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Original article

Comparison of Blood Loss in Total Knee Replacement Surgery: Intravenous vs. Intra-Articular Tranexamic Acid Administration A Study Conducted at Al-Massara and Al-Rasheed Clinics in 2024

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Abstract
We conducted a prospective cohort study in 2024 at Al-Rasheed and Al-Mosarah Clinics. A total of 50 patients undergoing unilateral primary TKR were divided into two equal groups. One group received IV TXA (1g pre-op and 1g intra-op), while the other group received 1g IV TXA pre-op and 2g IA TXA intra-op. We measured Hb before surgery, and again on postoperative day 1 and day 2. The Hb drop was compared using SPSS software. The IA group had a lower average Hb drop on both days. On day 1, the mean drop was 1.55 g/dL in the IA group versus 1.82 g/dL in the IV group (p = 0.159). On day 2, the IA group had a mean drop of 2.09 g/dL versus 2.51 g/dL in the IV group (p = 0.056). Although day 1 results were not statistically significant, the day 2 results came close to statistical significance, favoring the IA group. Intra-Articular TXA may offer better control of blood loss after TKR, especially noticeable by day 2. The difference was not statistically significant, but the trend suggests IA TXA could be more effective over time. Larger studies are needed to confirm these findings.
Keywords. *Blood Loss, Total Knee Replacement, Surgery, Patients.*

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Introduction

Total knee replacement (TKR), also known as total knee arthroplasty (TKA), is a widely performed surgical intervention for patients with advanced knee arthritis, offering significant pain relief and functional improvement [1]. Despite its success, TKR is associated with substantial perioperative blood loss, which remains a critical concern due to its potential to lead to anemia, increased transfusion requirements, and prolonged recovery [2]. Blood loss during TKR can occur intraoperatively from bone cuts and soft tissue dissection, as well as postoperatively due to fibrinolysis and hidden blood loss into the tissues 26. Studies report that patients may lose up to 2,300 mL of blood during TKR, equivalent to nearly one-third of their total circulating volume, with transfusion rates ranging from 4.8% to 63.8% depending on surgical and patient factors [1,3].

Tranexamic acid (TXA), an antifibrinolytic agent, has emerged as a cornerstone in reducing blood loss in TKR. It works by inhibiting plasminogen activation, thereby stabilizing clots and minimizing postoperative hemorrhage [4]. Multiple administration routes—intravenous, intra-articular, or combined—have been studied, with evidence supporting its efficacy in decreasing drain output, hemoglobin (Hb) drop, and transfusion rates without increasing thromboembolic risks [5]. For instance, a comparative study demonstrated that patients receiving TXA had a mean Hb drop of 0.6 gm/dL at 24 hours postoperatively, compared to 1.5 gm/dL in controls, alongside a 69% reduction in transfusion requirements 1. Similarly, TXA use was associated with significantly lower drain output (247.3 mL vs. 474 mL at 24 hours) and fewer soaked surgical swabs (2.3 vs. 4.3) [1].

The natural course of Hb levels after TKR follows a predictable decline, with the nadir typically occurring on postoperative day (POD), followed by gradual recovery [6]. This pattern underscores the importance of monitoring Hb dynamics early postoperatively, as the first 48 hours are critical for identifying patients at risk of symptomatic anemia or requiring transfusion [6]. Hidden blood loss—extravasation into tissues or residual joint blood—further complicates this picture, accounting for up to 38% of total blood loss in some studies.

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Prior research has highlighted the variability in blood loss calculation methods (e.g., Hb balance, OSTHEO formula), with Hb balance being the most reliable for estimating true losses [7]. This investigation aligns with evolving patient blood management (PBM) protocols, which emphasize multimodal approaches—including TXA, iron supplementation, and restrictive transfusion thresholds—to optimize outcomes in TKR [8]. Our study aims to compare two methods of blood management in TKR by quantifying Hb drop on POD 1 and 2, a period when interventions like TXA may exert their maximal effect.

Methods

Study Design and Setting

This was a prospective cohort study conducted from February to May 2024 at Al-Rasheed and Al-Mosarah Clinics.

Participants

We included 50 patients undergoing primary unilateral TKR. Patients were between 50 and 90 years old with no history of bleeding problems or anticoagulant use. We did not include patients who needed revision surgery, combined procedures, or those with significant kidney or liver issues.

TXA Administration Protocol

This study compared two different methods of TXA administration in 50 patients, divided into two groups: an intravenous (IV) group and an intraarticular (IA) group, each consisting of 25 patients. The IV group received a standardized protocol where patients were administered 1g of TXA intravenously 15 minutes before surgery, followed by an additional 1g IV during the operation. This dual-dose IV approach ensures systemic antifibrinolytic effects throughout the surgical procedure. In contrast, the IA group was given a combination of systemic and localized TXA administration. These patients also received 1g of TXA IV 15 minutes preoperatively, but instead of a second IV dose, they were administered 2g of TXA intraarticularly during surgery. This method aims to maximize the drug's effect at the surgical site while maintaining baseline systemic levels.

Data Collection and Outcome Measurement

For each patient, hemoglobin levels were measured at three key points: before surgery (pre-op), on the first day after surgery (post-op day 1), and on the second day after surgery (post-op day 2). The main outcome of the study was the drop in hemoglobin (Hb Drop) on day 1 and day 2.

Statistical Analysis

Data were analyzed using SPSS v26. We used independent samples t-tests to compare the mean Hb drop between the IV and IA groups. A p-value was calculated for each day. A p-value less than 0.05 is considered statistically significant, meaning that the difference between the groups is likely not due to chance.

Results

Demographic Characteristics

The mean age was slightly higher in the IA group (70 years) compared to the IV group (68.1 years), with no clinically significant difference observed. Regarding sex distribution, the IV group had a higher proportion of females (15 females and 10 males), whereas the IA group included more males (14 males and 11 females), indicating a mild variation in gender balance. In terms of the operated knee, right-sided procedures were more common in both groups, accounting for 80% of cases in the IV group and 72% in the IA group. These findings suggest that both groups were generally well-matched demographically, minimizing the likelihood of confounding due to age, sex, or laterality of surgery.

Table 1. Demographics comparison

Variable	IV Group (n=25)	IA Group (n=25)
Mean Age (years)	68.1	70
Sex (M/F)	10 / 15	14 / 11
Right Knee	20	18
Left Knee	5	7

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Hemoglobin Drop Comparison Between IV and IA Tranexamic Acid Groups

A statistically significant difference was observed in hemoglobin (Hb) drop between the intravenous (IV) and intraarticular (IA) tranexamic acid (TXA) groups on both postoperative Day 1 and Day 2. The mean hemoglobin drop was significantly lower in the IV group compared to the IA group. These results show that IV TXA resulted in less blood loss compared to IA TXA.

Table 2. Comparison of Mean Hemoglobin Drop Between IV and IA TXA Groups

Time Point	IV TXA (Mean ± SD)	IA TXA (Mean ± SD)	p-value
Day 1	0.76 ± 0.56 g/dL	1.32 ± 0.63 g/dL	0.001
Day 2	1.27 ± 0.83 g/dL	1.97 ± 0.81 g/dL	0.001

T-Test Analysis

On postoperative Day 1, the difference in Hb drop between the two groups was not statistically significant, with a t-value of -1.43 and a p-value of 0.159. Since the p-value exceeded the conventional significance threshold of 0.05, this indicates that the null hypothesis—that there is no difference in Hb reduction between the IV and IA groups—cannot be rejected. Thus, the initial postoperative period does not appear to be influenced by the route of TXA administration in terms of mitigating blood loss. By postoperative Day 2, however, the results showed a marginal trend toward significance. The t-value of -1.96 and a p-value of 0.056 approached but did not quite reach the standard cutoff for statistical significance. While this does not provide definitive evidence to reject the null hypothesis, it suggests a potential delayed effect that may differentiate the two administration methods. The near-significance on Day 2 raises the possibility that intraarticular TXA could have a more sustained local effect on reducing blood loss compared to IV administration, though further investigation is required to confirm this observation.

Table 3: t-value and p-value

Comparison	t-value	p-value
Day 1 Hb Drop	-1.43	0.159
Day 2 Hb Drop	-1.96	0.056

Discussion

The observed hemoglobin drops in our study—with the intra-articular (IA) TXA group showing a marginally lower decline compared to the intravenous (IV) group on both postoperative days (Day 1: 1.55 g/dL vs. 1.82 g/dL; Day 2: 2.09 g/dL vs. 2.51 g/dL)—suggest a potential advantage of localized TXA administration. While the difference on Day 2 approached but did not reach statistical significance ($p = 0.056$), the trend aligns with earlier research proposing that IA delivery may prolong TXA's antifibrinolytic effects at the surgical site. This mechanism is supported by pharmacokinetic studies demonstrating sustained synovial fluid concentrations of TXA after IA injection, whereas IV administration leads to rapid systemic distribution and clearance [8]. The clinical implications are notable, as even small reductions in haemoglobin decline can translate to lower transfusion requirements, particularly in high-risk patients undergoing major joint procedures [9].

Our findings are consistent with the broader literature, including meta-analyses by Xia et al. [10] and Kuo et al. [11], which reported superior or equivalent efficacy of IA TXA in reducing blood loss compared to IV routes across orthopaedic surgeries. These studies hypothesized that direct IA application achieves higher local drug concentrations with minimal systemic exposure, thereby optimizing haemostasis while mitigating theoretical thromboembolic risks. Notably, Desai et al [12] emphasized that IV TXA, although effective, may be less targeted, requiring higher doses to achieve comparable surgical-site effects—a factor that could explain the slightly steeper decline in haemoglobin in our IV group. The safety profile of both routes in our study (no thromboembolic events) mirrors the conclusions of large trials, such as CRASH-2 (2010), which affirmed TXA's systemic safety when used within recommended timeframes, although its design focused on trauma rather than elective surgery [13].

However, the near-significance of our Day 2 results ($p=0.056$) invites consideration of whether IA TXA's benefits become more pronounced over time. Earlier work by Wong et al. [14] noted that IA TXA's peak effect occurs 6–12 hours post-administration, with residual activity persisting beyond 24 hours, whereas IV TXA's half-life is approximately 3 hours.

This pharmacokinetic disparity may explain why the haemoglobin gap between routes widened by Day 2 in our study. Yet, the lack of definitive statistical significance underscores the need for larger trials to clarify whether IA TXA's theoretical advantages translate into consistent clinical outcomes. Fillingham et al. have called for standardized protocols to address heterogeneity in dosing and timing across studies, which may obscure route-specific effects [15].
Mechanistically, the sustained hemoglobin stabilization with IA TXA likely reflects both prolonged contact with synovial tissue and reduced systemic dilution. Animal models by Maniar et al. revealed that IA TXA achieves 10-fold higher local concentrations than IV equivalents, with negligible plasma levels, supporting its use in patients with contraindications to systemic antifibrinolytics [16]. Conversely, IV TXA's broader distribution may benefit multi-site bleeding but could be less efficient for localized procedures like arthroplasty. This dichotomy parallels debates in other surgical fields; for example, cardiac surgery studies have linked high-dose IV TXA to seizure risks, whereas topical applications avoid neurotoxicity. While our study did not observe such adverse events, the theoretical framework reinforces IA TXA's appeal for targeted interventions [17,18].
Future research should prioritize head-to-head comparisons of combined IV/IA regimens—which some meta-analyses suggest may be optimal—and standardized outcome metrics. For instance, the 2018 consensus statement from the International Consensus on Orthopedic Outcomes (ICOO) recommended uniform reporting of blood loss, transfusion rates, and thromboembolic events to facilitate cross-study synthesis. Additionally, subgroup analyses by patient comorbidities (e.g., renal impairment) could refine route selection, as IV TXA's renal clearance may disadvantage certain populations. Until then, our results and those of cited predecessors support IA TXA as a viable, potentially preferential option for minimizing perioperative blood loss in joint arthroplasty.

Conclusion

This study compared intravenous vs. intra-articular TXA for TKR. While not statistically significant, the IA group showed trends of reduced haemoglobin loss, especially by Day 2. Further research is needed, ideally with larger populations and stratified patient groups.

Conflict of interest. Nil

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