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ORIGINAL RESEARCH

Study on the Effects of Tranexamic Acid on Perioperative Inflammation, Long-Term Functional Recovery, and Satisfaction in Total Knee Arthroplasty: A Follow-up Study

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Purpose: To explore the anti-inflammatory effects and safety of Tranexamic Acid (TXA) during the perioperative period of Total Knee Arthroplasty (TKA) in patients with Knee Osteoarthritis (KOA), and to follow-up on long-term knee joint function and patient satisfaction.

Methods: A prospective non-randomized controlled cohort study evaluated TXA efficacy in 130 unilateral TKA patients with KOA between January 2019 and March 2021. Patients were randomized into TXA (n=65) and control (n=65) groups. The TXA group received both intravenous and intra-articular TXA as required Postoperative coagulation profiles, day-3 systemic inflammatory markers, 6-month DVT/complication rates, and 2-year functional outcomes (knee function, QoL [Quality of Life], satisfaction) were assessed.

Results: No significant differences in demographics, clinical data, or KOA severity were observed between the control and TXA groups (P>0.05). Only TXA group showed decreased post-operative Fibrinogen (FIB) levels, while Erythrocyte Sedimentation Rate (ESR)(decreased to 15.41 ±4.39 mm/h), C-reactive Protein (CRP) (decreased to 33.32 ±11.56 mg/L), and Interleukin 6 (IL-6) levels significantly decreased (decreased to 111.38 ±30.14 μg/mL) on the third day post-operation (P<0.001). During the 6 months, specific complications did not significantly differ, but the overall complication rate notably decreased in the TXA group (OR=0.23, 95% CI 0.08 to 0.61, P = 0.012). At 2-year follow-up, TXA group showed significantly better joint function and QoL (P<0.05). Postoperative satisfaction correlated with preoperative TXA use, neutrophil count, NLR, ESR, and CRP. Multivariate analysis identified TXA as an independent predictor of satisfaction (P<0.05). TXA group exhibited reduced inflammation, lower complication rates, and improved long-term outcomes, demonstrating favorable perioperative and long-term outcomes in KOA management.

Conclusion: TXA has a significant effect on perioperative inflammation, long-term functional recovery and satisfaction in TKA.

Keywords: total knee arthroplasty, tranexamic acid, observational study, quality of life, inflammatory response

Introduction

Knee osteoarthritis (KOA) is a prevalent degenerative joint disease characterized by chronic inflammation, progressive cartilage loss, and significant pain and functional impairment.[1] Inflammatory activation of synovial tissue occurs early in KOA, with macrophages and fibroblasts releasing pro-inflammatory cytokines such as IL-1β, TNF-α, and IL-6.[2] These molecules accelerate the degradation of cartilage extracellular matrix by activating the NF-κB pathway and promoting the expression of matrix metalloproteinases (MMPs) and platelet-responsive protein-containing deintegrin metalloproteinases (ADAMTS).[3] The infrapatellar fat pad (IFP) is a fibrous adipose tissue of the knee joint that plays an important role in the mechanisms that induce osteoarthritis (OA) disease onset and progression.[4] Critically, this inflammatory state is not confined to the joint; it contributes to systemic metabolic and immune dysfunction, exacerbating symptoms like muscle atrophy and pain sensitization.[5–7] While early-stage management involves lifestyle changes and physical therapy, total knee arthroplasty (TKA) remains the definitive solution for severe KOA to relieve pain and restore function.[8,9] However, TKA itself triggers a significant systemic inflammatory response due to surgical trauma, ischemia-reperfusion

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injury, and infection risk.[10–12] This response contributes to postoperative complications such as pain, swelling, reduced mobility, and potentially compromised outcomes.[13] Therefore, strategies mitigating perioperative inflammation are crucial for improving recovery.

Tranexamic acid (TXA), a potent antifibrinolytic agent, is a mainstay for reducing blood loss in TKA.[14] Beyond hemostasis, emerging evidence suggests TXA possesses direct anti-inflammatory properties. Animal models demonstrate TXA's protective effects against post-traumatic OA progression,[15] and clinical studies indicate its perioperative use in TKA may correlate with reduced systemic inflammatory markers like IL-6 and CRP, potentially contributing to decreased postoperative pain and swelling.[16,17] This positions TXA as a promising candidate for repurposing to address the inflammatory burden inherent in both KOA and TKA.[15] Despite this potential, a significant research gap exists. Previous studies primarily focus on TXA's blood-sparing effects or are limited to retrospective analyses or animal models of OA.[18] Crucially, the long-term functional consequences and the specific impact of TXA's anti-inflammatory action on patient-reported outcomes and joint function following TKA remain inadequately explored.

This study addresses this gap directly. We employ a prospective non-randomized controlled cohort design to specifically investigate the anti-inflammatory effects and safety of perioperative TXA in TKA patients. By comparing systemic inflammatory marker levels, detailed postoperative recovery metrics, and crucially, tracking knee joint function and patient satisfaction over a two-year follow-up period, this study aims to provide robust clinical evidence on TXA's potential benefits beyond hemostasis. Our prospective, longitudinal approach focusing on functional outcomes distinguishes this work from prior retrospective reviews or preclinical studies. The findings will offer new insights for optimizing perioperative management in TKA and the broader treatment of KOA inflammation.

Materials and Methods

General Materials

Selection

This is a prospective non-randomized controlled cohort study. A total of 130 patients who underwent unilateral TKA for OA at the Anqing Hospital affiliated with Anhui Medical University from January 2019 to March 2021 were selected. Patients were divided into a TXA group (intravenous TXA, n=65) and a control group (intravenous saline only, n=65) on the basis of preoperative doctor-patient shared decision-making. Grouping was based on patient acceptance of TXA and contraindication assessment, with non-randomized assignment. This study was approved by the Medical Ethics Committee of Anqing Hospital affiliated with Anhui Medical University (Medical Ethics Review (2019) No. 21). All procedures were performed in compliance with the Declaration of Helsinki, and informed consent was obtained from all participants and their close relatives.

Inclusion Criteria

Patients diagnosed with OA, indicating surgery, planning to undergo unilateral TKA for the first time; normal preoperative hemoglobin and coagulation markers; preoperative bilateral lower limb Doppler ultrasound showing no thrombosis.

The diagnosis of OA was confirmed by clinical evaluation (persistent knee pain, morning stiffness <30 minutes, and functional limitation) combined with radiographic evidence (Kellgren-Lawrence grade ≥2 on preoperative X-ray). In cases of diagnostic uncertainty, MRI was utilized to exclude other pathologies (such as meniscal tears) and assess cartilage degeneration (Outerbridge grade).

Exclusion Criteria

Previous history of TKA; preoperative anemia or coagulation dysfunction; history of allergy to TXA; severe underlying diseases that could not withstand surgery. Patients with other rheumatic diseases or autoimmune inflammatory diseases were also excluded.

Patient Data Collection

Demographic data of the patients, including age, gender, smoking and drinking history, Body Mass Index (BMI), and records of systemic comorbidities, such as diabetes and dyslipidemia, were collected.

TXA Intervention

All patients were given either spinal or general anesthesia, with a tourniquet applied preoperatively at a pressure of 35 kPa. A pneumatic tourniquet was applied to the proximal thigh at 35 kPa (≈263 mmHg), determined by adding a safety margin of 130 mmHg to the average preoperative systolic blood pressure (130 mmHg) to minimize tissue injury while ensuring effective hemostasis.[19] This pressure aligns with international guidelines for tourniquet use in lower limb arthroplasty. Anesthesia type (spinal or general) was selected based on patient contraindications and anesthesiologist evaluation. Spinal anesthesia was preferred unless contraindicated. All patients were treated with the LINK Gemini MK II posterior stabilized cemented prosthesis (Link, Germany) including femoral condylar component, tibial plateau and polyethylene liner, with preservation of the posterior cruciate ligament (PCL) and intramedullary localization system to ensure alignment of the lines of force (<3° deviation from the target mechanical axis). All TKA surgeries were performed by 3 senior orthopedic surgeons (all with more than 10 years of experience in joint replacement), using a standardized surgical procedure and instrumentation to ensure technical consistency. The lateral 1/3 of the fat pad was resected only when it was severely fibrotic or prevented exposure of the surgical field to avoid anterior knee pain and release of inflammatory factors due to complete resection. The IFP vascular nerve bundle was protected intraoperatively by blunt dissection and no IFP repair was performed postoperatively.

Preoperative Use

TXA was administered 10 minutes before releasing the tourniquet. The observation group received 1 g of TXA (produced by Zhejiang Jinhua Conba Pharmaceutical Co., Ltd., with the National Medicine Certificate number H20031172, batch number: DK1812002-3) dissolved in 100 mL of 0.9% sodium chloride solution intravenously. The control group was given 100 mL of 0.9% sodium chloride solution intravenously. After the prosthesis was installed and the bone cement had fully solidified, the tourniquet was released, hemostasis was achieved with electrocoagulation, the area was rinsed and sutured, and a drainage tube was placed. The surgery was controlled within 90 minutes.

Postoperative Maintenance

Intra-articular continuous infusion of 3 g of TXA dissolved in 100 mL of saline at a rate of 12.5 mL/hour through a drain tube over 24 hours postoperatively.[20] Postoperative intravenous maintenance is 1 g of TXA dissolved in 100 mL of saline every 8 hours for a total of three injections. Postoperative anticoagulation therapy was administered according to the standard treatment protocol. In patients with contraindications to TXA, the alternate antifibrinolytic drug aminocaproic acid (EACA) was used.

Laboratory Test Indicators

Venous blood was collected for routine blood analysis (used fasting blood sample), recording RBC count, Neutrophil count, Lymphocyte count, Monocyte count, and Platelet count. Additionally, the level of systemic inflammation was assessed using the following formula:[21]

$$\mathrm{NLR} = \text{neutrophil count}(10^9/\mathrm{L})/\text{lymphocyte count}(10^9/\mathrm{L});$$

$$\mathrm{PLR} = \text{platelet count}(10^9/\mathrm{L})/\text{lymphocyte count}(10^9/\mathrm{L});$$

$$\mathrm{SII} = \text{neutrophil count}(10^9/\mathrm{L}) \times \text{platelet count}(10^9/\mathrm{L})/\text{lymphocyte count}(10^9/\mathrm{L}).$$

Additionally, the levels of plasma prothrombin time (PT), plasma fibrinogen (FIB), and activated partial thromboplastin time (APTT) were measured preoperatively and 24 hours postoperatively for both groups. The level of inflammation was indicated by analyzing perioperative erythrocyte sedimentation rate (ESR), interleukin 6 (IL-6), and C-reactive protein (CRP) levels. Venous blood levels of ESR, IL-6, and CRP were measured preoperatively and on the third day postoperatively for both groups using the enzyme-linked immunosorbent assay (ELISA) method. CRP and IL-6 were detected using a Roche Cobas 8000 automatic biochemical immunoassay analyzer (Roche, Switzerland) with immunoturbidimetric (CRP) and chemiluminescent (IL-6) assays, respectively. ESR was detected using an Alifax Test 1 automatic ambulatory hemocytometer (Alifax, Italy). A 4 mL venous blood sample from all patients was centrifuged

at 3000 r/min for 10 minutes, and the serum was stored at −80°C for testing. All operations were strictly carried out by professional laboratory personnel according to the instruction manual. Systemic Inflammatory markers (ESR, CRP, IL-6) were measured preoperatively and on the third postoperative day (POD3) based on the dynamic trajectory of post-operative inflammation, where POD3 represents a critical phase for evaluating sustained inflammatory responses beyond the acute surgical stress period.

Deep Vein Thrombosis (DVT)

Both groups of patients underwent bilateral lower limb venous color Doppler ultrasound examinations preoperatively (LOGIQ E20, General Electric Company, America), one week postoperatively, and four weeks postoperatively to ascertain the presence of thrombus formation.

Follow-up Study

Postoperative follow-up was conducted routinely, with visits every 1–2 months during the first half-year and outpatient visits every 3 to 6 months after one year. At 6 months postoperatively, complications of TKA were tallied, including deep vein thrombosis (DVT), cerebrovascular accidents, myocardial infarction, pneumonia, pulmonary embolism, urinary tract infections, transfusions, and superficial skin infections, in both groups of patients. The occurrence of total complications was calculated. Patient revision cases were recorded for subsequent analysis. Two years after surgery, knee joint function was assessed using The Hospital for Special Surgery (HSS) Knee Score Questionnaire and range of motion (ROM). The first postoperative follow-up visit was made to assess the grade of healing and the presence of redness, swelling or oozing. The HSS knee score and SF-36 quality of life (QoL) scale were completed by a blinded assessor at the 3-month postoperative follow-up. The HSS score, SF-36 scale and 6-minute walk test (6MWT) were repeated at 6-month and 1-year postoperative follow-up. Final 2-year postoperative follow-up included a patient satisfaction survey (5-point Likert scale), need for revision surgery, and survival analysis.

Knee function (HSS score) and QoL (SF-36) were systematically assessed at multiple time points: preoperatively, 3 months, 6 months, 1 year, and 2 years postoperatively. However, the 2-year data were prioritized in the main analysis to reflect long-term outcomes and align with international consensus on TKA efficacy evaluation. Data from earlier time points (3 days, 6 weeks, 6 months) focused on monitoring acute recovery parameters.

QoL and Satisfaction

The SF-36 scale, a validated and widely accepted tool, was used to assess QoL in both physical and mental domains.[22] The physical health category includes the following subscales: physical functioning, role limitations due to physical health, bodily pain, and general health perceptions. The mental health category includes vitality, social functioning, role limitations due to emotional problems, and mental health. Scores range from 0 (worst health condition) to 100 (best health condition). The Chinese version of the SF-36 was used for assessing the QoL. The SF-36 questionnaire was administered preoperatively (baseline) and postoperatively at 3 months, 6 months, 1 year, and 2 years to track longitudinal changes in health-related QoL (HRQoL). HRQoL was evaluated using the validated Chinese version of the SF-36 Health Survey (version 2.0), which has demonstrated high reliability and validity in Chinese populations with knee osteoarthritis.[23]

Treatment satisfaction was assessed through patient ratings, ranging from 0 (least satisfied) to 100 (most satisfied), with a cutoff point of 90 for treatment satisfaction for analysis. Patient satisfaction was evaluated using a 5-point Likert scale specifically designed for postoperative TKA outcomes, with the following anchors: 1 = Very dissatisfied, 2 = Dissatisfied,3 = Neutral,4 = Satisfied, 5 = Very satisfied. Treatment satisfaction is the most crucial outcome variable.

Statistical Methods

Statistical analysis was performed using Graphpad (Graphpad Prism version 10.1.0 America). Quantitative data were presented as mean ± standard deviation (sd). Comparisons of baseline data and pre- and post-operative coagulation functions between groups were conducted using independent sample *t*-tests, while count data comparisons used chi-square tests. Changes in postoperative ESR, IL-6, and CRP peak levels and their levels on the third postoperative day

were analyzed by binary and multiple logistic regression analyses in relation to TXA use. Normality of continuous variables was assessed using the Shapiro–Wilk test (for sample sizes <50) or the Kolmogorov–Smirnov test (for sample sizes ≥50), and statistical significance was set at P>0.05 to indicate a normal distribution. For non-normally distributed data, appropriate transformations were performed before parametric analysis, and if the transformation did not normalize the distribution, non-parametric tests (Mann–Whitney U, Wilcoxon signed rank) were used. All missing values were not included in the final statistical analysis.

Results

General Analysis

421 potential candidates were screened in this study, and after excluding those not meeting the inclusion criteria and unable to participate, a total of 130 patients were ultimately included and evenly divided into the observation and control groups (Figure 1). The observation group comprised 65 patients, including 22 males and 43 females, with an average age of 65.32 ± 4.17 years and a BMI of 26.03 ± 3.40 kg/m^2, and an HSS score of 46.52 ± 9.15, and an VAS at rest score of 1.47 ± 0.62, and an VAS at movement of 2.14 ± 1.02, and an ROM(°) of 80.79 ± 17.83, and an SF-36 Physical score of 42.77 ± 15.29, and an SF-36 Mental score of 45.99 ± 16.68. The TXA treatment group consisted of 65 patients, with 31 males and 34 females; the average age was 65.48 ± 7.23 years, with a BMI of 24.95 ± 3.73 kg/m^2, and an HSS score of 45.73 ± 7.50, and an VAS at rest score of 1.43 ± 0.58, and an VAS at movement of 2.19 ± 0.97, and an ROM(°) of 84.22 ± 19.34, and an SF-36 Physical score of 45.16 ± 17.22, and an SF-36 Mental score of 47.19± 17.83. The distribution of anesthesia types was balanced between groups and adjusted for in statistical analyses to minimize confounding. No statistically significant differences were observed in these metrics between the groups (all P > 0.05). Furthermore, there were no statistically significant differences in demographic data, routine blood tests, and systemic inflammation indices between the two groups (Table 1, P > 0.05), indicating comparability.

Postoperative Coagulation Function

Given that TXA is an important medication for coagulation disorders, preoperative and postoperative coagulation markers were analyzed for both groups. As shown in Table 2, there were no statistically significant differences in preoperative PT, FIB, and APTT between the groups (P > 0.05). However, postoperative FIB levels in the TXA group (2.95 ± 1.16 g) were significantly lower than those in the control group (3.35 ± 0.90 g, P = 0.031).

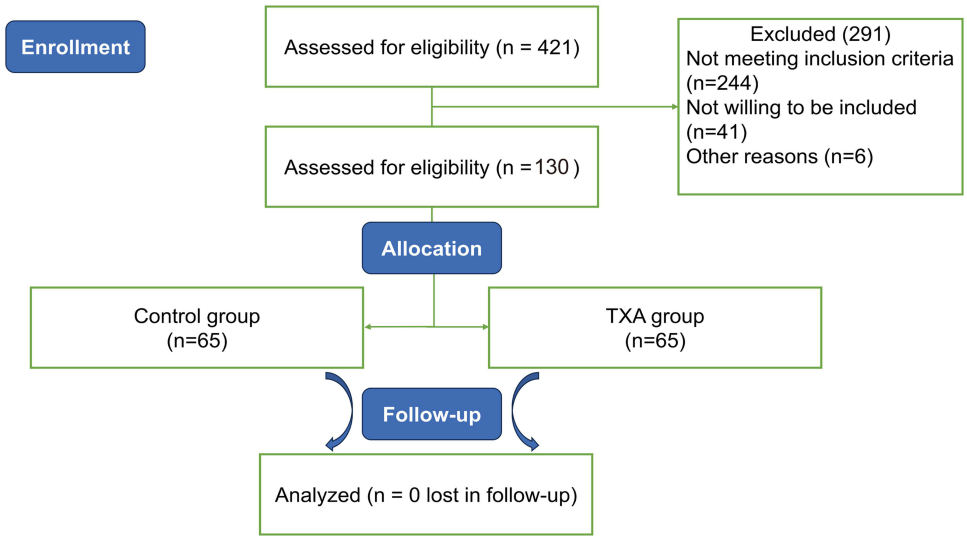

Figure 1 Study flow chart showing the data collection methodology and excluded cases.

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Table 1 Basic Characteristics of KOA Patients Treated by TKA with or without TXA

Characteristics	Control Group (n = 65)	TXA Group (n = 65)	P
Age (years)	65.32 ±4.17	65.48 ±7.23	0.883
Gender (male/female)	22/43	31/34	0.153
Smoking (ever/never)	10/55	15/50	0.374
Alcohol drinking (ever/never)	15/50	18/47	0.687
BMI (kg/m^2)	26.03 ±3.40	24.95 ±3.73	0.089
Obesity (yes/no)	8/57	6/59	0.778
Diabetes (yes/no)	14/51	12/53	0.827
Dyslipidemia (yes/no)	7/58	9/53	0.599
RBC count ($10^{12}/L$)	4.18 ±0.45	4.03 ±0.60	0.106
Neutrophil count ($10^{12}/L$)	7.65 ±2.79	6.61 ±3.21	0.052
Lymphocyte count ($10^{12}/L$)	1.36 ±0.33	1.31 ±0.27	0.388
Monocyte count ($10^{12}/L$)	0.74 ±0.29	0.68 ±0.29	0.254
Platelet count ($10^{9}/L$)	210.24 ±48.67	202.56 ±56.02	0.409
NLR	6.12 ±3.06	5.18 ±2.62	0.064
PLR	165.22 ±59.65	162.41 ±62.59	0.795
SII	1268.36 ± 707.48	1060.29 ± 592.97	0.074
HSS scale	46.52 ± 9.15	47.11 ± 9.23	0.719
VAS at rest	1.47 ± 0.62	1.43 ± 0.58	0.932
VAS at movement	2.14 ± 1.02	2.19 ± 0.97	0.748
ROM(°)	80.79 ± 17.83	84.22 ± 19.34	0.689
SF-36 Physical score	42.77 ± 15.29	45.16 ± 17.22	0.566
SF-36 Mental score	45.99 ± 16.68	47.19± 17.83	0.712

Abbreviations: BMI, Body Mass Index; RBC, Red blood cell; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet to lymphocyte ratio; SII, Systemic immune-inflammation index; HSS, Hospital for Special Surgery; VAS, Visual Analogue Scale; ROM(°), Range of Motion; SF-36, Short Form-36 Health Survey; TXA, Tranexamic Acid.

Table 2 The Coagulation Indexes of KOA Patients Treated by TKA with or without TXA

Characteristics	Control Group (n = 65)	TXA Group (n = 65)	P
Pre-operative PT (seconds)	14.92 ±2.70	14.09 ±3.24	0.114
Post-operative PT (seconds)	12.31 ±3.15	12.71 ±3.51	0.494
Pre-operative FIB (g/L)	3.20 ±0.91	3.32 ±1.06	0.495
Post-operative FIB (g/L)	3.35 ±0.90	2.95 ±1.16	0.031
Pre-operative APTT (seconds)	34.37 ±3.16	35.56 ±3.75	0.055
Post-operative APTT (seconds)	33.37 ±3.23	34.45 ±4.01	0.095

Abbreviations: PT, Prothrombin time; FIB, Fibrinogen; APTT, Activated Partial-Thromboplastin Time; TXA, Tranexamic Acid.

Postoperative Inflammation Markers

To further clarify the effect of TXA on postoperative inflammatory responses, blood samples were collected preoperatively and on the third day postoperatively to analyze ESR, CRP, and IL-6 levels. Preoperative results showed no significant differences between the two groups ($P > 0.05$). However, on the third day postoperatively, significant reductions in ESR, CRP, and IL-6 levels were observed in the TXA intervention group ($P < 0.05$, Table 3).

Table 3 The Inflammatory Indexes of KOA Patients Treated by TKA with or without TXA

Characteristics	Control Group (n = 65)	TXA Group (n = 65)	P
Pre-operative ESR (mm/h)	25.67 ±2.22	25.93 ±2.24	0.506
Post-operative ESR (mm/h)	22.39 ±4.82	15.41 ±4.39	<0.001
Pre-operative CRP (mg/L)	2.97 ±0.31	2.94 ±0.26	0.611
Post-operative CRP (mg/L)	45.26 ±13.38	33.32 ±11.56	<0.001
Pre-operative IL-6 (μg/mL)	2.21 ±0.26	2.21 ±0.24	1.000
Post-operative IL-6 (μg/mL)	161.61 ±45.47	111.38 ±30.14	<0.001

Abbreviations: ESR, Erythrocyte Sedimentation Rate; CRP, C-reactive protein; IL-6, Interleukin-6; TXA, Tranexamic Acid.

Postoperative Complications and Revision

An analysis of postoperative complications and revisions was conducted at the 6-month follow-up. As shown in Table 4, at 6 months postoperatively, there were no significant differences in DVT, cerebrovascular accident, myocardial infarction, pneumonia, pulmonary embolism, urinary tract infection, transfusions, and superficial skin infections ($P > 0.05$). Moreover, the overall incidence of total complications significantly decreased in the TXA group (OR = 0.23, 95% CI 0.08 to 0.61, P = 0.012). At 6 months postoperatively, 2 patients in the control group and 1 patient in the TXA group underwent revision, with no significant difference between the groups (OR = 0.49, 95% CI 0.04 to 5.57, P = 1.000). During the 2-year follow-up period, 8 patients (3 in the TXA group and 5 in the control group) underwent revision of the TKA. 3 cases had a delayed chronic infection, 1 case had an acute postoperative deep infection, 2 cases of aseptic loosening both with tibial prosthesis loosening, 1 case of polyethylene liner wear, and 1 case of joint stiffness. All revision cases were performed after confirmation of indications by a multidisciplinary team.

Postoperative Knee Function and QoL

The HSS score, VAS score, and ROM levels of both groups of patients were analyzed 2 years post-surgery. The HSS score in the TXA intervention group (92.43 ± 7.45) was significantly higher than that in the control group (86.38 ± 8.04, P<0.001), indicating that TXA intervention contributes to the long-term functional recovery of the knee joint post-TKA in KOA patients. Additionally, the long-term QoL, assessed through the SF-36, showed significant improvements in both physical and mental aspects in the TXA intervention group (P<0.001, Figure 2). We compared the changes in the HSS scale, VAS at rest, VAS at movement, ROM (°), SF-36 Physical score, and SF-36 Mental score between postoperative and preoperative assessments. The results revealed statistically significant differences in the change in HSS scale (P=0.011) and the change in ROM(°) (P=0.036), which further demonstrates the beneficial effect of TAX on patient outcomes (Table 5).

Table 4 Comparison of 6-month Complications and Readmissions in TKA Cases with or without TXA Treatment

Complications	Control Group (n = 65)	TXA Group (n = 65)	OR	95% CI	P Value
Deep vein thrombosis	2	0	–	–	0.496
Cerebrovascular accident	3	1	0.32	0.03~3.19	0.619
Myocardial infarction	1	0	–	–	1.000
Pneumonia	5	1	0.19	0.02~1.65	1.000
Pulmonary embolism	1	1	1.00	0.06~16.34	1.000
Urinary tract infection	2	1	0.49	0.04~5.57	1.000
Transfusions	3	1	0.32	0.03~3.19	0.619
Superficial skin infections	1	1	1.00	0.06~16.34	1.00
Total complications	18	6	0.23	0.08~0.61	0.012
Readmissions	2	1	0.49	0.04~5.57	1.000

Abbreviation: TXA, Tranexamic Acid.

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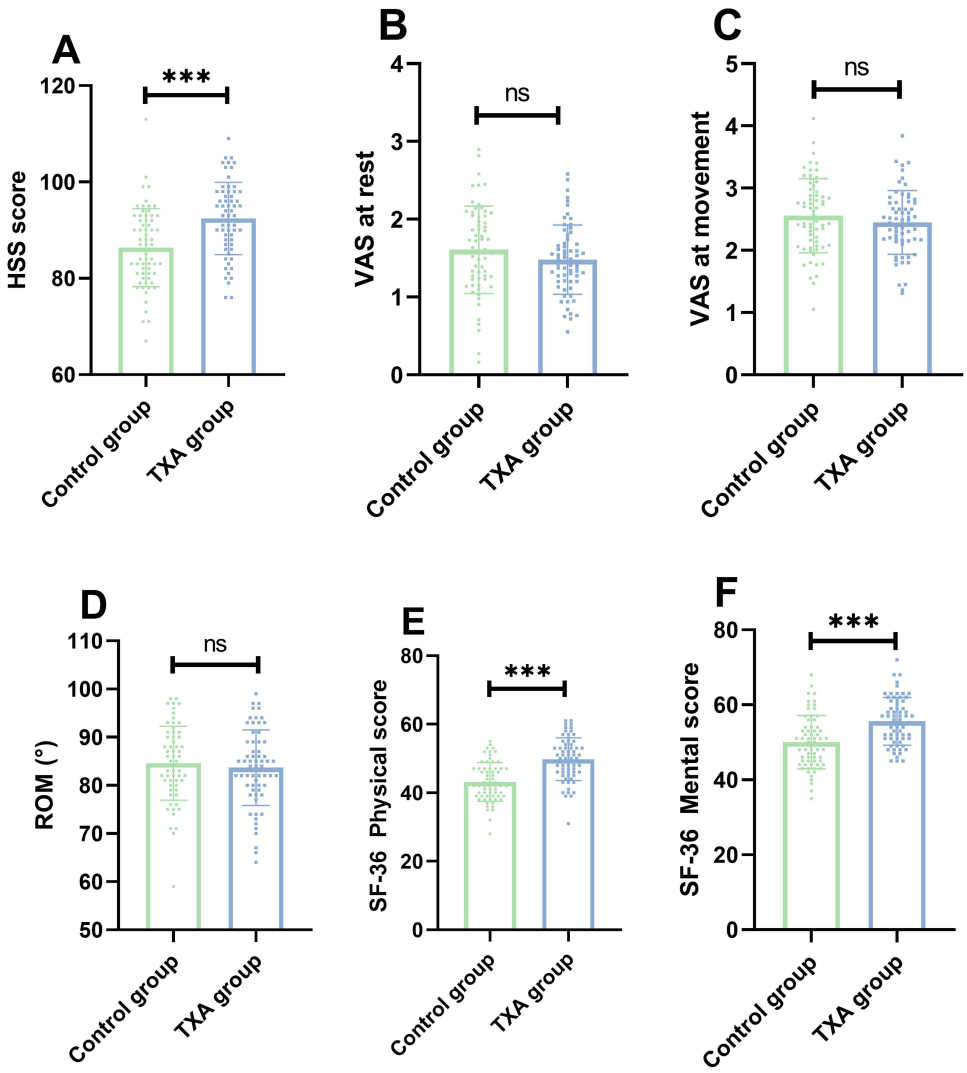

Figure 2 The long-term knee function and life quality in control and TXA group. (**A**) HSS score; (**B**) VAS at rest; (**C**) VAS at movement; (**D**) ROM; (**E**) SF-36 physical score; (**F**) SF-36 mental score. ***p < 0.001, ns: p>0.05.

Treatment Satisfaction Analysis

To analyze long-term patient satisfaction post-surgery, satisfaction scores were compared between the control and TXA groups. The satisfaction score in the TXA group (94.66 ± 2.85) was significantly higher than that in the control group (92.58 ± 4.89, P=0.004). Moreover, using a satisfaction threshold of 90 points, 63 patients in the TXA group were satisfied, compared to 53 in the control group, showing a statistical difference (P=0.009).

Table 5 Comparison of Changes in Key Outcome Measures at 6 Months in TKA Patients Treated with versus without TXA

Characteristics	Control Group (n = 65)	TXA Group (n = 65)	P
ΔHSS scale	40.37 ± 13.23	56.32 ± 11.39	0.011
ΔVAS at rest	1.01 ± 0.73	1.03 ± 0.69	0.875
ΔVAS at movement	1.01 ± 0.97	0.93 ± 0.76	0.443
ΔROM(°)	5.76 ± 3.43	10.32 ± 2.14	0.036
ΔSF-36 Physical score	20.74 ± 10.11	19.78 ± 9.33	0.175
ΔSF-36 Mental score	17.82 ± 5.67	18.89± 7.63	0.126

Abbreviations: HSS, Hospital for Special Surgery; VAS, Visual Analogue Scale; ROM(°), Range of Motion; SF-36, Short Form-36 Health Survey; TXA, Tranexamic Acid.

Further correlation analysis between satisfaction scores and preoperative baseline data revealed that postoperative satisfaction was associated with TXA treatment, neutrophil count, NLR, SII, ESR, and CRP (P<0.05, Table 6). Multivariate logistic regression analysis, including these factors, identified TXA intervention as an independent factor for postoperative satisfaction (OR=0.192, 95% CI 0.028 to 0.798, P=0.0419, Table 7). In addition, the Nagelkerke R^2 value is 0.512, indicating that the model has a relatively good predictive value. Hence, the intraoperative use of TXA plays a role in enhancing patient satisfaction.

Table 6 The Correlations Between Baseline Characteristics and Satisfaction Score in All the Participants

Characteristics	r	P
Age (years)	0.030	0.734
Gender (male/female)	5.764e-005	0.999
Smoking (ever/never)	0.067	0.448
Alcohol drinking (ever/never)	0.079	0.371
BMI (kg/m^2)	0.115	0.194
Obesity (yes/no)	0.052	0.554
Diabetes (yes/no)	0.008	0.926
Dyslipidemia (yes/no)	−0.030	0.735
RBC count (10^{12}/L)	0.001	0.993
Neutrophil count (10^{12}/L)	−0.226	0.010
Lymphocyte count (10^{12}/L)	0.009	0.920
Monocyte count (10^{12}/L)	−0.072	0.414
Platelet count (10^{9}/L)	−0.008	0.931
NLR	−0.231	0.008
PLR	−0.081	0.362
SII	−0.243	0.005
PT (seconds)	−0.030	0.738
FIB (g/L)	0.0162	0.855
APTT (seconds)	−0.149	0.091
ESR (mm/h)	0.174	0.047
CRP (mg/L)	−0.217	0.013
IL-6 (μg/mL))	0.0247	0.781
HSS scale	−0.085	0.339
TXA treatment	0.239	0.006

Abbreviations: NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet to lymphocyte ratio; SII, Systemic immune-inflammation index; PT, plasma prothrombin time; FIB, plasma fibrinogen; APTT, activated partial thromboplastin time; ESR, erythrocyte sedimentation rate; IL-6, interleukin 6; CRP, C-reactive protein; HSS, Hospital for Special Surgery; TXA, Tranexamic Acid.

Table 7 The Effects of Based Characteristics on the Long-Term Satisfaction Status Using a Logistic Regression Model

Characteristics	Odds Ratios	95% CI	P
TXA Treatment	0.192	0.028 to 0.798	0.0419
Neutrophil count (10^{12}/L)	1.075	0.737 to 1.59	0.7076
NLR	1.233	0.716 to 2.076	0.4302
SII	0.9999	0.998 to 1.002	0.9548
ESR (mm/h)	0.8538	0.625 to 1.139	0.2980
CRP (mg/L)	4.134	0.497 to 46.120	0.2130

Abbreviations: TXA, Tranexamic Acid; NLR, Neutrophil-to-Lymphocyte Ratio; PLR, Platelet to lymphocyte ratio; SII, Systemic immune-inflammation index; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

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Discussion

Principal Findings

This study demonstrates that intravenous TXA administration in knee osteoarthritis (KOA) patients undergoing TKA effectively reduces postoperative inflammation (IL-6, TNF-α) and hidden blood loss without impairing coagulation function or increasing deep vein thrombosis (DVT) incidence, consistent with its known safety profile even at high doses (30 mg/kg).[24,25] Crucially, TXA intervention was associated with enhanced functional recovery and identified as an independent protective factor for long-term patient satisfaction. We also found that elevated systemic inflammation markers (NLR, SII, ESR, CRP) correlated with reduced satisfaction—a novel observation underscoring the multifaceted impact of inflammation on recovery.

Comparison with Literature

Originally used to treat postpartum hemorrhage (PPH) due to its effective hemostatic properties, TXA has become a commonly used antifibrinolytic agent in clinical practice. Early studies found that TXA also has a role in reducing perioperative inflammatory responses, mainly in cardiac surgery, and has gradually been applied to other areas including cerebral and ocular hemorrhages.[26,27] Moreover, TXA intervention has potential orthopedic hemostatic applications; recent systematic reviews and network meta-analyses have shown TXA to be one of the most effective interventions for preventing bleeding in hip or knee replacement surgeries.[25] In this study, by comparing coagulation function and DVT incidence rates between two groups of patients postoperatively, results showed that TXA had little impact on coagulation function and did not increase the risk of venous thrombotic complications.

Clinical Implications

As TXA's application in orthopedics becomes more widespread, increasing research has focused on its potential anti-inflammatory effects, offering additional benefits to patients. In 2016, Xie et al included 151 patients undergoing TKA in a study and found that multiple postoperative intravenous infusions of TXA could effectively reduce postoperative serum CRP and IL-6 levels. Most importantly, by adding one more intravenous push of TXA, patients could achieve smaller decreases in Hb, less postoperative inflammatory response, less pain, and less knee joint swelling.[28] Moreover, multiple intravenous pushes of TXA effectively reduced hidden blood loss after primary THA.[29] Another study evaluating 640 patients undergoing surgery after elbow trauma found that the use of TXA was associated with a lower incidence of heterotopic ossification compared to not using TXA.[30] The results of this study showed that TKA surgeries with TXA intervention had lower levels of inflammation and higher functional recovery. Therefore, TXA has the potential for deeper application in the field of KOA.

Mechanistic Insights

The specific mechanisms of TXA's anti-inflammatory action are not yet clearly understood. D-dimers can increase the release of inflammatory cytokines. Therefore, although fibrinolysis and inflammation are largely independent processes, they are likely closely connected, and inhibiting the formation of fibrinolysis may help suppress the generation of inflammatory factors.[31]

Early studies on traumatic brain injury found that only higher doses of TXA could definitively eliminate penumbral leukocyte mobilization, thereby maintaining the integrity of the blood-brain barrier after brain injury and inhibiting cellular activation.[32] However, this study did not further explore the mechanisms, which remains a direction for future research by our team.

TXA demonstrates a favorable safety profile, with no evidence indicating that high doses (30 mg/kg) increase deep vein thrombosis risk. While our study confirms TXA does not impair coagulation or elevate thrombotic complications, its anti-inflammatory effects may exhibit dose dependency. Research in traumatic brain injury indicates that only higher TXA doses definitively suppress inflammatory pathways like penumbral leukocyte mobilization.[33] In orthopedics, TXA reduces systemic inflammatory markers (CRP, IL-6) and improves outcomes,[32] yet whether doses exceeding current regimens (eg, 30 mg/kg) could enhance anti-inflammatory efficacy remains unexplored. Future studies should investigate TXA's dose-response relationship for anti-inflammatory benefits in knee surgery.

Satisfaction-Inflammation Correlation

This study also focuses on the postoperative QoL and satisfaction with surgery among patients with KOA undergoing TKA. Patients with KOA are often older, have declining physical functions, poor psychological resilience, and a lack of exercise awareness and discipline. This can lead to non-compliance with medical advice on exercise and excessive rest during home rehabilitation, increasing the risk of complications such as joint stiffness. These complications are detrimental to postoperative recovery and can lead to a decrease in QoL. Research has shown that satisfaction improves within the first six months after TKA treatment, supporting the early identification of patients at risk of low satisfaction with TKA. This enables clinicians to provide timely targeted treatment and supportive interventions to improve patient outcomes.[34] Another multicenter cohort study indicated that low preoperative HRQoL scores, older age, severe obesity, certain comorbidities (such as depression and rheumatism), readmission or complications without discharge rehabilitation, are good predictors of long-term low benefits in HRQoL.[33] Unlike previous findings, our study focused on systemic inflammation levels, identifying multiple NLR, SII, ESR, and CRP as candidate factors leading to poor patient satisfaction. A unique aspect of this study was its focus on TXA, finding that TXA intervention plays a role in enhancing long-term patient satisfaction rates and acts as an independent protective factor. Thus, this study provides new evidence for the use of TXA in KOA interventions from a novel perspective.

Limitations

This study has the advantages of a wide range of test indicators and a long follow-up period, focusing on TXA as a potential key candidate adjunctive medication. However, there are some limitations to this study. Firstly, it is not a randomized controlled double-blind experiment, and the absence of blinding may introduce bias in subjective testing and scoring. Additionally, the sample size is still not large enough, and some results, such as complications, cannot provide more convincing conclusions. Moreover, the individual differences among patients and the technical gaps among surgeons cannot be simply ignored. Finally, the knee joint scoring is not detailed enough, and future research should incorporate imaging and structural-functional analysis. Furthermore, there is no evidence to suggest that high doses (30 mg/kg) of TXA pose a risk of deep vein thrombosis formation, making TXA a relatively safe hemostatic strategy with potential for further application. As for the study of drug efficacy, the most appropriate dosage of medication needs to be confirmed in future strict large-sample clinical cohort studies.

Conclusion

TXA has a certain inhibitory effect on perioperative inflammatory responses in TKA, alleviates patient discomfort, promotes functional recovery, and improves long-term knee joint function and patient satisfaction without increasing the risk of thrombosis formation. The observed weak correlations may be attenuated by measurement error or unaccounted mediators. Future studies incorporating repeated biomarker sampling and mixed-effects models could better delineate these relationships. The conclusions of this study require further confirmation through well-designed, large-sample research. In addition, there is a potential connection between satisfaction and inflammation, and this is also the direction we will continue to explore next.

Abbreviations

KOA, Knee Osteoarthritis; TKA, Total Knee Arthroplasty; TXA, Tranexamic Acid; OA, Osteoarthritis; PT, plasma prothrombin time; FIB, plasma fibrinogen; APTT, activated partial thromboplastin time; ESR, erythrocyte sedimentation rate; IL-6, interleukin 6; CRP, C-reactive protein; ELISA, enzyme-linked immunosorbent assay; DVT, Deep Vein Thrombosis; HSS, Hospital for Special Surgery; ROM, range of motion; PPH, postpartum hemorrhage; HRQoL, Health-Related Quality of Life; BMI, Body Mass Index. NLR: Neutrophil-to-Lymphocyte Ratio; PLR: Platelet to lymphocyte ratio; SII: Systemic immune-inflammation index.

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Disclosure

The authors declare that they have no conflicts of interest regarding this work.

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