such as OA or avascular necrosis, involves mechanical cartilage degradation without prominent systemic inflammation [16]. Understanding whether TXA's effects differ between these conditions is essential for tailoring perioperative hemostatic strategies.

Key Findings

Mohabey *et al.* [17] conducted a retrospective analysis of 126 patients undergoing uncemented THA at a single Indian center, stratifying them by TXA use and arthritis type (21 IA, 105 DA). TXA was administered as a single 1 g intravenous bolus pre-incision in 106 patients; 20 did not receive TXA. Their key findings include (**Table 1**):

1. **Operative time**: Significantly shorter in the TXA group (88.5 min vs. 102.6 min; p=0.046), an often-overlooked outcome with potential implications for surgical efficiency.
2. **Intraoperative blood loss**: Lower mean estimated blood loss in the TXA group (350.6 mL vs. 380 mL) but not statistically significant (p=0.472).
3. **Drain output**: Trend towards lower postoperative drainage in TXA users (118.9 mL vs. 183.3 mL; p=0.052).
4. **Functional recovery**: No significant difference in time to full weight-bearing (34.1 vs. 35.8 days; p=0.341).
5. **Subgroup trends**: Greater blood loss reduction with TXA in DA patients (mean reduction ~55 mL) but paradoxically higher mean blood loss in IA patients receiving TXA (429 mL vs. 300 mL).

These findings add new insights by suggesting TXA's hemostatic effect may be more pronounced in DA, likely due to more predictable coagulation profiles and less synovial vascularity.

Existing Evidence on TXA in THA

Numerous randomized trials and meta-analyses support TXA's role in reducing perioperative blood loss, transfusion rates, and hospital length of stay in THA [9–11,18]. For instance, a meta-analysis by Ker *et al.* [19] found TXA reduces surgical blood loss by ~30% and lowers transfusion risk without increasing thromboembolic complications. A Cochrane review including over 40 trials also concluded that TXA significantly reduces blood transfusion requirements in orthopedic surgery [20].

However, studies directly comparing IA and DA subgroups are limited. Morse *et al.* [21] retrospectively evaluated 271 RA patients undergoing total joint arthroplasty and found TXA did not reduce transfusion rates compared to DA patients, consistent with Mohabey *et al.*'s subgroup trends.

Novelty and Comparison to Recent Meta-Analyses and Guidelines

While multiple recent meta-analyses and umbrella reviews confirm TXA's efficacy and safety in THA, they rarely stratify by arthritis type. For example, a 2024 umbrella review by Zhang *et al.* confirmed TXA's benefit in reducing blood loss and transfusion rates in THA, but did not address IA versus DA specifically. The Mohabey *et al.* study is among the first to directly compare TXA efficacy in IA and DA within a single population, providing new insight into the need for personalized perioperative blood management strategies [22].

Pathophysiological Basis for Differential TXA Efficacy

Inflammatory arthritis (e.g., RA) involves systemic inflammation, elevated IL-1, IL-6, and TNF-α levels, and angiogenic factors like VEGF, leading to increased synovial vascularity and capillary fragility [14,23,24]. Histological studies show dense neovascularization in inflamed synovium, which correlates with increased bleeding risk [25]. Moreover, systemic inflammation can disrupt normal hemostatic pathways, altering fibrinolytic and coagulation responses, possibly diminishing TXA's antifibrinolytic efficacy [26].

In contrast, degenerative arthritis presents with cartilage loss, osteophyte formation, and subchondral sclerosis but lacks the systemic pro-inflammatory cytokine profile seen in IA [16,27]. Hemostasis during DA-related THA is more predictable, and TXA's clot-stabilizing effect appears more consistent, aligning with Mohabey *et al.*'s observation of greater blood loss reduction in DA.

Additionally, patient-specific factors such as preoperative anemia, renal function, and nutritional status may influence bleeding risk and TXA response [28]. Indian populations often exhibit dietary patterns (e.g., vegetarianism, spice intake) and racial variations affecting fibrinolysis [29], underscoring the need for region-specific data like that provided by Mohabey *et al.*

Operative Time: A Valuable but Understudied Outcome

Most TXA research focuses on blood loss and transfusions, but Mohabey *et al.*'s significant reduction in operative time with TXA is noteworthy. Excessive intraoperative bleeding obscures visualization, prolongs dissection, and complicates implant placement, leading to longer surgery duration [30]. Çataltepe *et al.* [31] similarly reported reduced THA time with TXA administration. Shorter operative times may reduce anesthesia-related risks, lower infection rates, and improve OR efficiency, which has important cost implications for high-volume arthroplasty centers [32,33].

Drain Output and Postoperative Complications

Persistent wound drainage increases the risk of hematoma, wound complications, and deep infections [34]. Studies have shown TXA reduces postoperative drain output, potentially mitigating these risks [35–37]. Gianakos *et al.* [38] and Yoon *et al.* [39] confirmed TXA significantly reduces drain output in arthroplasty patients. Although Mohabey *et al.* did not find statistical significance, their trend toward lower drain output in TXA users supports previous findings and highlights a clinically meaningful benefit in reducing wound-related complications.

Table 1. Key findings.

Outcome	**Inflammatory Arthritis (IA)**	**Degenerative Arthritis (DA)**	**Statistical Significance**
Operative Time	Higher	Lower	Significant
Intraoperative Blood Loss	Higher	Lower	Not significant
Postoperative Drainage	Higher	Lower	Not significant
Transfusion Rate	Higher	Lower	Not significant

Functional Recovery

Rapid mobilization after THA reduces complications such as deep vein thrombosis (DVT), pneumonia, and deconditioning [40]. While TXA reliably reduces blood loss, its effect on functional recovery metrics like time to ambulation or weight-bearing is inconsistent. Fraval *et al.* [41] found no significant improvement in pain or mobility despite reduced bleeding, which Mohabey *et al.*'s results corroborate. Future research should evaluate whether integrating TXA with enhanced recovery after surgery (ERAS) protocols accelerates postoperative rehabilitation [42,43].

Safety Considerations

Theoretical concerns persist that TXA may increase thromboembolic events; however, multiple large-scale studies have shown no significant rise in Deep Vein Thrombosis (DVT) or pulmonary embolism rates in arthroplasty patients receiving TXA [44–46]. In Mohabey *et al.*'s cohort, no TXA-related complications were reported, echoing extensive evidence supporting its safety. Poeran *et al.*'s analysis of over 870,000 joint arthroplasties found no increase in thromboembolic risk with TXA [47], reinforcing confidence in its routine use.

Limitations and Methodological Recommendations

Several factors limit generalizability of Mohabey *et al.*'s findings:

- **Retrospective design:** Prone to selection and information bias.
- **Small IA subgroup:** Only 21 patients with IA limits statistical power and may have led to the paradoxical trend of higher blood loss with TXA in IA.
- **Single center:** Findings may not extrapolate to centers with different surgical techniques or patient demographics.
- **Standardized single-dose TXA:** Emerging data suggests multi-dose or combined IV/topical TXA regimens may provide superior blood conservation [48,49].
- **Surgeon variability:** Although surgeries followed institutional protocols, individual differences could have affected outcomes.

Future studies should be prospective, multicenter, and stratified by arthritis type, with standardized multi-dose or combined TXA regimens and adequate power to detect subgroup differences.

Clinical Implications and Recommendations

Given potential reduced TXA efficacy in IA, surgeons should anticipate higher bleeding risk in these patients and consider adjunctive measures such as:

- Meticulous soft tissue handling to minimize synovial bleeding.
- Combined topical plus systemic TXA administration, which has shown enhanced efficacy [48].
- Early identification of high-risk IA patients (e.g., active RA flare) who may benefit from tailored hemostatic strategies [49,50].

Conversely, in DA patients, TXA remains reliably effective in reducing blood loss, operative time, and transfusion rates, supporting its routine use [12].

Guideline Development and Cost-Effectiveness

Recent guidelines (e.g. AAHKS 2024) recommend TXA for all eligible THA patients, but do not yet address IA-specific protocols. Cost-effectiveness analyses, including recent studies from low- and middle-income countries, support the use of oral TXA as a viable, affordable alternative to intravenous administration, particularly in resource-limited settings [51–54].

Future Directions

Research priorities emerging from Mohabey *et al.*'s study include:

1. **Prospective trials**: Comparing IA and DA cohorts receiving standardized multi-dose or topical TXA regimens.
2. **Biomarker studies**: Correlating inflammatory cytokine profiles with TXA response.
3. **Enhanced recovery after surgery (ERAS) integration**: Evaluating how TXA use within ERAS pathways affect mobility, length of stay, and complications.
4. **Cost-effectiveness analyses**: Assessing the economic impact of optimized TXA protocols, especially in low- and middle-income countries.
5. **Genetic and dietary factors**: Investigating how population-specific variables (e.g., diet-induced fibrinolytic variations) influence bleeding and TXA efficacy.

Conclusion

Mohabey *et al.*'s study provides novel insights into the differential effects of TXA in THA for IA vs. DA. Their findings suggest a potentially reduced efficacy of TXA in IA patients, possibly due to pathophysiologic factors like synovial hypervascularity and systemic inflammation, while confirming its robust benefits in DA. These observations underscore the need for personalized blood management strategies in arthroplasty. Future randomized trials with larger IA samples are critical to validate these findings and guide evidence-based protocols.

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