Efficacy and safety of intravenous combined with topical administration of tranexamic acid in reducing blood loss in opening wedge high tibial osteotomy procedure: A retrospective case-control study

Wei Luo1,*, Xin Fu2,*, Jing-min Huang1, Jiang Wu1, Xin-long Ma2

1Department of Arthroscopy, Tianjin Hospital, Tianjin, People’s Republic of China
2Department of Orthopedics, Tianjin Hospital, Tianjin, People’s Republic of China

ABSTRACT

Objective: This study aimed to evaluate the efficacy and safety of intravenous combined with topical application of tranexamic acid (TXA) in reducing blood loss in opening wedge high tibial osteotomy (OWHTO).

Methods: A total of 60 patients who underwent unilateral OWHTO between May 2018 and May 2019 were retrospectively reviewed. All the patients were then divided into one of the two groups (30 per group): the TXA group, patients receiving intravenous combined with topical application of TXA, and the control group, patients receiving no TXA. Outcome measures were drain volume, total blood loss, hidden blood loss, transfusion requirements, and incidence of complications.

Results: The mean follow-up of TXA group was 14.2±2.3 months (range, 13-16 months) and the mean follow-up for the control group was 14.4±2.1 months (range, 13-17 months). No significant difference was found for the follow-up of two groups (P=0.829). Drainage volume (141.3±65.4 mL vs 307.8±51.4 mL, P<0.001), hidden blood loss (156.7±63.8 mL vs 286.4±79.1 mL, P<0.001) and knee swelling (3.2±0.9 vs 6.5±2.1, P<0.001) in the TXA group was clearly less than that in the control group, and there was no statistical significance with regard to hospitalization time (P=0.746), transfusion requirements (P=1.000), wound complications (P=0.386), deep venous thrombosis (P=1.000), postoperative Lysholm knee score (P=0.681) and Knee Injury & Osteoarthritis Outcome subscales pain (P=0.752), symptoms (P=0.673), activities of daily living (P=0.871), sport/recreation function (P=0.816), and knee-related quality of life (P=0.576) at 6 months postoperatively.

Conclusion: This study has shown that administration of intravenous combined with topical TXA in OWHTO can effectively reduce perioperative blood loss without increasing the incidence of postoperative complications.

Level of Evidence: Level III, Therapeutic Study

Introduction

Opening wedge high tibial osteotomy (OWHTO) is a common treatment for patients suffering from medial compartment knee osteoarthritis (KOA) with varus malalignment.1 However, substantial blood loss may be associated with the surgical procedure, ranging from 400-800 mL.2 The decrease in hemoglobin (Hb) levels after osteotomy was reported to be in the range between 17 and 41 g/L.4,5 The resulting reduction in the hemoglobin level has a serious impact on patient health, especially in older individuals with a lower hematopoietic ability.8 Allogeneic blood transfusions are commonly used to correct postoperative anemia. However, allogeneic blood transfusions are associated with the risk of numerous adverse effects, including infectious disease, hemolysis, and anaphylactic reactions.9 Moreover, allogeneic blood transfusions also lead to longer hospital stays and higher medical costs.8 Reducing perioperative blood loss during HTO continues to be a challenge for surgeons.

Tranexamic acid (TXA) is a synthetic amino acid derivative that promotes hemostasis by competitively blocking the lysine-binding site of plasminogen.9 Tranexamic acid is widely used to reduce blood loss and transfusion requirements in orthopedic, hepatic, and cardiac surgeries.30 To date, intravenous or topical combined administration of TXA in total hip arthroplasty (THA) and total knee arthroplasty (TKA) has been well established in the literature.31 However, there are relatively few reports on the role of TXA in OWHTO, and most studies have focused on the effect of intravenous or topical application on blood loss.32,33 This study aimed to evaluate the efficacy and safety of intravenous combined with topical application of TXA in OWHTO.

Materials and Methods

Patient selection

The present study used retrospectively collected clinical data from patients who underwent the OWHTO procedure in our hospital from May 2018 to May 2019. From May 2018 to November 2018, 30 patients who underwent OWHTO without administration of TXA during the perioperative period were included in the control group. From December 2018 to May 2019,
30 patients who underwent OWHTO with intravenous combined with topical administration of TXA during the perioperative period were included in the TXA group. Ethical approval for this study was granted by the Ethics Committee of our hospital (2021052). The requirement for informed consent was waived because of the retrospective design of the study.

Inclusion and exclusion criteria
Inclusion criteria included: (1) patients with Kellgren–Lawrence grade III or above symptomatic medial compartment KOA, (2) varus deformity > 5 degrees, (3) good articular cartilage in the lateral compartment (International Cartilage Regeneration & Joint Preservation Society grade II or above), and (4) patients with postoperative follow-up time ≥ 12 months.

Exclusion criteria included: (1) patients with incomplete clinical data, (2) patients who did not conform to the protocol, (3) patients with anemia before surgery (male Hb < 120 g/L and female Hb < 110 g/L), (4) hinge fracture during surgery, (5) HTO for both knees, (6) simultaneous posterior root repairing of the medial meniscus or ligament reconstruction or (7) combined with femoral deformity and need for distal femur osteotomy, and (8) the contraindications of the TXA (anticoagulation therapy before surgery, severe cardiopulmonary disease, history of thromboembolic disease, congenital or acquired coagulopathy, and preoperative renal dysfunction).

From May 2018 to May 2019, 70 OWHTOs were performed; 6 patients (2 in TXA group and 4 in control group) were excluded because they underwent simultaneous bilateral OWHTO. Four patients (2 in each group) were excluded for combined distal femur osteotomy on their contralateral knee. Among them, 10 patients were excluded, and finally, 60 patients were enrolled in the final analysis including 30 patients who received TXA (TXA group) and 30 patients who were not administered TXA (control group).

Tranexamic acid protocol
In the TXA group, patients received 3 doses: the first dose was 1 g TXA dissolved in 100 mL normal saline intravenously 10 minutes before surgery, the second dose was 3 g TXA dissolved in 20 mL normal saline injected through the drainage tube after suturing the incision, and the third dose was 1 g TXA intravenously at 2 hours postoperatively. For intravenous administration, 1 g TXA was dissolved in 100 mL of normal saline. Tranexamic acid was not given in the control group.

Surgical procedure
Open wedge high tibial osteotomy was performed by the same senior surgeon with plentiful experience. The degree of correction, length of the osteotomy, and approximate length of the screws were templated preoperatively. All operations were performed under epidural anesthesia or general anesthesia. After anesthesia, the pneumatic tourniquet was inflated to 100-150 mmHg higher than the systolic blood pressure. Routine arthroscopic examination was done using anteromedial and anterolateral portals to explore the articular cartilage and menisci. If necessary, arthroscopic procedures, such as debridement, meniscectomy, meniscal repair, and/or microfracture chondroplasty, were done. A longitudinal incision was made on the superomedial side of the tibia, and a medial locked plate (TomoFix; Synthes, Solothurn, Switzerland) was used after bicipel osteotomy with a minimally invasive technique. After fixation of the plate with locking screws, allograft cancellous bone was grafted on the osteotomy gap. A drainage tube was applied to the osteotomy site, and it was retained for 48 hours after surgery. The tourniquet was deflated after applying the skin suture and knee banding with an elastic bandage.

Clinical evaluation
General demographic data were recorded, including age, gender, affected knee, body mass index, follow-up time, clinical function evaluation (Lysholm and Knee Injury & Osteoarthritis Outcome [KOOS] score), radiological evaluation (lower limb mechanical axis, medial proximal tibial angle and hip–knee–ankle angle), and clinical laboratory examination (Hb, hematocrit, albumin, activated partial coagulation time of whole blood, prothrombin time, fibrinogen, and D-dimer). Hospitalization days, operation time, incision length, drainage volume, hemoglobin level on the second day after surgery, and knee function at 1 year after surgery were also recorded. Total estimated blood loss was calculated by the formula of Nadler et al. and Gross et al. Hemoglobin levels were measured preoperatively and at 48 hours postoperatively. Hidden blood loss was calculated as proposed by Good et al. The circumference at the superior pole of the patella was measured preoperatively and at 72 hours postoperatively to assess knee swelling, and the increase compared with the preoperative measurement was calculated.

Postoperative care
Drainage volume was checked daily, and drainage was removed on postoperative day (POD) 2. Active and passive motion was initiated on the POD 1. The suture was removed 2 weeks postoperatively. Allogeneic blood transfusion was performed according to a trigger of Hb level less than 80 g/L. Wound complications were recorded, including hematoma, redness of the incision of more than 1 cm, superficial or deep infection, and deep venous thrombosis (DVT) during the hospital stay or within the initial 6-week postoperative period. Any clinical suspicion of DVT was investigated and confirmed by a Doppler ultrasound. For the prevention of postoperative thromboembolism, rivaroxaban was routinely administered at 10 mg per day until 2 weeks after surgery. Deep infection was diagnosed based on a positive culture from the wound. Patients were permitted to start partial weight-bearing with crutch ambulation by 4-6 weeks postoperatively. Full weight-bearing was started by 6-8 weeks postoperatively. The Lysholm and KOOS scores for knee function at 6 months postoperatively were recorded.

Statistical analysis
Statistical analysis was conducted with Statistical Package for Social Sciences v. 17.0 (SPSS Inc., Chicago, IL, USA) statistical software. Continuous data were expressed as the mean ± standard deviation (SD) and tested with Mann–Whitney U test for the difference. Categorical data were analyzed using Fisher's exact test. A two-sided \( P < .05 \) was considered to be statistically significant. A power analysis was performed using the effect size of total estimated blood loss (325.8 mL) with a common SD of 72.6 mL. On considering \( \alpha = 0.05 \) and sample size in each group = 30, the calculated power is more than 0.90.
Table 1. Demographic data of the patients

| Demographic characteristics | Control Group | TXA Group | P |
|-----------------------------|---------------|-----------|---|
| Age (years)                 | 60.3 ± 2.6    | 60.5 ± 2.7| 0.526 |
| Gender (male/female)        | 19/11         | 20/10     | 0.327 |
| Site (right/left)           | 16/14         | 13/17     | 0.564 |
| Body mass index (kg/cm²)    | 26.6 ± 2.93   | 27.6 ± 2.97| 0.821 |

Preoperative laboratory values

| Parameter                          | Control Group | TXA Group | P   |
|------------------------------------|---------------|-----------|-----|
| Hemoglobin (g/L)                   | 0.142         | 0.136     | 0.427 |
| Hematocrit (%)                     | 42 ± 3        | 43 ± 4    | 0.416 |
| Fibrinogen (g/L)                   | 3.3 ± 0.5     | 3.4 ± 0.4| 0.965 |
| Prothrombin time (seconds)         | 12.3 ± 1.1    | 12.9 ± 1.3| 0.758 |
| Partial thromboplastin time (seconds) | 32.4 ± 2.6 | 31.6 ± 2.8| 0.821 |
| D-dimer (mg/L)                     | 0.61 ± 0.39   | 0.63 ± 0.41| 0.753 |
| Preoperative function              |               |           |     |
| Lysholm knee score                 | 60.7 ± 2.8    | 61.3 ± 2.9| 0.647 |
| KOOS                               |               |           |     |
| Pain                               | 54.8 ± 7.4    | 56.6 ± 6.6| 0.632 |
| Symptoms                           | 55.3 ± 8.6    | 54.4 ± 8.2| 0.578 |
| Activities of daily living         | 58.1 ± 7.2    | 56.5 ± 8.6| 0.189 |
| Sport/recreation function          | 34.4 ± 13.6   | 32.5 ± 12.4| 0.529 |
| Knee-related quality of life       | 35.7 ± 8.5    | 38.5 ± 7.7| 0.142 |
| Weight-bearing line ratio, %       | 15.7 ± 2.1    | 16.3 ± 1.8| 0.753 |
| Hip-knee-ankle angle               | -8.7 ± 2.1    | -8.8 ± 2.2| 0.672 |
| Medical proximal tibial angle      | 83.5 ± 1.9    | 83.1 ± 2.1| 0.578 |

For TXA, tranexamic acid; KOOS, Knee Injury and Osteoarthritis Outcome Score.

Results

The mean follow-up of TXA group was 14.2 ± 2.3 months (range, 13-17 months), and the mean follow-up for the control group was 14.4 ± 2.1 months (range, 13-17 months). No significant difference was found during the follow-up of the 2 groups (P=.829). Demographic parameters were not statistically significantly different between the 2 groups (Table 1). There was no significant difference in the hospital stay (7.1 ± 0.7 vs. 7.2 ± 0.8, P=.746), surgical duration (76.8 ± 15.8 vs. 77.8 ± 14.9, P=.332), and incision length (8.4 ± 0.6 vs. 8.3 ± 0.5, P=.895) between the 2 groups (Table 2). Total blood loss (325.8 ± 72.6 vs. 612 ± 68.3, P < .001), drainage volume (143.3 ± 65.4 vs. 307.8 ± 51.4, P < .001), hidden blood loss (156.7 ± 63.8 vs. 286.4 ± 79.1, P < .001), and knee swelling (3.2 ± 0.9 vs. 6.5 ± 2.1, P < .001) in the TXA group were obviously less than that in the control group (Table 2). No wound complications were found in the TXA group. One superficial wound infection was observed in the control group, and it was cured after debridement and anti-infection treatment. There was no serious deep infection, blood transfusion, or DVT in either group. No significant difference was found between 2 groups for the Lysholm knee score (P=0.681) and KOOS subscales pain (P=0.752), symptoms (P=0.673), activities of daily living (P=0.871), sport/recreation function (P=0.816), and knee-related quality of life (P=0.576) at 6 months postoperatively. All OWHTOs achieved bone healing and had no loss in correction at 1 year postoperatively.

Discussion

The purpose of our study was to evaluate the efficacy and safety of intravenous combined with topical application of TXA in OWHTO. The most important finding of the present study was that intravenous combined with topical application of TXA in OWHTO can significantly reduce postoperative drainage volume and hidden blood loss without increasing the incidence of postoperative complications.

Table 2. Postoperative parameters compared among groups

| Parameter                          | TXA Group (n=30) | Control Group (n=30) | P  |
|------------------------------------|------------------|----------------------|----|
| Surgical duration (minutes)        | 76.8 ± 15.8      | 77.8 ± 14.9          | 0.332 |
| Skin incision length(cm)           | 6.4 ± 0.6        | 8.3 ± 0.5            | 0.895 |
| Hospital stay (day)                | 7.1 ± 0.7        | 7.2 ± 0.8            | 0.746 |
| Correction angle                   | 12.5 ± 1.6       | 12.6 ± 1.9           | 0.863 |
| Medial proximal tibial angle       | 91.3 ± 1.6       | 91.6 ± 1.4           | 0.817 |
| Increasing rate of knee circumference (%) | 3.2 ± 0.9  | 6.5 ± 2.1            | <0.001 |
| Blood loss                         |                  |                      |     |
| Total blood loss (mL)              | 325.8 ± 72.6     | 612 ± 68.3           | <0.001 |
| Drainage volume (mL)               | 143.3 ± 65.4     | 307.8 ± 51.4         | <0.001 |
| Hidden blood loss (mL)             | 156.7 ± 63.8     | 286.4 ± 79.1         | <0.001 |
| Postoperative laboratory values    |                  |                      |     |
| Hemoglobin (g/L)                   | 112 ± 23         | 93 ± 29              | 0.004 |
| Hematocrit (%)                     | 38 ± 3           | 31 ± 4               | 0.02 |
| Fibrinogen (g/L)                   | 3.7 ± 0.5        | 3.6 ± 0.6            | 0.561 |
| Prothrombin time (seconds)         | 13.4 ± 1.8       | 13.3 ± 1.7           | 0.429 |
| Partial thromboplastin time (seconds) | 34 ± 6        | 35 ± 6               | 0.637 |
| D-dimer (mg/L)                     | 0.93 ± 0.41      | 1.19 ± 0.71          | 0.03 |
| Blood transfusion                  | 0                | 0                    | 1.000 |
| Wound infection                    | 0                | 1                    | 0.386 |
| DVT                                | 0                | 0                    | 1.000 |
| Postoperative function             |                  |                      |     |
| Lysholm knee score                 | 76.1 ± 4.7       | 73.1 ± 4.8           | 0.681 |
| KOOS                               |                  |                      |     |
| Pain                               | 68.4 ± 6.3       | 66.7 ± 6.5           | 0.752 |
| Symptoms                           | 67.2 ± 6.9       | 68.5 ± 6.5           | 0.673 |
| Activities of daily living         | 69.1 ± 6.5       | 68.4 ± 7.5           | 0.871 |
| Sport/recreation function          | 51.2 ± 8.5       | 50.7 ± 8.5           | 0.816 |
| Knee-related quality of life       | 59.1 ± 8.7       | 58.6 ± 7.8           | 0.576 |

DVT, deep vein thrombosis; TXA, tranexamic acid; KOOS, Knee Injury and Osteoarthritis Outcome Score.
Opening wedge high tibial osteotomy creates a bone gap at the metaphysial level and releases extensive soft tissue that may induce extensive bone bleeding. A tourniquet is commonly used during HTO to decrease intraoperative blood loss and keep a clear operative field. However, abnormal fibrinolysis induced by tourniquet deflation may increase postoperative blood loss.10 Suh et al10 studied 30 patients who underwent OWHTO and found that the topical application of TXA effectively reduced postoperative blood loss after OWHTO. Palanisamy et al2 reported that 2 g intravenous TXA used 10 minutes before the use of a tourniquet and 3 hours after HTO could reduce postoperative blood loss. Gaussen et al24 reported that TXA had the strongest hemostatic effect in the first 24 hours, as its half-life period is approximately 3 hours. A meta-analysis showed that the combination of intravenous and topical TXA was relatively more effective in controlling bleeding without increased risk of VTE than intravenous or topical TXA in TKA.26 In the present study, 1 g TXA was administered intravenously before surgery and 2 hours after surgery, and 3 g TXA dissolved in 20 mL normal saline injected through the drainage tube after suturing the incision. Our study demonstrated that total blood loss, drainage volume, and Hb level in TXA group were significantly lower than those in the control group (P < .001). Postoperative hidden blood loss and knee swelling in TXA group were also significantly lower than those in the control group (P < .001). However, there was no blood transfusion in either group. Li et al21 attributed it to OWHTO having less blood loss compared with TKA or THA. Current studies have confirmed that intravenous combined with local application of TXA significantly reduces perioperative blood loss and knee swelling with the OWHTO procedure.

Bone healing is important in OWHTO. Recently, several published literature reported that TXA has a significant effect on reducing postoperative bleeding and bleeding-related complications of HTO.2,3,4,12,13 However, none of them has shown the effect of TXA on bone healing of OWHTO. The effects of TXA on fracture healing remain unclear. Çevik et al21 explored the effect of topical and systemic TXA on fracture healing in a rat surgical model. They found that the application of topical TXA during orthopedic fracture surgery may accelerate fracture healing and that systemic use may delay. In the present study, we found that topical and systemic administration of TXA did not affect bone healing of OWHTO.

Postoperative function and pain determine the overall efficacy of HTO. Visual Analogue Scale (VAS) is a patient-assessed score and has been used extensively in the literature to record patient pain following surgery. Palanisamy et al3 reported that patients who underwent OWHTO in the TXA group had lower VAS scores than those in the control group on the second day after surgery. The reason may be that TXA reduced postoperative hidden blood loss and knee swelling in the early postoperative period. The present study suggests that there is no significant difference in the Lysholm and KOOS scores of knee joint function between the TXA group and control group at 6 months postoperatively.

Owing to a lack of soft tissue coverage around the proximal medial tibia, there is a greater risk of wound complications in OWHTO. Severe hemorrhage may lead to hematoma, stiffness, infection, delayed healing, and DVT. Several studies24,25 have reported the incidence of wound complications after medial opening wedge HTO to be approximately 4%-5%. Therefore, reducing perioperative blood loss in HTO could result in less complications and improve the curative effect of the operation. In the present study, there was 1 wound complication in the control group and none in the TXA group. This case was cured after debridement and anti-infection treatment.

Recently, Onishi et al22 reported that the overall incidence of DVT is 13.8% after osteotomy around the knee even with the use of prophylactic anticoagulant. Deep venous thrombosis may develop into pulmonary embolism and result in death. Theoretically, TXA inhibits fibrinolytic activity and may increase the risk of DVT.27 Astedt et al24 found that intravenous TXA did not suppress fibrinolytic activity in the normal vein wall. Numerous studies25,26 have confirmed the safety of TXA, without increases in the incidence of either DVT or PE. In the present study, no significant difference was found in the postoperative coagulation parameters between the combined group and control group, and no patient had symptomatic DVT. These results suggest that intravenous combined with topical application of TXA appears to be safe in HTO.

This study has several limitations. First, it is a retrospective case–control study. Second, this study lacked an intravenous or topical group using TXA alone for analysis and research. Third, more outcomes are needed to find the most effective dose of TXA. A prospective randomized, controlled study with larger sample size is needed in the future to further demonstrate its safety and effectiveness.

In conclusion, intravenous combined with topical TXA administration in HTO can effectively reduce perioperative blood loss without increasing the incidence of postoperative complications.

**Ethics Committee Approval:** Ethics committee approval was received from the Ethics Committee of Tianjin hospital. (Approval No: 2021052).

**Informed Consent:** The requirement for informed consent was waived because of the retrospective design of the study.

**Author Contributions:** Concept - W.L., X.M.; Design - W.L., X.F.; Supervision - J.H., J.W.; Funding - W.L., X.F.; Materials - W.L., J.W.; Data Collection and/or Processing - W.L., J.W.; Analysis and/or Interpretation - W.L., J.M.; Literature Review - J.H., X.M.; Writing - W.L., X.F.; Critical Review - J.H., X.M.

**Acknowledgments:** The authors are grateful for Ru-Xin Sun’s contribution to the statistical analysis.

**Declaration of Interests:** The authors have no conflicts of interest to declare.

**Funding:** The authors declared that this study has received no financial support.

**References**

1. Akizuki S, Shibakawa A, Takizawa T, Yamazaki I, Horiiuchi H. The long-term outcome of high tibial osteotomy: a ten- to 20-year follow-up. *J Bone Joint Surg Br*. 2008;90(5):592-596. [CrossRef]
2. Kim KJ, Kim HJ, Kim GB, Ban SH. Tranexamic acid is effective for blood management in open-wedge high tibial osteotomy. *Orthop Traumatol Res Rev*. 2018;104(7):1003-1007. [CrossRef]
3. Palanisamy JV, Das S, Moon KH, Kim DH, Kim TK. Intravenous tranexamic acid reduces postoperative blood loss after high tibial osteotomy. *Clin Orthop Relat Res*. 2018;476(11):2148-2154. [CrossRef]
4. Suh DW, Kyung BS, Han SB, Cheong K, Lee WH. Tranexamic acid is effective for hemostasis in patients undergoing high tibial ostectomy. *J Knee Surg*. 2018;31(1):50-55. [CrossRef]
5. Ogbumudia AO, Bafor A, West-Osemwengie L. Reactionary haemorrhage reduction with adrenaline infiltration in proximal tibial ostectomy: a randomized clinical study of safety and efficacy. *Arch Orthop Trauma Surg*. 2012;132(2):213-218. [CrossRef]
6. Li N, Williams L, Zhou Z, Wu Y. Incidence of acute transfusion reactions to platelets in hospitalized pediatric patients based on the US hemovigilance reporting system. *Transfusion*. 2014;54(6):1666-1672. [CrossRef]
7. Hart A, Khalil JA, Carlil A, Huk O, Zukor D, Antoniou J. Blood transfusion in primary total hip and knee arthroplasty. Incidence, risk factors, and thirty-day complication rates. *J Bone Joint Surg Am*. 2014;96(23):1945-1951. [CrossRef]
8. Varney SJ, Guest JP. The annual cost of blood transfusions in the UK. *Transfus Med*. 2003;13(4):205-218. [CrossRef]
9. Henry DA, Carless PA, Moxey AJ, et al. Anti-fibrinolytic use for minimising perioperative allogeneic blood transfusion. *Cochrane Database Syst Rev*. 2011;2011(3):CD001886.
10. Franchini M, Liuzzi Bruno GM. The key role of tranexamic acid in Patient Blood Management programmes. Blood Transfus. 2018;16(6):471-472. [CrossRef]
11. Li JF, Li H, Zhao H, et al. Combined use of intravenous and topical versus intravenous tranexamic acid in primary total knee and hip arthroplasty: a meta-analysis of randomised controlled trials. J Orthop Surg Res. 2017;12(1):22. [CrossRef]
12. DeMeo PJ, Fau JE, Jiang PP, et al. Midterm follow-up of opening-wedge high tibial osteotomy. Am J Sports Med. 2010;38(10):2077-2084.
13. Roos EM, Roos HP, Lohmander LS, Ek达尔 C, Beynnon BD. Knee Injury and Osteoarthritis Outcome Score (KOOS)—development of a self-administered outcome measure. J Orthop Sports Phys Ther. 1998;28(2):88-96. [CrossRef]
14. Briggs KK, Steadman JR, Hines SL. Lysholm score and Tegner activity level in individuals with normal knees. Am J Sports Med. 2009;37(5):899-903. [CrossRef]
15. Nadler SB, Hidalgo JH, Bloch T. Prediction of blood volume in normal human adults. Surgery. 1962;51(2):224-232.
16. Gross JB. Estimating allowable blood loss: corrected for dilution. Anesthesiology. 1983;58(3):277-280. [CrossRef]
17. Good L, Peterson E, Lisander B. Tranexamic acid decreases external blood loss but not hidden blood loss in total knee replacement. Br J Anaesth. 2003;90(5):596-599. [CrossRef]
18. Aglietti P, Baldini A, Vena LM, Abbate R, Fedi S, Falciani M. Effect of tourniquet use on activation of coagulation in total knee replacement. Clin Orthop Relat Res. 2000;371(1):169-177. [CrossRef]
19. Gausden EB, Qudsi R, Boone MD, O’Gara B, Ruzbarsky JJ, Lorich DG. Tranexamic acid in orthopaedic trauma surgery: a meta-analysis. J Orthop Trauma. 2017;31(10):513-519. [CrossRef]
20. Sun Q, Li J, Chen J, Zheng C, Liu C, Jia Y. Comparison of intravenous, topical or combined routes of tranexamic acid administration in patients undergoing total knee and hip arthroplasty: a meta-analysis of randomised controlled trials. BMJ Open. 2019;9(1):e024350. [CrossRef]