

Comparison of the effectiveness and safety of intravenous and topical regimens of tranexamic acid in complex tibial plateau fracture: a retrospective study

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Abstract

Background Previous studies have demonstrated the effectiveness and safety of tranexamic acid (TXA) in orthopedics. However, no study has investigated TXA in complex tibial plate surgery. Therefore, the purpose of this study was to confirm the safety and effectiveness of IV (intravenous) TXA and topical TXA. **Material and methods** This was a retrospective analysis of prospectively collected data. The control group received an equal amount of placebo (physiological saline solution); the IV group received 1.0 g TXA by intravenous injection before the tourniquet was inflated and before the surgical incision was closed, and the topical group received 3.0 g TXA in 75 mL of physiological saline solution before 5 min prior to the final tourniquet release. Perioperative blood loss, vascular events, wound complications, and adverse reactions were compared for the three groups. The pain functional and quality of life (QoL) assessment based on their corresponding scoring system. **Results** Baseline data were comparable for all groups. The IV group showed the best results for total blood loss (TBL) and hidden blood loss (HBL) (424.5 ± 29.4 ml, 219.3 ± 33.4 ml, respectively, all p values < 0.001). The topical group performed excellently with regard to postoperative vascular events, wound complications, and adverse reactions, but there was no statistical significant in the incidence of these between the groups. In addition, the topical group benefited in reducing postoperative pain and better QoL. **Conclusion** This study presents the first information to show that both IV TXA and topical TXA are safe and effective for complex tibial plateau fractures. The IV regimen effectively reduced blood loss during the perioperative period, whereas the topical regimen had a better safety profile and QoL.

Background

Tibial plateau fractures are mostly caused by a high-energy direct impact; however, the incidence of osteoporotic fracture of the tibial plateau increases with age^{1,2}. For this type of fracture, surgical treatment can improve the patient's quality of life and improve knee function³. Most simple types of tibial plateau fractures (Schatzker I–IV) are not difficult to treat. Owing to the special local anatomic characteristics of the posterior and lateral sides of the tibial plateau, exposure and fixation of complex tibial plateau fractures (Schatzker V and VI) represent major challenges⁴. The use of tourniquets during surgery and the increase in exposed area in patients with complex tibial plateau fracture often result in excessive fibrinolysis and massive blood loss after surgery. Antifibrinolytic therapy, as an important part of blood management, has emerged as a particular focus of research.

Tranexamic acid (TXA) is a traditional antifibrinolytic drug that binds to lysine and forms a reversible complex with plasminogen and plasmin; it is an effective agent against plasmin, tissue plasminogen activators, and plasminogen⁵. Several studies reported that TXA could effectively reduce the perioperative RBC transfusion, blood loss, and blood drainage, and did not increase the risk of DVT formation; in addition, it has been shown to be cost-effective^{6–8}.

The purpose of this study was to investigate the effectiveness and safety of different TXA regimen in the application of complex tibial plateau fracture.

Materials And Methods

The present study was a part of a RCT, which was registered in the Chinese Clinical Trial Registry (ChiCTR-TRC-1800017754), so this was a retrospective analysis of prospectively collected data. Approval was obtained from the Clinical Trials and Biomedical Ethics Committee of Hong Hui Hospital (Approval Number: 2018002), and written informed consent was obtained from all participants.

Patients

Ninety patients with a diagnosis of Schatzker V and VI tibial plateau fractures from January 2018 to October 2019 were recruited. The inclusion criteria were: (1) more than 18 years of age; (2) the presence of a unilateral closed tibial plateau fracture, image inspection that conformed to Schatzker \square and \square classification standards; (3) no coagulopathy or abnormal hemoglobin before the operation; (4) fresh fracture, with a period between injury to hospital admission of less than 3 days; (5) and preoperative ultrasonography that shows deep vein thrombosis (DVT). The exclusion criteria were: (1) patients with severe brain, heart, liver, and kidney dysfunction who could not tolerate surgery; (2) patients with blood system diseases; (3) patients with pathological fractures or tumors; (4) bilateral tibial plateau fractures or other injuries; (5) contraindications for the use of TXA or anticoagulant drugs; (6) patients with incomplete data. In addition, if the surgeon chose to fill the collapsed articular surface with an autologous bone graft during surgery, the patient's data were also excluded from the statistical analysis, as it was considered that the extra wound incision and blood loss from the iliac bone may have affected the results.

Intervention

Patients were divided into the control group, IV group, and topical group based on a computer-generated randomization schedule. The control group received an equal amount of placebo (physiological saline solution) IV or topical. The IV group received 1.0 g IV TXA before the tourniquet was inflated and before the surgical incision was closed. Five minutes prior to final tourniquet release, the topical group received 3.0 g TXA in 75 mL of physiological saline solution and the IV group received 75 mL of saline solution directly on the wound. The therapeutic doses of these regimens were determined from previous studies⁹⁻¹².

Surgical Methods and Postoperative Management

All other drugs, except for TXA and physiological saline solution during general anesthesia, were same in all three groups. The pressure of the balloon-type tourniquet on the affected limb was set to 450 mmHg, and the mean arterial blood pressure (MAP) was maintained at 60–70 mmHg. This surgical technique has been described previously^{13,14}. Briefly, a medial and lateral double incision approach, combined with double locking steel plates, was used to fix the fracture block. Primarily, a medial incision (posterior medial approach) was performed to expose the fractured end of the medial platform, Kirschner wire was used for temporary reduction, and this area was fixed with the anatomical locking plate of the proximal

tibia. Then, the joint was opened through a lateral incision (anterolateral approach) to fully expose lateral condyle, the lateral dissection plate of the proximal tibia was used for fixation, and then use artificial bone grafts. Before the incision was closed, two drainage tubes were placed in patients in group, the incision was sutured layer by layer, and the tourniquet was loosened with compression with elastic bandage. Drainage pipes for each patient were temporary clamped for 4 h after the operation. Postoperatively, the leg was raised for 3 to 4 days, and the drainage tubes were removed within 48 h. Functional exercises related to the active and passive range of motion were started approximately 2 weeks after surgery. The RBC transfusion indications formulated by our institution were: 1) $Hb < 70 \text{ g/L}$; 2) $70 \text{ g/L} < Hb < 100 \text{ g/L}$, when the patient has symptoms of dizziness, palpitation, asthma, and lassitude.

Study Objectives

The following demographic data were recorded for each patient: sex, age, body mass index, medical history, American Society of Anesthesiologists score¹⁵ (ASA), fracture type, preoperative hemoglobin (Hb), preoperative hematocrit (Hct), preoperative D-dimer, and preoperative fibrinogen (FIB). The operation time and intraoperative blood loss were also included in the statistics. Furthermore, routine blood tests and coagulation tests (e.g., Hb, Hct, D-dimer, and FIB) were evaluated 24 h after surgery on and the third postoperative day (POD #3). To evaluate the safety of TXA in this study, the following parameters were evaluated: any vascular event that occurred within 12 weeks after surgery, including deep vein thrombosis of the lower extremity (DVT, confirmed by ultrasound), pulmonary embolism (PE, confirmed by pulmonary spiral CT), cerebrovascular accidents (confirmed by spiral CT or MRI), and gastrointestinal hemorrhage. In addition, we recorded the incidence of wound complications (e.g., dehiscence, hematoma, edge necrosis, and infection). Potential adverse side effects of TXA, including epilepsy, rash, headache, nausea, and vomiting, were also monitored^{16,17}. HSS, SF-12 and VAS pain were evaluated patient outcomes. Due to the particularity of the SF-12 scoring system, we divided it into two parts, PCS and MCS, for comparison.

Calculation of perioperative blood loss

Perioperative total blood loss (TBL) and hidden blood loss (HBL) were the items that this research focuses on. The intraoperative blood loss (IBL) was estimated from the weight of the surgical sponges and the measurement of the volume of blood collected by the suction canisters; the weight of the irrigation fluids added to the surgical field and the sponge weight were then subtracted from this value¹⁸. The total postoperative drainage (TPD) was the weight of fluid in the drainage bag collected over 48 h.

Primarily, the preoperative blood volume (PBV) was calculated by Nadler's equation, $PBV (L) = K_1 \times h^3 + K_2 \times w + K_3$, [h: height (m), w: weight (kg)]; for male patients, $K_1 = 0.3669$, $K_2 = 0.03219$, and $K_3 = 0.6041$; for female patients, $K_1 = 0.3561$, $K_2 = 0.03308$, and $K_3 = 0.1833$ ¹⁹.

Then, the total blood loss (TBL) was calculated according to the Gross Eq. 2⁰, $TBL (ml) = PBV \times (Hct_1 - Hct_2) \div Hb_{trans}$. Hct_1 is the first routine blood test after the patient was admitted to the hospital; Hct_2 is the lowest value obtained by routine blood tests after surgery; Hb_{trans} is the weight of the transfused packed

red blood cells (PRBCs), and two units of PRBCs can cause an increase of approximately 5.2 g/dL in Hb²¹. All transfused blood products were fresh and stored frozen.

Finally, the hidden blood loss (HBL) were calculated as follows:

$HBL (mL) = TBL - IBL - TPD.$

Statistical Analysis

Statistical analyses were computed by using GraphPad Prism 8.0. Continuous variables were reported as the mean and standard deviation. One-way analysis of variance (ANOVA) was used to compare the differences among multiple groups. Student's t-test was utilized to compare the difference between two groups, and the Chi-square test was used for the analysis of categorical data. P-values of < 0.05 were considered to indicate a statistically significant difference.

Results

Patient Demographics

All 90 patients included in the study were followed up for 12 weeks postoperatively; no patients were lost to follow-up. There was no significant difference in demographic data and preoperative blood test results between the three groups of patients (Table 1).

Table 1
Patient demographic data and preoperative blood test results

Variable	Control group (30 patients)	IV group (30 patients)	Topical group (30 patients)	P value (between group)
Patient characteristics				
Age (yr)	44.6 ± 6.7	43.8 ± 5.5	45.1 ± 6.3	0.715 ^a
Gender(male/female)	24/6	25/5	28/2	0.311 ^b
BMI	23.1 ± 1.4	22.9 ± 1.5	23.2 ± 1.7	0.745 ^a
Medical history				
Diabetes mellitus	1	1	1	0.964 ^b
Hypertension	3	1	2	
Arrhythmia	1	2	2	
No	25	26	25	
ASA score				
I	24	24	23	0.966 ^b
II	4	5	5	
III	2	1	2	
Schatzker type				
I	14	17	11	0.300 ^b
II	16	13	19	
Preoperative blood tests				
Hb (g/dL)	12.7 ± 1.0	12.8 ± 0.9	13.1 ± 1.4	0.360 ^a
Hct (%)	39.2 ± 2.7	39.1 ± 2.1	40.1 ± 3.1	0.283 ^a
D-dimer (mg/L)	6.3 ± 1.2	6.7 ± 1.7	6.1 ± 0.8	0.191 ^a
FIB (g/L)	4.6 ± 1.1	5.2 ± 1.5	4.8 ± 1.2	0.172 ^a
Abbreviations: BMI, Body mass index; ASA, American Society of Anesthesiologists; Hb, Hemoglobin; Hct, Hematocrit; FIB, fibrinogen.				
Intergroup comparisons performed using ANOVA or Chi-square test (^a ANOVA; ^b Chi-square test).				

Operation Time, IBL, and TPD

The mean operation time in control group, IV group, and topical group was 117.7 ± 19.4 min, 109.1 ± 17.5 min, 115.3 ± 20.5 min, respectively; there was no significant difference between these values ($p = 0.206$), although the time in the IV group was shorter than in the other groups. The average values of IBL in control group, IV group and topical group were 144.5 ± 21.1 mL, 116.5 ± 15.2 mL, and 137.5 ± 19.2 mL, respectively; these were significantly different ($p < 0.001$); the best effect occurred in the IV group ($p < 0.001$). The topical group showed the greatest reduction in TPD among three groups, but the difference was not significant compared with the IV group (44.1 ± 6.3 mL versus 46.5 ± 5.2 mL, $p = 0.113$) (Table 2).

Table 2
Postoperative data and postoperative blood test results

Variable	Control group (30 patients)	IV group (30 patients)	Topical group (30 patients)	P value (between group)	Intergroup comparison		
					P ₁	P ₂	P ₃
Duration of surgery (min)	117.7 ± 19.4	109.1 ± 17.5	115.3 ± 20.5	0.206 ^a	-	-	-
IBL (ml)	144.5 ± 21.1	116.5 ± 15.2	137.5 ± 19.2	< 0.001 ^a	< 0.001	0.184	< 0.001
TPD (ml)	56.3 ± 7.6	46.5 ± 5.2	44.1 ± 6.3	< 0.001 ^a	< 0.001	< 0.001	0.113
Postoperative blood tests							
HB (g/dL)							
24 h	11.7 ± 1.1	12.2 ± 2.2	11.9 ± 0.8	0.430 ^a	-	-	-
POD#3	11.2 ± 2.4	12.5 ± 3.4	11.6 ± 1.2	0.125 ^a	-	-	-
Hct (%)							
24 h	33.5 ± 4.1	34.1 ± 3.9	33.7 ± 4.4	0.849 ^a	-	-	-
POD#3	33.7 ± 2.9	34.6 ± 2.4	34.1 ± 3.1	0.466 ^a	-	-	-
D-dimer (mg/L)							
24 h	9.6 ± 3.4	8.1 ± 2.9	8.4 ± 3.3	0.165 ^a	-	-	-
POD#3	11.2 ± 4.1	9.8 ± 3.1	10.3 ± 3.8	0.335 ^a	-	-	-
FIB (g/L)							

Abbreviations:POD#3, the third postoperative day.

P₁ represents the p value obtained by comparison between control group and IV group;

P₂ represents the p value obtained by comparison between control group and topical group;

P₃ represents the p value obtained by comparison between IV group and topical group;

Intergroup comparisons performed using AVONA or Chi-square test (^aANOVA; ^bChi-square test).

Variable	Control group (30 patients)	IV group (30 patients)	Topical group (30 patients)	P value (between group)	Intergroup comparison		
					P ₁	P ₂	P ₃
24 h	5.7 ± 2.1	5.1 ± 1.9	5.4 ± 2.3	0.546 ^a	-	-	-
POD#3	7.4 ± 2.6	6.4 ± 1.3	6.8 ± 2.9	0.264	-	-	-
Real Hb decrease (g/dL)	1.8 ± 0.6	0.9 ± 0.3	1.3 ± 0.7	< 0.001 ^a	< 0.001	0.004	0.006
Transfusion rate (%)	6.7%	0	0	0.129 ^b	-	-	-
Abbreviations:POD#3, the third postoperative day.							
P ₁ represents the p value obtained by comparison between control group and IV group;							
P ₂ represents the p value obtained by comparison between control group and topical group;							
P ₃ represents the p value obtained by comparison between IV group and topical group;							
Intergroup comparisons performed using AVONA or Chi-square test (^a ANOVA; ^b Chi-square test).							

Postoperative Blood Tests

The results of routine blood tests and blood coagulation tests in the three groups were summarized in Table 2. The mean value of post-operative Hb of 24 hours in control group, IV group and topical group were 11.7 ± 1.1, 12.2 ± 2.2, 11.9 ± 0.8 g/dL respectively, and no significant difference between groups (p = 0.430). The mean value of POD#3 Hb in control group, IV group, and topical group was 11.2 ± 2.4, 12.5 ± 3.4, and 11.6 ± 1.2 g/dL respectively; there was no significant difference between groups (p = 0.125). Similarly, there were no significant differences in mean Hct values for the above two time points between each groups. However, there was a statistically significant difference in the average real Hb reduction between the three groups (p < 0.001): the values were 1.8 ± 0.6 g/dL in the control group, 0.9 ± 0.3 g/dL in the IV group, and 1.3 ± 0.7 g/dL in the topical group. The best effect was observed for the IV group (p = 0.006 versus the topical group).

The mean value of post-operative D-dimer after 24 h in the control group, IV group and topical group was 9.6 ± 3.4, 8.1 ± 2.9, and 8.4 ± 3.3 mg/L, respectively, with no significant difference between groups (p = 0.165). The mean value of POD #3 D-dimer in the control group, IV group, and topical group was 11.2 ± 4.1, 9.8 ± 3.1, 10.3 ± 3.8 mg/L, respectively, with no significant difference between groups (p = 0.335). Similarly, there were no significant differences between three groups for mean FIB values at the above two time points.

Blood Loss and Transfusion

After careful calculation and verification, we found that there were significant differences in TBL between the three groups ($p < 0.001$). The pairwise comparisons and statistical analysis, namely, control group vs IV group, IV group vs topical group, and control group vs topical group, all showed statistically significant differences (Fig. 1). The same results were also found for HBL: HBL in control group, IV group and topical group was 341.1 ± 43.7 , 219.3 ± 33.4 , and 224.5 ± 33.6 mL, respectively (all intergroup p values < 0.001) (Fig. 2).

The final analysis revealed that two patients in the control group were transfused with 2 units of PRBCs owing to postoperative anemia symptoms, whereas no patients in the IV group and the topic group required blood transfusion treatment. No statistical differences were found in the transfusion rate between three groups ($p = 0.129$) (Table 2).

Vascular Events, Wound Complications, and Adverse Reactions

In this study, the venous plexus of calf muscle was the most common site for DVT, followed by the popliteal vein. No severe complications, such as pulmonary embolism, myocardial infarction, or cerebral infarction, occurred in this study. There were no significant differences in wound complications and adverse reactions between three groups. The specific data are described in Table 3.

Table 3

Vascular events, wound complications, and adverse reactions resulting from TXA

Variable	Control group (30 patients)	IV group (30 patients)	Topical group (30 patients)	P value (between group)
Vascular events				
DVT	9	11	7	0.530
MI	0	0	0	-
CI	0	0	0	-
PE	0	0	0	-
GIH	0	1	0	0.364
Total	9	12	7	0.373
Wound complications				
Dehiscence	0	0	0	-
Hematoma	0	0	0	-
Edge necrosis	1	0	0	0.364
Infection	2	1	0	0.355
Total	3	1	0	0.160
Adverse reactions				
Epilepsy	0	0	0	-
Rash	0	1	0	0.364
Headache	2	4	1	0.338
Nausea and Vomiting	1	1	1	1.000
Total	3	6	2	0.260
Abbreviations: TXA, tranexamic acid; DVT, deep vein thrombosis; MI, myocardial infarction; CI, cerebral infarction; PE, pulmonary embolism; GIH, gastrointestinal hemorrhage.				
Chi-square test for intra-group comparison.				

Pain, Functional and QoL assessment(Figures. 3,4,5)

According to our results, topical regimen TXA own the best effect on pain control in the early postoperative period (POD#2 and POD#4,with p value:0.002 and 0.025), but also this advantage continues into the later period(6 weeks post-operative,with p value < 0.001).

The knee function HSS scores was used to assess patient's knee function both pre- and post-operatively. Although there was no significant difference in postoperative follow-up among the three groups (p values: 0.052 and 0.432), it is worth mentioning that the topical group benefited the most, followed by the IV group.

To assess the function, we used both PCS and MCS of SF-12. In PCS aspect of view, the topical group showed a sustainable development advantage from the 6th week to the 12th week post-operative (p values: 0.237 and 0.051). This advantage is likely to become more significant as the follow-up time increases. On the contrary, in the postoperative follow-up, there was no significant difference in PCS between the three groups, although they were improved to varying degrees compared with pre-operative.

Discussion

Schatzker type I and II tibial plateau fractures are usually caused by severe crushing and collapse of the medial and lateral condyles owing to high-energy trauma; however, the internal and external double incision approach, combined with bone grafting and double steel plate fixation, can achieve ideal results¹⁴. As there are an abundance of blood vessels around the knee joint, an increase in the incision exposure range and the use of tourniquets can lead to a large amount of blood loss and fibrinolytic response during the perioperative period²². The safety and effectiveness of TXA has been proven in general surgery, joint surgery, and spine surgery. Currently, TXA is administered as intravenous, intramuscular, topical, and oral regimens. As the safety of intramuscular and oral regimens has not been supported by a large number of clinical trials, these methods were excluded from this study. Some scholars have suggested that when TXA is used topically in the joint cavity, joint cavity drainage must not be placed after surgery, to avoid loss of drug efficacy^{23,24}. Therefore, to reduce the bias in the test results, a temporary clamping scheme for the drainage tube for 4 h after operation was used in this study^{11,25}. Given the encouraging results for TXA, the purpose of this study was to confirm which approach was more effective and safe in complex tibial plateau fracture.

In this study, the use of TXA reduced IBL and TPD. Compared with the topical regimen, the IV regimen effectively reduced blood loss by approximately 28 mL (p < 0.001). The topical regimen can effectively reduce TPD by approximately 12 mL, but there was no significant difference to intravenous application; this conclusion was also reached by Artit et al.²⁶ The IV regimen more effectively reduced the real Hb reduction during the perioperative period, similar to the results of Tzatzairis et al.²⁷

Sehat et al.²⁸ first proposed the concept of HBL and studied the HBL of 63 patients that underwent TKA; they found that HBL accounted for approximately 50% of the TBL. Gao et al.²⁹ found that the TBL of perioperative patients in hip replacement was approximately 859 mL, and the HBL was approximately 525 mL, which accounted for 61% of the TBL. Foss et al.³⁰ studied the hidden blood loss after hip fracture and found that different surgical schemes caused a hidden blood loss of 500 mL to 1473 mL, which was approximately 2 to 3 times greater than the visible blood loss. Therefore, to reduce the blood

loss in orthopedic surgery, reduction of the HBL should be the first priority. The main finding of our study was that both intravenous and topical use TXA can effectively reduce TBL during the perioperative period, and that the IV regimen had the strongest effect (approximately 50 mL compared with the topical group, $p < 0.001$). Similarly, the perioperative HBL was also reduced, but there was no significant difference between the IV regimen and topical regimen.

It has been proposed that the use of tourniquets will lead to excessive fibrinolysis and blood loss within the first 6 h of surgery³¹. In the current study, the second TXA application in the IV group was before the tourniquet was released and its effect may have been weakened as the fibrinolytic response was already in progress. The topical application of TXA allows it to rapidly reach the active bleeding point and directly interact with the wound, inhibit the fibrinolytic reaction in the blood, promote the formation of fibrin and maintain a stable clot, reduce the leakage of blood to the surface of the damaged tissue, and exert hemostatic effects³². Thus, this explains why there were no great differences between the IV group and topical groups in TBL and HBL.

Thus far, most orthopedic clinical trials have been designed to test the hemostatic effect of TXA instead of safety. For rare complications, such as pulmonary embolism, the current clinical trial sample size cannot reach a definitive conclusion. The results of this study show that patients were safe whether they received IV or topical treatment. The IV regimen appeared to increase the incidence of vascular events and adverse reactions, but with fewer wound complications compared with the control group; however, the difference was not significant. Some studies have confirmed that plasmin not only promotes the activation of monocytes, platelets, and endothelial cells, but also plays an important role in stimulation of the release of inflammatory mediators and the induction of related proinflammatory gene expression. TXA is an inhibitor of plasmin, so ammonia TXA also has potential anti-inflammatory effects^{33,34}. In addition, reducing the perioperative blood transfusion rate may reduce the incidence of wound complications³⁵. We have reduced blood loss by the application of TXA and therefore may also reduce the incidence of wound complications. Hence, we believe that the application of TXA in this study has been shown to be safe.

Another interesting study in this study found that pain in the topical group was significantly reduced in the early and late postoperative periods. In addition, the HSS of this group of patients has a slight advantage in postoperative knee function. This advantage is reflected in the fact that patients can perform a wider range of knee mobility exercises and early ambulation. This can well explain the long-term, higher PCS in the topical group in terms of postoperative quality of life. However, the application of TXA without improve the psychological impact of patients caused by orthopedic trauma.

There are some limitations to our study. First, the sample size of this study was small and the results are from a single center. A large-scale prospective, randomized case-control study is needed to confirm these results. Second, according to the perioperative rehabilitation guidelines for major orthopedic surgery designated by our institution, all patients received preventive anticoagulation after admission, which may have affected blood loss. Third, blood loss in postoperative wound dressings was not measured.

Conclusion

In summary, for complex tibial plateau fractures of Schatzker type Ⅱ and Ⅲ, the use of TXA is reasonable, safe, and effective. The IV regimen offers the advantage of lower perioperative blood loss, whereas the topical regimen can reduce the incidence of vascular events, wound complications, and adverse reactions, and own advantages in reducing pain and increasing PCS in patients.

Abbreviations

TXA, tranexamic acid; IV, intravenous; QoL, quality of life; TBL, total blood loss; HBL, hidden blood loss; RBC, red blood cell; DVT, deep vein thrombosis; MAP, mean arterial blood pressure; ASA, American Society of Anesthesiologists score; Hb, hemoglobin; Hct, hematocrit; FIB, fibrinogen; BMI, body mass index; VAS, visual analogue scale; PE, pulmonary embolism; IBL, intraoperative blood loss; TPD, total postoperative drainage; PBV, preoperative blood volume; PCS, Physical health score; MCS, mental health score.

Declarations

Ethics approval and consent to participate

Approval was obtained from the Clinical Trials and Biomedical Ethics Committee of Hong Hui Hospital (Approval Number: 2018002), and written informed consent was obtained from all participants.

Consent for publication

Not applicable.

Availability of data and material

All data generated or analyzed during this study are included in this published article.

Declaration of conflict of interest

The authors declare no conflict of interest.

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Authors' contributions

BZ and KZ were responsible for the study design, the definition of intellectual content, and for literature research. ZMW, YL and CR analyzed and interpreted data. LLS and TM performed the statistical analysis.

ZMWYL and QW drafted the manuscript. TM, CR ZL and JRY revised the manuscript. All authors read and approved the final manuscript.

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Figures

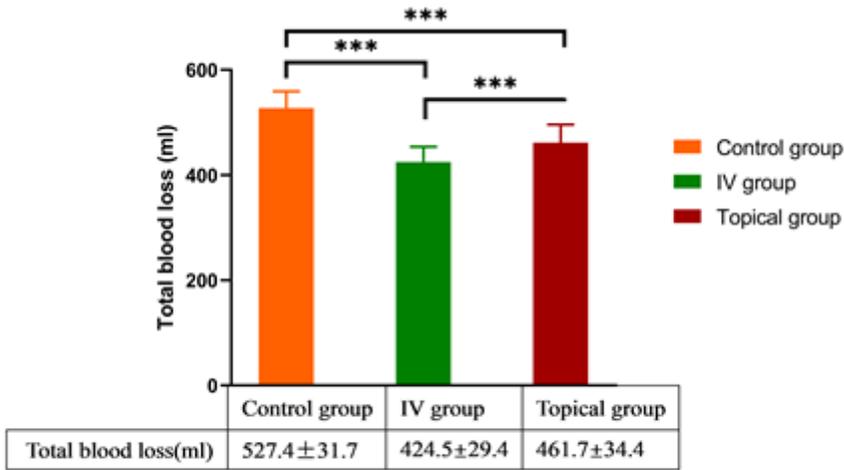


Figure 1

Comparison of TBL in the three groups.

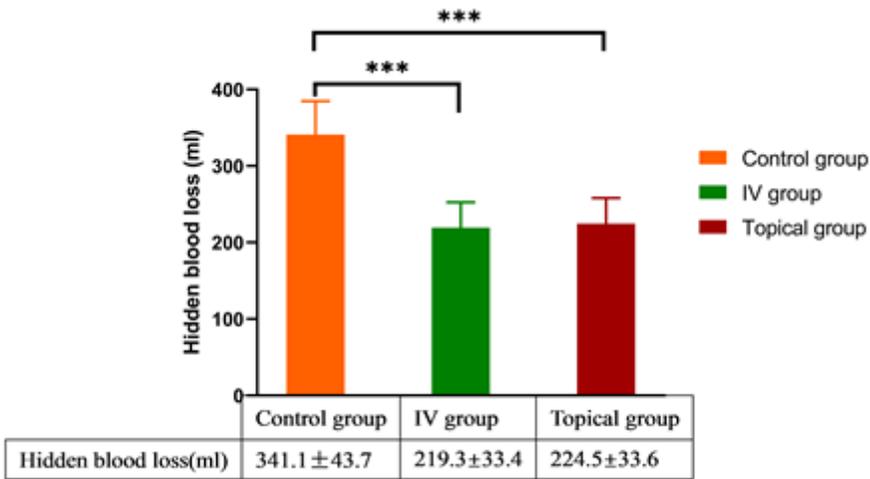


Figure 2

Comparison of HBL in the three groups.

VAS pain score

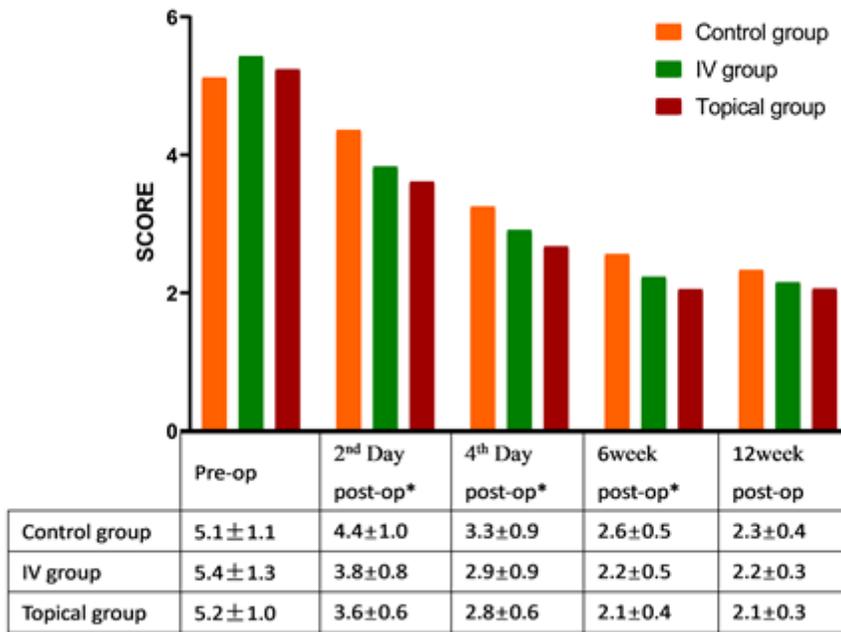


Figure 3

Comparison of VAS pain in the three groups.

Knee HSS score

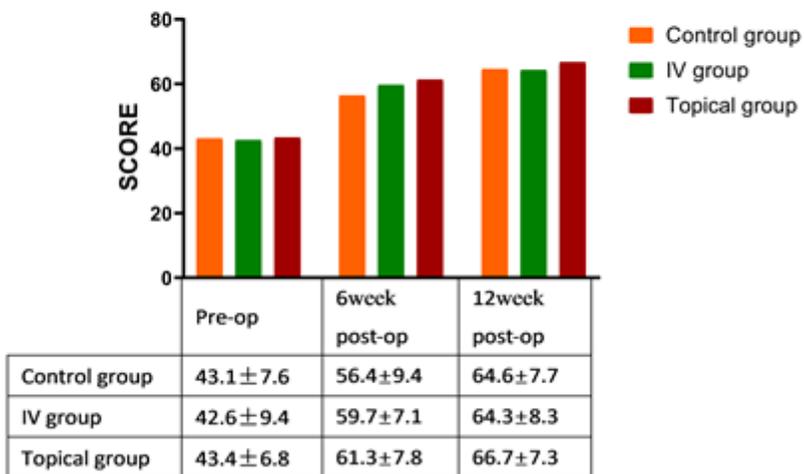


Figure 4

Comparison of functional in the three groups.

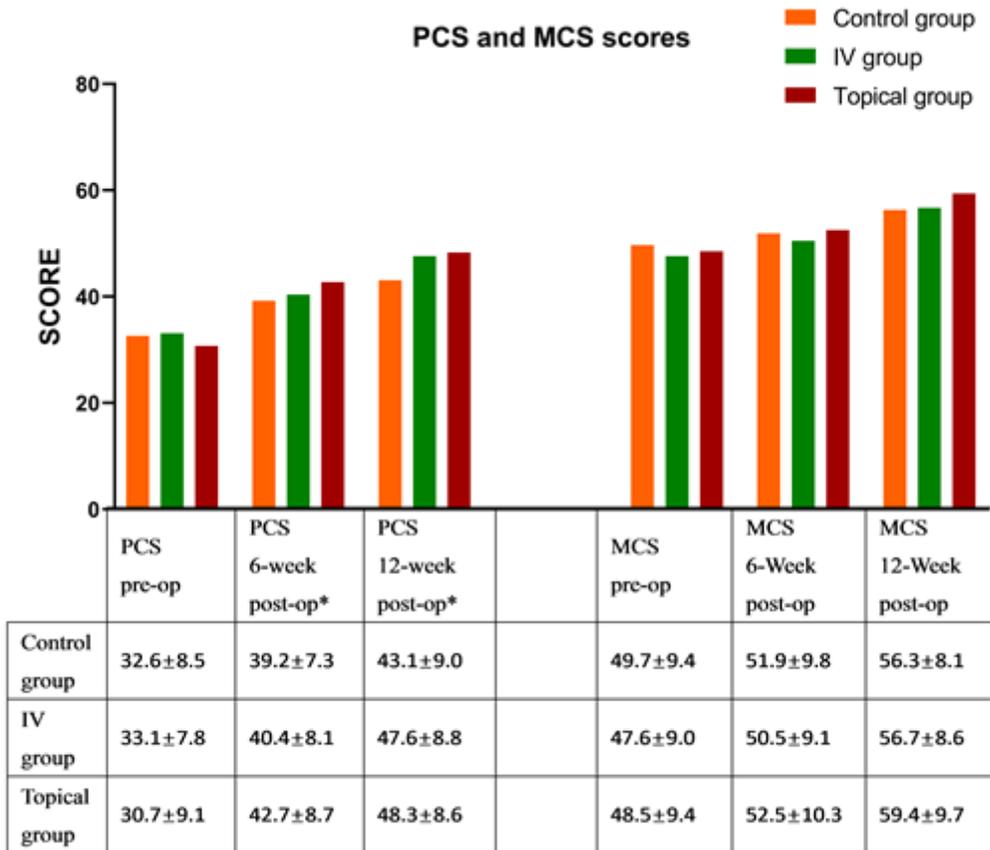


Figure 5

Comparison of PCS and MCS in the three groups.