ORIGINAL RESEARCH

Effects of Different Applications of Tranexamic Acid on Perioperative Blood Transfusion Rate and Postoperative Pain in Unilateral Total Knee Arthroplasty

Xiaodong Zhang • Deli Ma • Jiang Pan • Liang Wen

X. Zhang • D. Ma • J. Pan • L. Wen (✉)

Department of Orthopaedics, Beijing Chao-Yang Hospital, Capital Medical University, Beijing, China

Email: sclhjo@163.com

ABSTRACT

Introduction: The current study was conducted in order to evaluate the effect of different applications of tranexamic acid (TXA) on perioperative blood transfusion rate and postoperative pain in unilateral total knee arthroplasty.

Methods: This prospective study included a total of 102 patients undergoing unilateral total knee arthroplasty in our hospital from November 2017 to October 2019. Based on different TXA administration methods, these patients were randomly assigned to Surface Treatment Group (50 cases were treated with intraoperative spraying and drug-soaked gauze to cover the wound combined with local injection into the articular cavity) and control group (52 cases were given TXA by intravenous drip combined with local injection into articular cavity) by random number table method. Clinical Data were recorded and evaluated in the two groups. A total of 8 surgeons participated in the study.

Results: In the Surface Treatment Group, the operation time, hospital stay, tourniquet time and blood transfusion rate were significant lower compared with the control group, and there was no sighificant difference in the incision length between the two groups. Our results showed the intraoperative blood loss, postoperative drainage, postoperative blood loss, total blood loss and the incidence of deep venous thrombosis in the surface treatment group were signifcantly lower than those in the control group. Our results demonstrated that the Surface Treatment Group reported significantly lower degree of pain compared with the control group at 1 day and 3 days after operation. However, 7 days after operation, the degree of pain in the surface treatment group did not differ significantly from that in the control group. In addition, the results of blood coagulation indexes showed that the values of PT, APTT, Fib, D-D and HGB in the surface treatment group did not differ significantly from those in the control group before operation ($P>0.05$).

Conclusion: In terms of applications of TXA, the method of intraoperative spraying and drug-soaked gauze covering the wound combined with local injection into the articular cavity can reduce the amount of bleeding and the rate of blood transfusion, alleviate the degree of pain with high safety profile.

Keywords: Blood transfusion rate; Perioperative period; Total knee arthroplasty; Tranexamic acid; Unilateral

Key Summary Points

Why carry out this study?

- Epidemiological studies are available to show that over 80 million people suffer from knee osteoarthritis each year in China.
- our study specifically focused on the effects of different applications of TXA on the perioperative pain degree and blood transfusion rate in unilateral total knee arthroplasty, further aimed to improve the efficiency of TXA in clinical practice.

What was learned from the study?

- TXA may be appropriate for wide application in grass-roots hospitals
- Applications of TXA, the method of intraoperative spraying and drug-soaked gauze covering the wound combined with local injection into the articular cavity can achieve several beneficial value, including the effective reduction of amount of blood loss and the rate of blood transfusion in total knee arthroplasty without affecting blood coagulation, and the alleviation of postoperative pain with high safety.

DIGITAL FEATURES

This article is published with digital features, including a summary slide, to facilitate understanding of the article. To view digital features for this article go to https://doi.org/10.6084/m9.figshare.13325933.

INTRODUCTION

Epidemiological studies are available to show that over 80 million people suffer from knee osteoarthritis each year in China, about 200,000 of whom have late-stage knee osteoarthritis. It mainly occurred among middle-aged and elderly people. The intensification of the aging population in China further contribute to the increased incidence of late-stage knee osteoarthritis. Given the disease accompanied with high disability rate, severe deformity and pain, the physical and mental health of patients are seriously affected(1). In clinical practice, total knee arthroplasty has been regarded as one of the best approaches for late-stage knee disease, which is able to restore the walking ability of patients, relieve the deformity and pain, and effectively improve the life quality of patients(2). However, massive bleeding may occur during surgery using this method, and most patients suffer from lower limb swelling and pain due to postoperative tissue oozing, even deep venous thrombosis, which is not conducive to the prognosis of these patients. Therefore, focus should been laid on the reduction of the perioperative blood transfusion rate as well as the pain alleviation of patients. Tranexamic acid (TXA) has been confirmed to exert great effect in terms of reducing the blood loss of patients. However, the best application of tranexamic acid remains unknown for clinical practice with no related study concerning the postoperative pain in patients. For the reasons given above, our study specifically focused on the effects of different applications of TXA on the perioperative pain degree and blood transfusion rate in unilateral total knee arthroplasty, further aimed to improve the efficiency of TXA in clinical practice.

METHODS

General Data

From November 2017 to October 2019, 102 patients admitted to our hospital were recruited and enrolled in this prospective study. These patients were randomly divided into surface treatment group (n = 50) and control group (n = 52) according to the different applications of tranexamic acid by random number table method. The general clinical characteristics of patients were collected before surgery, including age (years old), gender, time of course (months), BMI (kg/m^2), preoperative hemoglobin (g/L), preoperative hematocrit (g/L), location in total knee surgery (left or right) and complications. There were no significant differences in these general data between the two groups (P >0.05)(Table 1). Informed consent was obtained from all patents before enrollment. This study protocol was approved by Beijing Chao-Yang Hospital. The work was performed in accordance with the Helsinki Declaration of 1964 and its later amendments.

Selection Criteria

Inclusion Criteria

The inclusion criteria were as follows: 1) patients who underwent unilateral total knee arthroplasty for the first time; 2) patients suffering from pain, swelling, dysfunction and deformity of knee joint, and with ineffective pain treatment for over 6 months; 3) complete clinical data were available; 4) the total score was ≥ 6 according to RA grading and scoring standard of American College of Rheumatology (ACR) and European League Against Rheumatism(4); 5) patients met the indication of operation and tolerated surgery; 6) patients in stage Ⅲ to Ⅳ based on Kellgren-Lawrence X-ray classification(5). Each of these 6 criteria had to be met by every patient.

Exclusion Criteria

The exclusion criteria were as follows: 1) patients undergoing reoperation, simultaneous or staged bilateral total knee arthroplasty; 2) patients with malignant tumor, tuberculosis, active infection and other diseases; 3) patients with severe hepatorenal insufficiency, or patients with high risk of thrombosis such as atrial fibrillation, stent implantation, use of cardiac pacemaker, etc.; 4) patients with history of cardiovascular diseases such as myocardial infarction before operation; 5) patients receiving anticoagulants within one week before operation and with abnormal coagulation function; 6) patients with arterial occlusion in both lower extremities, venous thrombosis or related medical history before operation; 7) patients with poor compliance or with mental disorder; 8) patients who were allergic to drugs used in this research; 9) patients who were unable to complete the research due to various reasons. Patients meeting either of these criteria were excluded.

Preoperative Analgesia

All patients were given aspirin (aspirin, Guangdong Jiuming Pharmaceutical Co., Ltd., H44021139) for 7 days before operation, and were given 200mg ropivacaine cocktail (ropivacaine hydrochloride injection, Guangzhou Jiabo Pharmaceutical Co., Ltd., H20113381), 5mg dexamethasone (dexamethasone sodium phosphate injection, Tianjin Jinyao Group Hubei Tianyao Pharmaceutical Co., Ltd., H42020019), and 0.2ml epinephrine (epinephrine, Shanxi Zhendong Taisheng Pharmaceutical Co., Ltd., H14020817). After operation, NSAIDs was given for these patients.

Administration of TXA

In the surface treatment group, 3g TXA (tranexamic acid, Xi'an Libang Pharmaceutical Co., Ltd., H20093031) was dissolved in 150mL 0.9% NaCl (sodium chloride injection, Chenxin Pharmaceutical Co., Ltd., H20093938), two pieces of sterile gauze were placed on the sterile tray to be soaked with 20mL above solution and to cover the patella and articular capsule for 5 minutes during the

operation. During the operation, the remaining TXA solution was sprayed every 10min until the joint capsule was ready to be sutured. After suturing, 20ml TXA solution(1g TXA: 20mL 0.9% NaCl) was injected into the articular cavity at one time.

In control group, the application of TXA included intravenous drip combined with articular local injection. 15mg/kg TXA was dissolved in 100mL 0.9% NaCl before operation, and 20ml TXA solution(1g TXA: 20mL 0.9% NaCl) was injected into the articular cavity at one time when suturing joint capsule.

Surgical Approaches

The operation bed was covered with towels, the patients were supine and general anesthesia was used. The the balloon tourniquet was fixed at the root of the affected thigh before operation, and the intraoperative pressure was approximately 38 kPa (285 mmHg). The incision was in the anterior middle of the knee joint, and medial parapatellar approach. The total knee arthroplasty was performed routinely. The prosthesis was purchased from Xerox Company and LINK Company, but without patellar replacement. When suturing, the drainage was placed in the articular cavity, and the negative pressure of the drainage bottle was removed.

All patients were not given autologous blood transfusion after operation. The laboratory test results and clinical symptoms of patients were comprehensively observed to determine whether to give allogeneic blood transfusion. In our research center, the criteria of blood transfusion are as follows: 1) the hemoglobin value of the patient is less than 70g / L; 2) the hemoglobin value of the patient is 70-100g / L, and the patient has poor mental state, anorexia, dizziness and low fever.

According to the above blood transfusion indications, experienced senior doctors decided whether to give blood transfusion based on the patient's condition and clinical experience, and patients were given allogeneic red blood cell suspension transfusion when they needed blood transfusion.

Postoperative Management

The drainage was opened 3 hours after the operation, and the lower limb elastic socks were worn. The drainage volume at 24 hours after operation was recorded. One day after operation, 4000 IU low molecular weight heparin calcium (low molecular weight heparin calcium injection, Laboratoire GlaxoSmithKline, H20030633) was injected once a day for 14 days. Rivaroxaban (Rivaroxaban tablets, Bayer Pharma AG, H20181081) was taken orally for 14 days. After the end of anesthesia, patients were instructed to perform isometric contraction exercise of lower limb muscles, and exercise of ankle joint activity, straight leg raising and knee flexion. 2 to 3 days after operation, the patient could be instructed to walk on the ground.

After the operation, the patient performed long contraction exercises for the lower extremity muscles (25 times per group, 5 groups/day), and gradually performed ankle joint activities, straight leg elevation and knee bending exercises (initial angle is set to 35°, 2h/day, increase by 10-15° per day). The patients can walk moderately according to their own tolerance and increase the activity intensity appropriately 2-3 days after operation. The patient can be discharged after completing the standard knee-lifting action. In our research center, the specific criteria are as follows: 1) stable vital signs, no fever, dry surgical incision and no redness, swelling and exudation; 2) The joint on the surgical side can be actively flexed (100°) and extended (-5°); 3) VAS ≤ 3 points after activity; use a walker Can walk alone (>70m); 4) The mental state, diet, and urine and feces are basically recovered; 5) The imaging examination shows that the prosthesis is in good position and there is no looseness.

Observation Indicators

Intraoperative Blood Loss

Intraoperative blood loss included intraoperative and postoperative dominant blood loss and hidden blood loss. The amount of intraoperative blood loss = the amount of blood in the gauze during the operation + (the total amount of fluid in the suction bottle-the amount of flushing fluid during the operation). Postoperative dominant bleeding volume = net increment of dressing gauze after operation-amount of fluid injected into articular cavity (50mL) + postoperative drainage volume. Hidden blood loss = the amount of blood in postoperative blood transfusion + (total blood loss-dominant blood loss).

Postoperative Coagulation Index

Prothrombin time (PT), activated partial thromboplastin time (APTT) and fibrinogen (Fib) were detected before operation, 1 day, 3 days and 7 days after operation. At the same time, hemoglobin (HGB) level and D-dimer (D-D) were examined.

Evaluation of Pain

The degree of pain was recorded and evaluated at 1 day, 3 days and 7 days after operation based on VAS scores.

Incidence of Deep Venous Thrombosis

Both lower extremities were examined by color Doppler ultrasound before operation, 24 hours and 7 days after operation, and the occurrence of deep venous thrombosis was monitored. The

incidence of deep venous thrombosis = (the number of cases with deep venous thrombosis)/(the total number of cases) × 100%.

Statistical Analysis

All the data in this study were analyzed by SPSS21.0 software. Measurement data were expressed as the mean ± standard deviation (mean ± SD),and the differences between two groups were examined by Student's t-test. The categorical data were represented by the number of cases and percentage, and their comparison between two groups was performed by chi-squared test. A p value of less than 0.05 was considered statistically significant.

RESULTS

Comparison of Postoperative Conditions Between the Two Groups

All the 102 cases were successfully operated, and they were followed up for (5.61 ± 0.91) months, who had undergone a good postoperative recovery (Figure 1, Figure 2). Compared with the control group, the operation time, hospital stay, tourniquet time and blood transfusion rate in the surface treatment group were significant lower ($P < 0.05$), and there was no significant difference in the incision length between the two groups ($P > 0.05$)(Table 2).

Comparison of Blood Loss and Blood Coagulation Indexes Between the Two Groups

Our results showed the intraoperative blood loss, postoperative drainage, postoperative blood loss and total blood loss in the surface treatment group were signifcantly lower than those in the control group ($P <0.05$) (Table 3).

In addition, the results of blood coagulation indexes showed that the values of PT, APTT, Fib, D-D and HGB in the surface treatment group did not differ significantly from those in the control group before operation ($P>0.05$). In both groups, the values of PT, APTT and HGB at 1 day, 3 days and 7 days after operation were significantly lower than those before operation ($P<0.05$), while Fib and D-D were significantly higher than those before operation ($P<0.05$). 1 day, 3 days and 7 days after operation, there were no significant differences in the values of PT, APTT, Fib and D-D between the two groups ($P>0.05$). Meanwhile, the values of HGB in the surface treatment group were significantly higher than that in the control group at 1 day, 3 days and 7 days after operation ($P<0.05$)(Table 4).

Evaluation of Pain Between the Two Groups

Before operation, there was no significant difference in scores of VAS between the two groups (P<0.05). Compared with the control group, the scores of VAS in the Ssurface treatment group at 1 day and 3 days after operation were significantly lower (P <0.05), namely that the surface treatment group reported lower degree of pain . However, 7 days after operation, the scores of VAS in the surface treatment group did not differ significantly from that in the control group (Table 5).

Comparison of the Incidence of Deep Venous Thrombosis Between the Two Groups

The incidence of deep venous thrombosis in the surface treatment group was significantly lower than that in the control group after operation (2.00% vs. 15.38%, P <0.05).

DISCUSSION

Due to the ineffective conservative treatment for knee joint disease, total knee arthroplasty elicits several beneficial effect such as relieving pain and improving the function of patients(6,7). At present, TXA has been widely used in clinical practice and in total knee arthroplasty to achieve good hemostatic effect, but issues such as the application methods of TXA, perioperative blood transfusion rate and postoperative pain remain largely unsolved. Hence, the current study explored the effects of the method of intraoperative spraying and drug-soaked gauze covering the wound combined with local injection into the articular cavity, compared with TXA intravenous drip combined with local injection. The effects of two different administration methods on the perioperative blood transfusion rate and postoperative pain in patients undergoing total knee arthroplasty were also investigated in our study. The results showed that the operation time, hospital stay, tourniquet time, blood transfusion rate and blood loss in the surface treatment group were significantly lower than those in the control group. The reason may be related to the magnifying cascade reaction of fibrinolytic activation. Lysine peptide chain is composed of fibrinogen and lytic fibrin, and produce fibrin degradation products, resulting in clot lysis and bleeding(8). TXA is a synthetic antifibrinolytic drug with a chemical structure that is similar to lysine, which can strongly block the binding sites of tissue-type plasminogen activator lysine, plasminogen and plasminogen, thus it is able to quickly stop bleeding in surgical wounds(9,10). And intraoperative administration of TXA can reduce the permeability of vascular wall, reduce blood loss and blood transfusion rate, block the exudation of blood to the surrounding tissue, thus reduce the amount of local bleeding. However, intravenous injection combined with intra-articular injection of TXA can not achieve the effective drug concentration of direct coverage and intraoperative spraying, so the hemostatic effect is relatively weak.

It is well known that the PT and APTT can reflect the status of exogenous and endogenous coagulation,respectively, and fibrin can promote platelet aggregation, which leads to erythrocyte adhesion and thrombosis. The hemostatic function of TXA is closely related to the proportion of antifibrinolysis in the factors of abnormal coagulation function. Hence our study exerted attempts to explore the effect of different application of TXA on blood coagulation function. Based on the results, the values of PT, APTT and HGB at 1 day, 3 days and 7 days after operation were significantly lower than those before operation, while Fib and D-D were significantly higher than those before operation. However, the values of HGB in the Surface Treatment Group were significantly higher than that in the control group at 1 day, 3 days and 7 days after operation. 1 day, 3 days and 7 days after operation, there were no significant differences in the values of PT, APTT, Fib and D-D between the two groups, which was consistent with the results of Lopez-Hualda et al.(11), indicating that the antifibrinolytic effect of TXA is to prevent the fibrinolysis from changing from coagulation state to dissolved state. Moreover, intraoperative bleeding and operative bleeding lead to hypercoagulable state of blood, which leads to the change of coagulation function and consumes a lot of Fib, leading to the decrease of Fib. It is not directly linked to the application of TXA, while bleeding can activate the endogenous coagulation pathway and decrease the content of thrombin, thus prolonging the time of APTT. HGB is the main component of red blood cells, and two different applications of drug after operation both can lead to the decrease of HGB. However, intravenous injection combined with intra-articular injection of TXA was shown to result in a greater decrease of HGB, indicating that there was more loss of HGB, which was similar to the results of Pan et al.(12). It was demonstrated that the method of intraoperative spraying and drug-soaked gauze covering the wound combined with local injection of TXA into the articular cavity can significantly stop bleeding during the perioperative period, and the postoperative APTT was prolonged, suggesting that the operation can activate the internal and external coagulation pathway, but the coagulation function of the method of direct covering and intraoperative spraying of TXA elicited greater effects compared with that of intravenous injection of TXA.

The main function of total knee arthroplasty is to relieve pain and restore knee joint function. However, acute pain after total knee arthroplasty has a negative impact on early functional exercise, sleep quality and psychology stress of patients, which increases the incidence of complications. The satisfaction of surgical treatment is affected, not to mention the prolonged stay and increased cost of hospitalization. Currently multimodal analgesia has been greatly introduced in clinic(13), which can relieve the pain after surgery of total knee arthroplasty, but the postoperative pain always affects the prognosis of patients. Cocktail has a good effect on early postoperative acute pain(14), and taking NSAIDs drugs before operation also shows the effect of preemptive analgesia. Opioids are

recommended when the postoperative analgesic effect is not good. Rannou et al.(15) confirmed that oral administration of NSAIDs drugs before operation and opioids when postoperative analgesia was not effective could effectively reduce the pain degree of patients. According to studies supported by Kuo et al.(16), intraarticular injection of TXA could effectively relieve the pain degree of patients. The results of this study showed that the degree of pain in the Surface Treatment Group was significantly lower than that in the control group, suggesting that the method of intraoperative spraying and drug-soaked gauze covering the wound combined with local injection into the articular cavity could effectively reduce the pain degree of the patients. Considering both groups used painkillers before operation, and the analgesic effect of the Surface Treatment Group was better than that of the control group, it may be due to the fact that direct coverage and intraoperative spraying of TXA can reduce the amount of bleeding and a large amount of blood in the knee joint, which was closely associated with the obvious relieving effect on the tension in the articular cavity and the degree of tissue edema. TXA is an antifibrinolytic agent, but limited research exists on whether it can cause blood coagulation disorder in clinical practice. Tanaka et al.(17) and Wong et al.(18) have confirmed that different applications and different doses of TXA were safe and could not increase the incidence of deep vein thrombosis. Based on our results, the incidence of deep venous thrombosis in the surface treatment group was significantly lower than that in the control group, suggesting that the method of intraoperative spraying and drug-soaked gauze covering the wound combined with local injection into the articular cavity can effectively reduce the incidence of deep venous thrombosis, which may attribute to the good effect of local application of TXA. On the basis of years of experience in clinical practice, the aurthors believe the following factors may cause deep venous thrombosis: 1) the middle-aged and elderly patients with different degrees of cardio-cerebrovascular diseases received total knee arthroplasty and TXA, but with higher incidence of venous thrombosis; 2) postoperative pain made patients unwilling to move and afraid of aggravating pain. A series of procedures during the operation, such as reaming and osteotomy, can activate the fibrinolytic system, thus increasing the probability of deep venous thrombosis of lower extremities. One of the serious postoperative complications is thrombosis and Hourlier et al.(19) suggested that intravenous injection of TXA could increase the probability of deep venous thrombosis. However, in the current study, only 2 cases of deep venous thrombosis occurred in group of TXA intravenous drip combined with intra-articular local injection, which was not consistent with the results of previous studies. As a fibrinolytic inhibitor, TXA can theoretically make the blood in a hypercoagulable state, which can increase the incidence of thrombosis, especially intermuscular vein thrombosis. However, there is not enough evidence to prove the harmfulness of intermuscular thrombosis. From 2012 to 2014, a large sample, prospective clinical study with a sample size of 2352 cases found that the

incidence of DVT after tranexamic acid during joint replacement surgery was 17.55%, which was greater than 9.35% in the control group. Most of the difference in the incidence of DVT comes from the difference in the intermuscular veins, and there is no difference in the incidence of symptomatic deep vein thrombosis and pulmonary embolism (20). Regarding the harmfulness of intermuscular vein thrombosis, studies have suggested that proximal deep vein thrombosis is more likely to develop into pulmonary embolism than distal intermuscular vein thrombosis (21, 22). Some scholars believe that thrombosis may develop into pulmonary embolism when it reaches above the knee joint. Distal intermuscular venous thrombosis does not need to be treated. However, there are reports in the literature that if intermuscular venous thrombosis is not treated, some patients (<15%) will develop into proximal deep vein thrombosis (23). Therefore, sufficient attention should be paid to TXA-induced intermuscular venous thrombosis.

There are some limitations in the study. The present analysis included strict inclusion and exclusion criteria and bias of cases existed, which may lead to errors in the study. It was unlikely to discover asymptomatic deep venous thrombosis in perioperative period, and venous thrombosis was not excluded when selecting cases. During the whole operation, it was completed by the same team, and the prostheses were purchased from the same company. But different cutters used based on the specific conditions of the patients may affect the results to some extent.

CONCLUSION

In conclusion, for the applications of TXA, the method of intraoperative spraying and drug-soaked gauze covering the wound combined with local injection into the articular cavity can achieve several beneficial value, including the effective reduction of amount of blood loss and the rate of blood transfusion in total knee arthroplasty without affecting blood coagulation, and the alleviation of postoperative pain with high safety. Therefore, it may be appropriate for wide application in grass-roots hospitals.

ACKNOWLEDGEMENTS

We thank the participants of the study.

Funding: No funding or sponsorship was received for this study or publication of this article. The Rapid Service Fee was funded by the authors.

Authorship: All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Authorship Contributions: Xiaodong Zhang and Liang Wen contributed to the conception and design of the study; Deli Ma and Jiang Pan performed the experiments, collected and analyzed data; Xiaodong Zhang and Liang Wen wrote the manuscript; All authors reviewed and approved the final version of the manuscript.

Disclosures: Xiaodong Zhang, Deli Ma, Jiang Pan and Liang Wen have nothing to disclose.

Compliance with Ethics Guidelines: Informed consent was obtained from all patents before enrollment. This study protocol was approved by Beijing Chao-Yang Hospital. The work was performed in accordance with the Helsinki Declaration of 1964 and its later amendments.

Data Availability: The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

REFERENCES

1. Wallace IJ, Worthington S, Felson DT, et al. Knee osteoarthritis has doubled in prevalence since the mid-20th century. *Proceedings of the National Academy of Sciences of the United States of America* 2017:114: 9332-9336.

2. Katchy AU, Njeze NR, Ezeofor S, et al. Geometrical Analysis of the Proximal Femur and the Clinical Application in Total Hip Replacement: A Study of the Igbo Population of South East Nigeria. *Nigerian journal of clinical practice* 2019:22: 1728-1736.

3. Agha R, Abdall-Razak A, Crossley E, et al. STROCSS 2019 Guideline: Strengthening the reporting of cohort studies in surgery. *International journal of surgery* 2019:72: 156-165.

4. Arnett FC, Edworthy SM, Bloch DA, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. *Arthritis Rheum* 1988:31: 315-324.

5. Yoshida K, Barr RJ, Galea-Soler S, et al. Reproducibility and Diagnostic Accuracy of Kellgren-Lawrence Grading for Osteoarthritis Using Radiographs and Dual-Energy X-ray Absorptiometry Images. *J Clin Densitom* 2015:18: 239-244.

6. Kim WJ, Park JS, Won SH, et al. Total hip arthroplasty in hereditary multiple exostoses with secondary osteoarthritis: A case report. *Medicine* 2019:98: e18175.

7. Yaseen MK, Gorial FI. An observational descriptive cross sectional multicenter study of health related quality of life among Iraqi patients after total hip replacement. *Annals of medicine and surgery (2012)* 2019:48: 118-121.

8. Cid J, Lozano M. Tranexamic acid reduces allogeneic red cell transfusions in patients undergoing total knee arthroplasty: results of a meta-analysis of randomized controlled trials. *Transfusion* 2005:45: 1302-1307.

9. Kawaguchi K, Kinoshita S, Ishikawa M, et al. Tranexamic acid-induced fixed drug eruption confirmed by the drug lymphocyte transformation test. *Clinical case reports* 2019:7: 2074-2075.

10. Faraoni D, Levy JH. Tranexamic Acid for Acute Hemorrhage: When Is Enough Evidence Enough? *Anesthesia and analgesia* 2019:129: 1459-1461.

11. Lopez-Hualda A, Dauder-Gallego C, Ferreno-Marquez D, et al. Efficacy and safety of topical tranexamic acid in knee arthroplasty. *Medicina clinica* 2018:151: 431-434.

12. Pan DQ, Chen LL, Sun B, et al. [Effect of tranexamic acid combined flexion position of hip and knee on perioperative bleeding following unilateral total knee arthroplasty]. *Zhongguo gu shang = China journal of orthopaedics and traumatology* 2019:32: 759-764.

13. Bi RB, Ji L, Wang XK. [Effect analysis of multimode analgesia of parecoxib sodium during laparoscopic cholecystectomy]. *Zhonghua yi xue za zhi* 2013:93: 2727-2729.

14. Liu P, Guo WS, Zhang QD, et al. [Efficacy and safety of compound betamethasone cocktail therapy in primary unilateral unicompartmental knee arthroplasty]. *Zhonghua yi xue za zhi* 2019:99: 3100-3104.

15. Rannou F, Pelletier JP, Martel-Pelletier J. Efficacy and safety of topical NSAIDs in the management of osteoarthritis: Evidence from real-life setting trials and surveys. *Seminars in arthritis and rheumatism* 2016:45: S18-21.

16. Kuo FC, Lin PY, Wang JW, et al. Intravenous tranexamic acid use in revision total joint arthroplasty: a meta-analysis. *Drug design, development and therapy* 2018:12: 3163-3170.

17. Tanaka N, Sakahashi H, Sato E, et al. Timing of the administration of tranexamic acid for maximum reduction in blood loss in arthroplasty of the knee. *The Journal of bone and joint surgery British volume* 2001:83: 702-705.

18. Wong J, Abrishami A, El Beheiry H, et al. Topical application of tranexamic acid reduces postoperative blood loss in total knee arthroplasty: a randomized, controlled trial. *The Journal of bone and joint surgery American volume* 2010:92: 2503-2513.

19. Hourlier H, Fennema P. Chemoprophylaxis without intra-articular wound drainage can replace autotransfusion in primary TKA. *Orthopedics* 2011:34: 154.

20. Jinwei X, Jun M, Pengde K, et al. Does tranexamic acid alter the risk of thromboembolism following primary total knee arthroplasty with sequential earlier anticoagulation? A large, single center, prospective cohort study of consecutive cases. *Thromb Res* 2015:136: 234-238.

21. Michael GR, Geoffrey HW, Hollis GP, et al. Effect of mechanical compression on the prevalence of proximal deep venous thrombosis as assessed by magnetic resonance venography. *J Bone Joint Surg Am* 2002:84: 1998-2004.

22. Arie M. Origin and natural history of deep vein thrombosis of the legs. *Semin Vasc Med* 2005:5: 65-74.

23. Clive K, Elie AA, Anthony JC, et al. Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012:141: e419S-e496S.

Table 1 Comparison of general clinical characteristics of patients

Item	Surface Treatment Group (n = 50)	Control Group (n = 52)	t/χ^2	p
Age (years old)	65.19 ± 6.87	64.81 ±7.08	0.275	0.784
Gender				
male	16	18	0.078	0.779
female	34	34		
Duration of Symptoms (months)	26.87± 1.82	26.78 ± 1.78	0.252	0.802
BMI (kg/m^2)	25.81 ± 0.99	25.67 ±1.02	0.703	0.484
Total knee arthroplasty				
left	21	22	0.001	0.975
right	29	30		
Preoperative hemoglobin (g/L)	115.81 ±10.91	114.87 ±10.27	0.448	0.655
Preoperative hematocrit (g/L)	38.81 ±4.92	38.09 ±5.01	0.732	0.466
Comorbidities			0.275	0.784
hypertension	8	7		
diabetes mellitus	11	12		

Table 2 Comparison of postoperative conditions between the two groups (%, n)

Group	Incision length (cm)	Surgery time (min)	Hospital stay (d)	Tourniquet time (cm)	Blood transfusion rate (%)
Surface Treatment Group (n=50)	13.89±2.81	71.08±7.72[b]	10.13±2.81[b]	70.82±8.91[b]	14.00（7/50）[b]
Control Group(n=52)	14.01±3.21	77.08±8.06	11.02±2.31	75.01±7.39	44.23（23/52）
t	-0.201	-3.837	-2.284	-2.589	11.22
p	0.841	＜0.001	0.03	0.011	0.001

Note: [b], compared with the control group, P <0.05.

Table 3. Comparison of blood loss and blood coagulation indexes between the two groups

Group	Intraoperative blood loss (ml)	Postoperative drainage (ml)	Postoperative blood loss (ml)	Total blood loss (ml)
Surface Treatment Group (n=50)	109.89±12.81	179.08±7.72	865.13±22.81	2328.82±108.91
Control Group(n=52)	131.01±9.21	187.08±8.06	978.09±20.06	2875.01±107.39
t	9.589	-5.116	-26.586	-25.501
p	＜0.001	＜0.001	＜0.001	＜0.001

Table 4 Comparison of blood coagulation indexes between the two groups

	Before surgery		1d after surgery		3d after surgery		7d after surgery	
	Surface Treatment Group	Control Group	Surface Treatment Group	Control Group	Surface Treatment Group	Control Group	Surface Treatment Group	Control Group
PT（s）	17.97±1.72	17.91±1.92	11.42±1.02	11.61±1.32	11.40±0.97	11.71±1.21	11.19±0.28	11.43±0.99
t	0.166		-0.811		-1.424		-1.68	
p	0.868		0.419		0.158		0.098	
APTT（s）	28.56±4.63	28.49±4.08	28.21±3.87	28.29±3.76	27.42±3.01	27.91±3.28	27.51±2.76	27.81±3.19
t	0.081		-0.106		-0.785		-0.413	
p	0.936		0.916		0.434		0.681	
Fib（mg/L）	28.89±3.97	28.01±3.01	39.82±4.01	37.32±3.08	39.39±3.08	38.89±3.82	38.06±2.97	38.72±3.71
t	1.265		1.183		0.741		-0.989	
p	0.209		0.24		0.46		0.325	
D-D(mg/L)	0.43±0.12	0.44±0.19	0.44±0.15	0.44±0.21	0.47±0.19	0.45±0.22	0.48±0.18	0.46±0.21
t	-0.316		-0.316		0.491		0.504	
p	0.753		0.75		0.624		0.615	
HGB(g/L)	125.67±6.17	125.73±5.92	117.98±5.02	112.9±4.67	111.01±4.09	103.08±5.02	103.09±3.09	95.03±4.09
t	-0.05		5.211		8.727		11.196	
p	0.96		＜0.001		＜0.001		＜0.001	

Table 5. Comparison of pain between the two groups

Group	Before surgery	1d after surgery	3d after surgery	7d after surgery
Surface Treatment Group (n=50)	2.76±0.19	4.02±0.37	3.37±0.34	1.87±0.19
Control Group (n=52)	2.71±0.21	5.52±0.06	4.67±0.27	2.08±0.09
t	1.259	-28.848	-21.428	-7.178
p	0.211	＜0.001	＜0.001	＜0.001

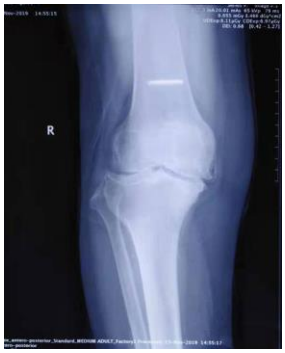

Figure 1: X-ray of knee joints before operation

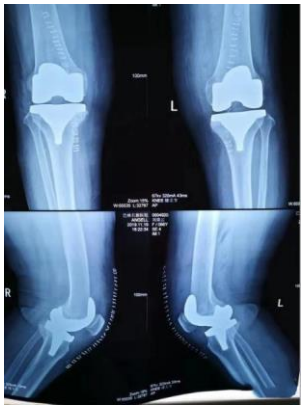

Figure 2: X-ray of knee joints after operation

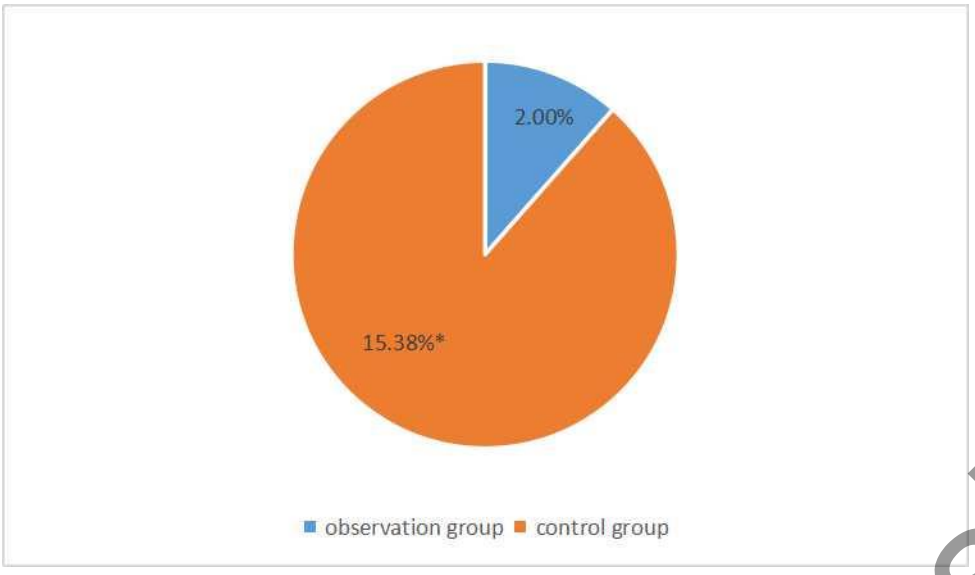

Figure 3: comparison of the incidence of deep venous thrombosis between the two groups

Note: *, compared with the control group,P＜0.05.