CLINICAL ARTICLE

Intravenous Combined with Topical Tranexamic Acid Administration Has No Additional Benefits Compared with Intravenous Administration Alone in High Tibial Osteotomy: A Retrospective Case-Control Study

Songlin Li[1], Qunshan Lu[1], Xingzhi Guo[2], Meng Zhang[1], Zhuang Miao[1], Desu Luo[1], Peilai Liu[1]

[1]*Department of Orthopedics, Qilu Hospital of Shandong University, Jinan and* [2]*Department of Orthopedics, Boxing County Hospital of Traditional Chinese Medicine, Binzhou, China*

Objective: To investigate whether intravenous combined with topical administration of tranexamic acid (TXA) is superior to intravenous administration alone in terms of blood loss, incision complications, functional recovery, and pain relief in high tibial osteotomy (HTO).

Methods: Clinical data of patients with knee osteoarthritis (OA) treated with unilateral HTO were retrospectively reviewed. The patients were grouped according to the TXA administration method, with 24 patients in the combined group and 21 in the solo group. In the combined group, 100 mL saline containing 1 g TXA was intravenously administered before application of a tourniquet, and 20 mL saline containing 2 g TXA was injected through a drainage tube after closure of the incision. Alternatively, 100 mL of saline containing 1 g TXA was intravenously administered before application of a tourniquet in the solo group. The blood loss and adverse events were compared between the two groups.

Results: All patients were followed for more than half a year. The drainage volume on the first day and total blood loss on the second day after surgery in the combined and single treatment groups were 130.06 ± 29.22 and 165.35 ± 43.08 mL ($P < 0.05$), respectively, and 327.17 ± 64.26 and 385.45 ± 63.31 mL ($P < 0.05$). There were no blood transfusions in either group. One case of delayed incision healing was observed in the solo group, and no such event occurred in the combined group. There were no significant differences between the two groups in terms of the following factors: the activated partial thromboplastin time (APTT) and prothrombin time (PT); levels of fibrinogen (FIB) and D-dimer on the second day after surgery; numbers of hospitalization days and thromboembolism events; and knee joint function and visual analog score 6 months after surgery.

Conclusion: Intravenous combined with topical TXA administration in HTO is superior to intravenous administration alone for reducing postoperative blood loss and drainage volume without thromboembolic complications. However, even with only intravenous TXA administration, no cases of blood transfusion and only 1 case of incision complication occurred. At the same time, the combined use of TXA did not improve the recovery of knee joint function and pain relief after HTO.

Key words: Blood loss; High tibial osteotomy; Knee osteoarthritis; Tranexamic acid

Address for correspondence Peilai Liu, Department of Orthopedics, Qilu Hospital of Shandong University, 107 Wenhua West Road, Jinan City, Shandong Province 250012, China. E-mail: gklpl@163.com

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Orthopaedic Surgery

Introduction

In terms of knee preservation, high tibial osteotomy (HTO) has become an effective method for the treatment of isolated compartment knee osteoarthritis (OA) with varus deformity. Compared with total knee arthroplasty (TKA), HTO retains most of the original joint structure, prevents further wear and tear on the cartilage, alleviates pain, and improves knee function by correcting the negative weight-bearing line of the knee joint, thus avoiding or delaying knee joint replacement[1,2]. Furthermore, HTO, as one of the effective methods for the treatment of isolated compartment OA of the knee, has advantages including minimal trauma, rapid recovery, and preservation of knee function. However, due to the exposure of the cancellous bone surface during osteotomy, intraoperative and postoperative bleeding is still unavoidable and may lead to substantial hemorrhage. Hemorrhage after HTO can lead to hematomas, delayed wound healing, anemia, and allogeneic blood transfusion[3–6]. Homologous blood transfusion can cause complications, including fever, infection, allergic reaction, and hemolysis[7,8]. Therefore, finding an effective method to reduce bleeding after HTO is worth further study and discussion.

As one kind of plasminogen inhibitor, tranexamic acid (TXA) can be strongly adsorbed on the surface of a wound and on the exposed plasminogen lysine binding site to make it saturated. Therefore, it cannot continue to undertake the effective binding of plasminogen with fibrin containing lysine residues. Thus, fibrin cannot be degraded to achieve hemostasis[9]. TXA has been widely used in various orthopaedic operations[10–13]. It can reduce the perioperative loss of blood and the transfusion rate, while it does not increase the risk of complications such as deep venous thrombosis (DVT). However, its application in HTO has been rarely studied[14–17]. TXA has many methods of administration, including intravenous, intramuscular, topical and oral administration; among these methods, intravenous and topical administration, are commonly used in orthopaedics[18]. It has been reported that blocking the fibrinolytic system at the initial stage can achieve the best hemostatic effect[19]. Blood loss during surgery will activate the fibrinolytic system, so intravenous administration should be used before surgery. Topical administration of TXA can be quickly absorbed locally, and the physiological half-life of the articular fluid can be maintained for approximately 3 h[9], thus achieving the effect of local hemostasis.

At present, there are few studies on the efficacy and safety of TXA in HTO, and all studies are retrospective. In a 2017 study, Suh et al.[14] analyzed blood loss and incision complications after topical application of TXA in HTO, with 15 cases in each group. Suh *et al.* found that topical administration of TXA could reduce drainage and hemoglobin decline on the first day after surgery. There were no incision complications in the TXA group. Therefore, it is considered that the topical application of TXA in HTO can reduce the amount of blood loss and the incidence of incision complications. In 2018, Kim et al.[16] retrospectively analyzed the effect of intravenous TXA in open wedge HTO. The patients received intravenous medication three times during the perioperative period: before the tourniquet was released, 6 h after the operation, and 24 h after the operation. The amount of postoperative hemoglobin reduction, postoperative drainage, and total blood loss in the TXA group were lower than those in the control group. There was no blood transfusion in the TXA group, and there were 2 patients in the control group. For the first time, this study investigated the effect of TXA on DVT of lower extremities in patients with HTO. No thrombosis was found in postoperative routine CT angiography of lower extremities, and no thrombosis-related symptoms were found in any patients. Palanisamy et al. [15] also conducted a retrospective study on the effect of intravenous TXA in HTO, but TXA was used 10 min before the use of a tourniquet and 3 h after the operation. Palanisamy et al. suggest that TXA can reduce blood loss in patients after HTO, but no blood transfusion occurred even without TXA. Moreover, due to the limitations of the sample size and follow-up time, Palanisamy[15] believes that the value of TXA in the prevention of incisional complications and DVT is uncertain. Therefore, TXA is not recommended in the perioperative period of HTO. A meta-analysis[17] included in these three studies also showed that topical or intravenous TXA alone could reduce perioperative blood loss but may not affect the rate of blood transfusion and the incidence of incisional complications. There is no study on the efficacy and safety of intravenous and topical combination of TXA used in HTO. Therefore, the purpose of the present study was to investigate the following. First, is intravenous combined with topical TXA administration superior to intravenous injection alone in reducing postoperative blood loss and the blood transfusion rate? Second, is there a difference between the two methods in the incidence of incision complications and deep vein thrombosis? Third, is the combination method more beneficial to the functional recovery and pain relief of patients after the operation?

Methods

Patients

Inclusion and Exclusion Criteria

Inclusion criteria were: (i) patients with isolated compartment knee osteoarthritis with varus deformity who underwent HTO; (ii) patients who underwent unilateral surgery; and (iii) a follow-up time of over half a year.

Exclusion criteria were: (i) patients with incomplete follow-up data; (ii) patients who underwent distal femoral osteotomy at the same time; (iii) patients with anemia before surgery (men: Hb < 120 g/L, women: Hb < 110 g/L); and (iv) previous history of thromboembolic disease.

The present study retrospectively collected clinical data from patients who underwent the HTO procedure in our hospital from May 2016 to January 2018. During the study period, the same surgeon performed a total of 56 HTO, and

all surgical procedures consisted of medial open wedge HTO (OWHTO). From May 2016 to April 2017, all patients only accepted 1 g of intravenous TXA 15 min before application of the tourniquet for the procedure. From May 2017 to January 2018, all patients underwent HTO with TXA application in combination with 1 g of intravenous and 2 g of topical application. According to the inclusion and exclusion criteria, 45 patients were included: 24 patients were treated with topical and intravenous TXA, and 21 patients were treated with intravenous TXA alone (Fig. 1).

This study was approved by the ethics committee of the local hospital, and because it was a retrospective study, permission for the exemption of informed consent was obtained.

Surgical Methods

All operations were performed by the same chief surgeon with 20 years of experience. Medial OWHTO was performed. After successful laryngeal mask general anesthesia, the patient was placed in the supine position, an inflatable tourniquet was fixed to the lower limbs at the root of the thigh, and the pressure was adjusted to 45 kPa for intraoperative hemostasis. The lower limb distal to the tourniquet was routinely disinfected and draped. Arthroscopic devices were inserted into the knee joint via an anterior approach. The superior patellar capsule, medial and lateral compartments, and the intercondylar fossa were explored thoroughly. The proliferative synovium was removed. If there was obvious cartilage wear on the medial articular surface and no obvious cartilage wear on the lateral articular surface, OWHTO was performed. After irrigation of the articular cavity, the arthroscopic devices were withdrawn, and the incision was sutured. A longitudinal incision of approximately 5–8 cm was made in the one-third anterior–posterior portion of the proximal tibia 1 cm from the articular surface. Skin and subcutaneous tissue were reflected, in turn, to expose the superficial layer of the goose foot tendon and the superficial layer of the medial collateral ligament with subperiosteal dissection. Two Kirschner wires were inserted approximately 5 cm below the articular surface (upper edge of the goose foot tendon) under fluoroscopy and pointed towards the tip of the fibula capitulum. HTO was performed along the direction of Kirschner's needle, and the angle was opened according to the preoperative plan. Under fluoroscopy, the corrected lower limb alignment was identified. A Tomofix locking plate was installed and fixed. Fluoroscopy was used to check the internal fixation position. If the correction angle of the varus deformity was too large (more than 12°) or if the distraction distance was too wide (more than 14 mm) and if there was a "hinge" fracture, then the artificial bone material tricalcium phosphate (OSferion, Olympus Terumo Biomaterials, Tokyo, Japan) was implanted at the osteotomy. After irrigation of the incision, a uniform type of drainage tube approximately 5 cm in length was placed around the osteotomy site. Then, the incision was sutured layer by layer, and the tourniquet was released after suturing.

Tranexamic Acid Protocol

In the combined group, 100 mL of saline containing 1 g of TXA (Zhejiang Jinhua Kangenbei Biopharmaceutical) was administered intravenously before application of the tourniquet, and 20 mL of saline containing 2 g of TXA was injected through the drainage tube after suturing the incision. In the solo group, only 100 mL of saline containing 1 g of TXA was administered intravenously before application of the tourniquet.

Postoperative Treatment

After the operation, the knee joint in the straight position was covered with an elastic bandage from the foot to the distal thigh with the use of a spiral bandage, with 50% overlap

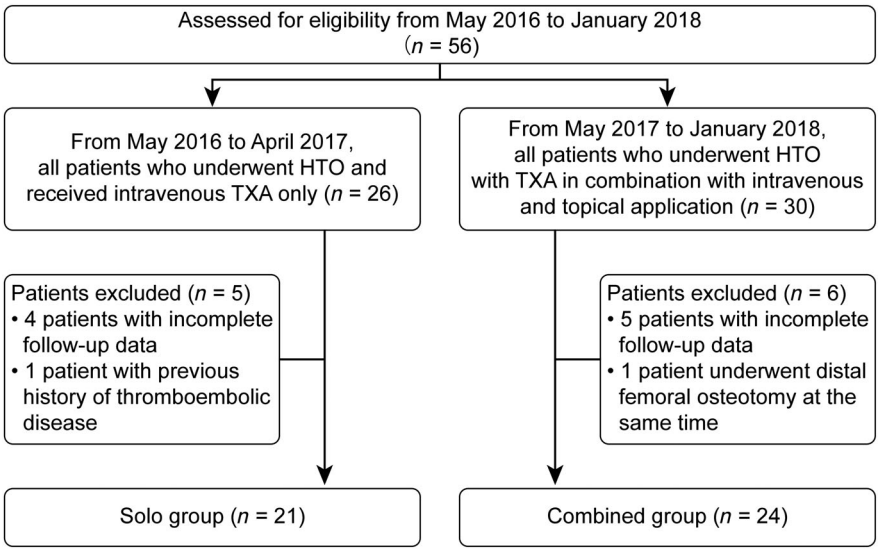

Fig. 1 The flow chart shows the grouping of the patients. HTO, high tibial osteotomy; TXA, tranexamic acid.

between the bandages. The drainage tube was closed for 3 h and removed 1 day after the operation. Quadriceps muscle strength exercises could be performed 1 h after surgery, and partial weight-bearing exercises began 1 day after surgery with the assistance of a walker. Full weight-bearing activity was performed 5 weeks after the operation.

Clinical Assessments

General Conditions During Perioperative Period
General demographic data were recorded, including gender, age, side of the operative limb, height, weight, and body mass index (BMI). Hospitalization days, operative time, range of motion, the length of the incision, and the number of cases that underwent bone grafting were also recorded.

Drainage Volume
Drainage volume refers to the volume of blood flowing through the drainage tube, which is measured on the first day after the operation. The amount of drainage can reflect the amount of blood loss, especially the amount of dominant blood loss.

Hemoglobin Reduction
Hemoglobin reduction refers to the patient's hemoglobin value on the second day after surgery minus the preoperative hemoglobin value, which can indirectly reflect the amount of blood loss.

Total Blood Loss Volume
Total blood loss was equal to the preoperative total blood volume multiplied by the preoperative hematocrit level subtracted from the postoperative hematocrit level plus the transfusion volume. Preoperative total blood volume was calculated with the Nadler equation[20]: before the procedure, total blood volume = K1 * height (m) + K2 * body mass (kg) + K3; males: K1 = 0.3669, K2 = 0.03219, K3 = 0.6041; females: K1 = 0.3561, K2 = 0.03308, K3 = 0.1833.

Allogeneic Blood Transfusion Cases and Volume
If the postoperative hemoglobin level was <80 g/L, allogeneic transfusion was performed and the number of transfusions was recorded. The number of blood transfusion cases and blood loss volume are obtained from the medical record information.

Coagulation Series
The coagulation series includes activated partial thromboplastin time (the normal values range from 28.00 s to 45.00 s), prothrombin time (the normal values range from 11.00 s to 14.50 s), fibrinogen (the normal values range from 2.00 g/L to 4.00 g/L) and D-dimer (the normal value <0.5 μg/mL). They can reflect the coagulation function of patients and the assessment and diagnosis of the risk of venous thrombosis. They were measured preoperatively and postoperatively on the second day.

Visual Analogue Score
The visual analogue scale (VAS) was used to evaluate pain. The method involves using a ruler approximately 10-cm long, with 10 scales on one side, and "0" and "10" at both ends, respectively. The score criteria were as follows: 0 indicates no pain; 1–3 was defined as mild pain, not affecting sleep; 4–6 was defined as moderate pain, mildly affecting sleep; 7–10 was defined as severe pain, which can result in the inability to sleep or wake up from sleep. A detailed explanation was provided to the patient before the process; we ensured that the patient understood the concept of the method and the relationship between pain measurement and real pain, and let the patient mark the corresponding position of pain on the straight line. The VAS was used to evaluate the degree of pain in the 6th month after the operation.

Hospital for Special Surgery Knee Scoring System
The Hospital for Special Surgery (HSS) knee scoring system is used to evaluate knee joint function, which mainly includes six aspects: pain, function, range of motion, muscle strength, flexion deformity, and stability. A total score <59 is considered a poor score, 60–69 fair, 70–84 is good, and >85 is considered excellent. It was measured in the 6th month after the operation.

Deep Vein Thrombosis
Deep venous thrombosis refers to the abnormal coagulation of blood in the deep vein, which is an important index to evaluate the safety of an operation. In the case of severe pain, circumference change, swelling of the limbs, and positive Homan's sign, lower extremity vascular ultrasound examination was performed to exclude DVT. The number of DVT cases is obtained from the medical record information.

Incision Complications
Incision complications include incision hematoma, delayed healing, and superficial cellulitis. Postoperative hematoma refers to the skin swelling around the incision caused by blood oozing at the operation site. It can be relieved after the fluid is extracted by the puncture. The occurrence of postoperative hematomas means that there is more bleeding around the incision. Delayed healing of the incision means that the incision is still not healed on the 14th day after the operation, which can be characterized by an exudation of the incision and skin necrosis or rupture of the cutting edge, but there is no sign of infection such as redness or swelling. Superficial cellulitis was defined by redness, swelling, and warmth on the edges of the wound, but the patient's body temperature was normal and erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) revealed no signs of systemic infection.

Statistical analysis
All data were analyzed with SPSS 23.0 (IBM, Chicago, IL, USA). The statistical power was calculated to be 0.850 considering alpha = 0.05 and beta = 0.2 for the current sample

size (n = 45). The measurement data were expressed as the mean ± standard deviation. The count data were represented factors such as sex, side of lower limb, the number of people who underwent bone grafting or blood transfusion, and the number of people who experienced incision complications or DVT. Statistical analysis was performed using χ^2-tests for the comparison of categorical parameters and t-tests for the comparison of continuous normally distributed parameters. A P-value <0.05 was considered statistically significant.

Results

General Conditions During the Perioperative Period

There was no significant demographic difference between the two groups. See Table 1 for details. There were no significant differences in the number of hospitalization days, operative time, the length of the incision, or bone grafting between the two groups ($P > 0.05$). See Table 2 for details.

Drainage Volume

The drainage volume was 130.06 ± 29.22 mL in the combined group and 165.35 ± 43.08 mL in the solo group. The drainage volume in the combined group was lower than that in the solo group ($P < 0.05$), which decreased by 21.34% compared with the solo group. See Table 2 for details; detailed amounts of the drainage volume for all patients are listed in Tables 3 and 4.

Hemoglobin Reduction

The postoperative hemoglobin and hematocrit levels in the two groups were lower than those before the operation. The hemoglobin and hematocrit levels on the second day after the operation in the combined group were significantly higher than those in the solo group ($P < 0.05$). Compared with the combined group, hemoglobin and hematocrit decreased by 7.83% and 13.78%, respectively, on the 2nd day after the operation in the solo group. The hemoglobin reduction was 17.04 ± 5.56 g/L in the combined group and 25.95 ± 4.09 g/L in the solo group. Compared with the solo group, the hemoglobin reduction in the combined group was reduced by 34.33%. There was significant difference between the two groups ($P < 0.05$); see Table 2 for details. The amounts of hemoglobin reduction of all patients are listed in Tables 3 and 4.

Total Blood Loss Volume

The total blood loss volume was 327.17 ± 64.26 mL in the combined group and 385.45 ± 63.31 mL in the solo group. The amount of total blood loss in the combined group was lower than in the solo group ($P < 0.05$), which decreased by 15.12 % compared with the solo group; see Table 2 for details. The total blood loss volumes of all patients are listed in Tables 3 and 4.

Allogeneic Blood Transfusion Cases and Volume

All patients had postoperative hemoglobin levels greater than 80 g/L, with a minimum of 89 g/L. There was no blood transfusion in either group. See Tables 2 and 4 for details.

TABLE 1 Demographic characteristics of the study participants (mean ± standard deviation)

	Combined group (n = 24)	Solo group (n = 21)	P-value
Sex (M/F)	10/14	10/11	0.692
Age (y)	58.63 ± 7.10	58.86 ± 7.696	0.947
Side (L/R)	11/13	12/9	0.454
Height (cm)	164.71 ± 7.55	163.81 ± 6.95	0.739
Weight (kg)	73.79 ± 12.96	71.33 ± 12.35	0.295
BMI	27.34 ± 5.394	26.59 ± 4.21	0.100
Preop ROM (°)	114.83 ± 8.28	113.10 ± 6.98	0.666
Preop Hb (g/L)	138.50 ± 11.95	137.90 ± 12.76	0.634
Preop Hct (%)	41.21 ± 3.10	41.79 ± 3.44	0.655
Preop blood volume (L)	4.54 ± 0.53	4.48 ± 0.54	0.855
Preop Aptt (s)	31.65 ± 2.80	31.04 ± 3.85	0.147
Preop Pt (s)	11.22 ± 0.60	11.18 ± 0.62	0.910
Preop Fib (g/L)	3.06 ± 0.59	3.28 ± 1.02	0.269
Preop D-dimer (μg/mL)	0.15 ± 0.13	0.15 ± 0.13	0.461

APTT, activated partial thromboplastin time; BMI, body mass index; F, female; Fib, fibrinogen; Hb, hemoglobin; Hct, hematocrit; L, left; M, male; Preop, preoperative; PT, prothrombin time; R, right; ROM, range of motion.

TABLE 2 Comparison after surgery (mean ± standard deviation)

	Combined group (n = 24)	Solo group (n = 21)	P-value
Hospitalization days (d)	10.21 ± 2.04	9.95 ± 1.91	0.974
Operative time (min)	143.54 ± 43.43	157.86 ± 46.71	0.655
Length of incision (cm)	4.97 ± 0.61	5.00 ± 0.34	0.110
Bone grafting (Y/N)	9/15	8/13	0.742
Hb Pod2 (g/L)	121.46 ± 12.43	111.95 ± 10.55	0.008*
Hb reduction (g/L)	17.04 ± 5.56	25.95 ± 4.09	0.001*
Hct Pod2 (%)	31.57 ± 5.60	27.22 ± 3.03	0.029*
Drainage volume Pod1 (mL)	130.06 ± 29.22	165.35 ± 43.08	0.002*
Blood loss Pod2 (mL)	327.17 ± 64.26	385.45 ± 63.31	0.004*
Aptt Pod2 (s)	31.15 ± 3.92	29.66 ± 3.52	0.987
Pt Pod2 (s)	12.71 ± 1.02	12.83 ± 1.15	0.367
Fib Pod2 (g/L)	3.58 ± 0.87	3.71 ± 0.95	0.557
D-dimer Pod2 (μg/mL)	0.81 ± 0.451	0.60 ± 0.438	0.720
Incision complications (Y/N)	0/24	1/20	0.285
DVT	0/24	0/21	1.000
Blood transfusion (Y/N)	0/24	0/21	1.000
VAS	1.54 ± 0.51	1.52 ± 1.60	0.628
HSS scores	75.99 ± 3.93	77.55 ± 5.63	0.252

*Statistically significant.; APTT, activated partial thromboplastin time; DVT, deep vein thrombosis; Fib, fibrinogen; Hb, hemoglobin; Hct, hematocrit; HSS, Hospital for Special Surgery; N, no; Pod, postoperative day; PT, prothrombin time; VAS, visual analog score; Y, yes.

[Correction added on 20 March 2020, after first online publication: blood transfusion values under the columns 'Solo group' and 'P-value' have been corrected.]

TABLE 3 Main indicators of blood loss and adverse events for each patient in the combined group

Patient	Hb Preop (g/L)	Hb Pod2 (g/L)	HB decrease (g/L)	Drainage volume (mL)	Blood loss (mL)	Adverse events
1	158	151	7	90	210.42	N
2	155	136	19	95	256.64	N
3	150	130	20	100	270.94	N
4	139	122	17	120	316.52	N
5	142	128	14	119	286.73	N
6	132	116	16	135	358.28	N
7	137	122	15	126	339.06	N
8	125	106	19	168	386.44	N
9	129	103	26	200	471.48	N
10	129	113	16	160	370.04	N
11	151	134	17	100	266.47	N
12	136	119	17	129	341.77	N
13	130	113	17	140	367.62	N
14	154	134	20	99	265.2	N
15	157	129	28	118	283.41	N
16	141	124	17	120	297.42	N
17	134	118	16	129	353.94	N
18	144	137	7	95	223.78	N
19	150	130	20	111	283.1	N
20	120	113	7	140	360.23	N
21	139	122	17	123	335.75	N
22	124	104	20	169	409.93	N
23	117	107	10	166	383.49	N
24	131	104	27	170	413.54	N
Mean	138.5	121.46	17.04	130.06	327.17	
SD	11.95	12.43	5.56	29.22	64.26	

Hb, hemoglobin; Pod, postoperative day; Preop, preoperative; SD, standard deviation.

TABLE 4 Main indicators of blood loss and adverse events for each patient in the solo group

Patient	Hb Preop (g/L)	Hb Pod2 (g/L)	HB decrease (g/L)	Drainage volume (mL)	Blood loss (mL)	Adverse events
1	161	128	33	90	233.31	N
2	146	120	26	143	383.05	N
3	134	109	25	181	408.43	N
4	121	100	21	227	452.27	Delayed healing
5	149	123	26	119	320.26	N
6	135	112	23	163	396.95	N
7	131	105	26	187	435.72	N
8	141	114	27	162	394.46	N
9	118	89	29	251	458.17	N
10	145	120	25	147	390.98	N
11	150	124	26	103	306.46	N
12	145	114	31	160	393.01	N
13	132	105	27	185	416.79	N
14	160	124	36	102	256.12	N
15	125	105	20	191	440.04	N
16	119	93	26	237	453.32	N
17	134	111	23	168	407.61	N
18	147	121	26	139	346.74	N
19	122	104	18	196	444.55	N
20	133	109	24	184	413.71	N
21	148	121	27	139	342.6	N
Mean	137.9	111.95	25.95	165.35	385.45	
SD	12.76	10.55	4.09	43.08	63.31	

Hb, hemoglobin; Pod, postoperative day; Preop, preoperative; SD, standard deviation.

Coagulation Series

There was also no significant difference in the APTT and PT or FIB and D-dimer levels between the two groups ($P > 0.05$). The indicators are in the normal range. See Table 2 for details.

Visual Analogue Score

At the 6th month postoperatively, the visual analogue scores were 1.54 ± 0.51 and 1.52 ± 1.60 in the combined group and the solo group, respectively. There was no significant difference in the VAS between the two groups ($P > 0.05$). See Table 2 for details.

Hospital for Special Surgery Knee Scoring System

At the 6th month postoperatively, the HSS scores were 75.99 ± 3.93 and 77.55 ± 5.63 in the combined group and the solo group, respectively. There was no significant difference in HSS scores between the two groups ($P > 0.05$). See Table 2 for details.

Deep Vein Thrombosis

No symptomatic DVT occurred in the two groups after the operation ($P > 0.05$). See Table 2 for details.

Incision Complications

There was only 1 patient who had an unhealed incision 14 days after surgery in the solo group. The patient healed by the 23rd day after surgery following repeated dressing changes; there were no complications due to the incision in the combined group ($P > 0.05$). See Tables 2 and 4 for details.

Discussion

There is a high incidence of OA in elderly individuals. The surgical methods of knee OA mainly include TKA, unicompartmental knee arthroplasty (UKA), and HTO[21]. For patients with isolated medial compartment OA of the knee with varus deformity and normal lateral cartilage and meniscus function, HTO has been proven to provide a good curative effect and patient satisfaction[1,2]. HTO is a minimally invasive surgical knee procedure for the treatment of knee osteoarthritis that preserves the normal structure of the knee joint. However, because the osteotomy is located in the proximal tibia with blood-rich cancellous bone, the periosteum and other fibrous soft tissues cannot adhere to the osteotomy site. Around the cancellous bone, it is not easy to prevent bleeding, so blood loss after HTO is still inevitable. Postoperative blood loss can lead to postoperative complications such as anemia, hemorrhage, hematoma formation, and blood transfusion, which may affect postoperative outcomes, patient satisfaction, and hospitalization costs[21–24]. As an anti–fibrinolytic drug, TXA can increase the stability of fibrin clots and achieve hemostasis. It has achieved good results in TKA and total hip arthroplasty (THA)[10,11]. However, few studies have been conducted on the role of TXA in HTO[14–17], and most of the research has only concentrated on the effects of intravenous or topical application alone on blood loss. The aim of the present study was to explore the efficacy and safety of the combined administration of TXA after HTO.

In this study, the amount of blood loss and drainage volume, and the decrease of the hemoglobin level in the combined group were lower than those in the solo group; the difference was statistically significant ($P < 0.05$). Postoperative hemoglobin and hematocrit levels in the combined group were higher than those in the solo group ($P < 0.05$). This suggests that the combination of TXA can reduce more perioperative blood loss with the HTO procedure than with the use of intravenous TXA alone. However, there was no blood transfusion in either group. Three studies confirmed that intravenous and topical administration of TXA alone can reduce blood loss after HTO. In a retrospective study, Suh et al.[14] compared 15 HTO patients treated with TXA and 15 HTO patients who represented a control group. The TXA group received 20 mL of saline containing 2 g of TXA through the drainage tube after closure of the incision. The results showed that the decrease in the drainage volume and hemoglobin 1 day after the operation in the TXA group was lower than that in the solo group, and the difference was statistically significant ($P < 0.05$). Through a retrospective study of 66 HTO patients, Palanisamy et al.[15] found that intravenous administration 10 minutes before application of the tourniquet and intravenous administration of TXA 3 h after the operation could reduce blood loss. In another retrospective study, Kim et al.[16] injected TXA at a dose of 10 mg/kg before and 6 h after tourniquet application and 24 h after the operation. The results showed that the hemoglobin level in the TXA group was higher than that in the control group 1, 2 and 5 days after the operation ($P < 0.001$). The hemoglobin level and drainage volume in the TXA group 1, 2 and 5 days after the operation were lower than those in the control group ($P < 0.001$). However, a meta-analysis of these three studies by Yao et al.[17] showed that TXA could reduce the blood loss after HTO but did not reduce the blood transfusion rate and incision complications. This is similar to the results of our study, even if TXA was used intravenously alone, there was no blood transfusion, and only 1 patient had incision complications. However, the combined method of TXA has been widely used in TKA and THA. Current studies have confirmed that the combined regimen of intravenous infusion of TXA combined with intra-articular local injection is superior to the single-route regimen[25–29]. Through a prospective study of 150 patients, Huang et al.[30] found that the combined regimen of TXA in TKA could reduce the overall effect of perioperative bleeding and even replace the role of the tourniquet. On the one hand, this may be because the quantity of involved patients who underwent HTO and TXA was not large enough; on the other hand, HTO itself is not an operation with a large amount of blood loss compared with TKA or THA. From this point of view, although the combined use of TXA can reduce blood loss in patients, it may not bring additional benefits.

Deep venous thrombosis has been a serious complication of orthopaedic surgery and is associated with a high mortality rate[31]. Poeran et al.[32] conducted a retrospective study of 872 416 patients with joint replacement and found that the use of TXA did not increase or even reduce the incidence of perioperative thrombotic events. A meta-analysis of 211 related studies by Xu et al.[33] found that intravenous or topical TXA in total knee and total hip arthroplasty did not increase the risk of postoperative thrombosis. There are few reports on the application of TXA in HTO to the study of postoperative coagulation and venous thrombosis. Palanisamy et al.[15] did not observe symptomatic DVT in 66 patients with HTO who underwent intravenous TXA administration during the perioperative period. Kim et al.[16] performed CT venography 5 days after surgery in 75 patients with TXA, and no DVT was found. In our study, there was no significant difference in the postoperative coagulation parameters between the combined group and the solo group and no patient had symptomatic DVT. In this study, intravenous combined with topical application of TXA appears to be safe in HTO.

In terms of the functional recovery of the knee joint after surgery, Palanisamy et al.[15] found that the VAS scores of HTO patients in the TXA group were lower than those in the control group on the second day after surgery. In our study there was no significant difference in VAS and HSS of knee joint function between the combined group and the solo group. The reason may be that we evaluated knee function only 6 months postoperatively; TXA can reduce postoperative bleeding at the surgical site, which may reduce limb swelling, improve the range of motion of the knee, and reduce pain in the early postoperative period. However, this significant difference might be clinically unrelated and it has been unclear whether the use of TXA can improve the recovery of knee function after HTO. Further research is needed.

The present study has several limitations. First, this study is a retrospective study with a small sample size, even though the statistical power is high. However, for events with a low incidence such as DVT and incision complications, larger sample sizes are necessary for a safe conclusion. Second, this study only counted the total blood loss and drainage volume; the difference in invisible blood loss was not recorded or compared. Third, there was no blank control group or simple topical approach group. Future prospective randomized controlled studies with larger sample sizes are required to determine the most effective application methods of TXA and their efficacy and safety.

Conclusion

Intravenous combined with topical TXA administration in HTO is superior to the use of intravenous administration alone for reducing postoperative blood loss and drainage volume without thromboembolic complications. However, the combined use of TXA did not affect the rate of blood transfusion and the incidence of incision complications, and had no additional benefit for the recovery of knee joint function or pain relief. Therefore, intravenous combined with topical application of TXA is not necessary in HTO.

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